

## 1 SCOPE AND APPLICABILITY

- 1.1 The scope and purpose of this standard operating procedure (SOP) is to describe the application requirements that must be met by Principal Investigators (PIs) or Study Chairs (SCs) and Local Site Investigators (LSIs) for submitting new projects involving multi-site human subject research to the VA Central IRB for review. This includes the following:
- 1.1.1 VA Central IRB PI and LSI application forms to include study team personnel issues, conflict of interest requirements, recruitment restrictions, and other general application requirements.
  - 1.1.2 Required elements of informed consent, the process of obtaining informed consent, documentation of informed consent, and requirements for waiver or alteration of the informed consent process and/or a waiver of documentation of informed consent. The VA Central IRB does not review or approve the use of broad consent or short forms at this time.
  - 1.1.3 Requirements involving research with vulnerable populations and other special categories of research participants that may need additional safeguards. This includes pregnant women, prisoners, individuals with impaired decision-making capacity, and children. It also includes other special categories of participants that could potentially be susceptible to undue influence or coercion and/or that may require additional safeguards and protections of their rights and welfare such as participants who are illiterate or non-English speaking; students and VA employees; the terminally ill; economically or educationally disadvantaged participants; and patients of the investigators.
  - 1.1.4 Requirements for the use of investigational drugs, devices, and biologics. The VA Central IRB does not review any activities constituting emergency use of test articles as described in Food and Drug Administration (FDA) regulations. The VA Central IRB also does not review any requests for the use of humanitarian devices. These types of reviews are best conducted by other IRBs of record for local VA facilities.
  - 1.1.5 VA privacy and information security requirements. This includes requirements concerning obtaining an authorization for the use of protected health information (PHI) as required by the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule (45 CFR Parts 160 and 164) as well as restrictions regarding use of certain types of equipment and software programs due to VA information security requirements.
- 1.2 This SOP applies to all new projects submitted to the VA Central IRB for review. Currently, the VA Central IRB accepts for review funded multisite studies involving two or more VA sites. A single site pilot project that has the potential to expand to a multi-site project can also be accepted for review.
- 1.2.1 Funding can be provided by sources within VA, such as the Office of Research and Development (ORD) or VHA Central Office; other government agencies such as a non-profit organization or consortium; or the project can be commercially sponsored. Due to resource constraints, the VA Central IRB must limit the number of studies it accepts for review and it is highly recommended that investigators contact the VA Central IRB administrator regarding a proposed submission prior to completing the submission paperwork to ensure the submission will be accepted.

1.2.2 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 allowed for research on fetuses in utero under 45 CFR 46.208(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 and will not be accepted for review.

1.3 This SOP does not pertain to requests for exemption or for human subjects engagement determinations. These are covered in VA Central IRB SOP 102, Requests for Exemptions and Requests for Determination of Human Subjects Engagement.

1.4 It is the policy of the VA Central IRB that a project is not scheduled for initial review by the VA Central IRB until all application requirements as detailed in this SOP are met. New project applications and associated documents must contain a sufficient description of the proposed research for the VA Central IRB to make an informed determination regarding all required regulatory approval criteria, as well as VA and VA Central IRB requirements.

1.5 This SOP applies to all VA investigators and members of their project teams who submit studies involving the use of human subjects to the VA Central IRB for review. It also pertains to VA Central IRB members and the VA Central IRB administrative staff.

## 2 DEFINITIONS

2.1 **Certificate of Confidentiality.** A Certificate of Confidentiality is a document issued by a component of HHS pursuant to The Public Health Service Act Section 301(d), 42 U.S.C. 241(d) amended by Section 2012 of the 21<sup>st</sup> Century Cures Act, Public Law 114-255, to protect the privacy of individuals who are subjects of certain specified research activities by authorizing investigators to withhold from all persons not connected with the conduct of such research the names or other identifying characteristics of such subjects. Persons so authorized to protect the privacy of such individuals may not disclose information in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings to identify such individuals. (VHA Handbook 1200.05)

2.2 **Children.** Children are persons who have not attained the legal age to consent to treatments or procedures involved in the research under the applicable State law of the jurisdiction in which the research will be conducted. (VHA Handbook 1200.05)

2.3 **Clinical Investigation.** The Food and Drug Administration (FDA) considers the term clinical investigation to mean any experiment that involves a test article and one or more human subjects, and that either: (1) meets the requirements for prior submission to the FDA under Sections 505(i) or 520(g) of the Federal Food, Drug, and Cosmetic Act, codified at 21 U.S.C. 355(i) and 360j(g) respectively; or (2) does not meet the requirements for prior submission to the FDA under these sections of the Federal Food, Drug, and Cosmetic Act, but the results of which are intended to be submitted later to, or held for inspection by, the FDA as part of an application for a research or marketing permit (21 CFR 56.102(c)).

2.4 **Collaborative Research.** Collaborative research is human subjects research activities involving investigators from VA and at least one non-VA institution. Collaborative research includes VA and non-VA institutions. (VHA Handbook 1200.05)

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

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

2.7 **Financial Interest.** Financial interests are limited to those owned by the employee or by the employee's spouse or minor children. It includes any current or contingent ownership, equity, or security interest in real or personal property or a business and may include indebtedness or compensated employment relationship. It includes interests stocks, bonds, partnership interests, fee and leasehold interests, mineral and other property rights, deeds of trust, and liens. It extends to any right to purchase or acquire any such interests, such as a stock option or commodity future. It does not include a future interest created by someone other than the employee, the employee's spouse, or dependent child or any right as a beneficiary of an estate that has not been settled. It does include service, with or without compensation, as an officer, director, trustee, general partner, or employee of any person, including a nonprofit entity, whose financial interests are imputed to the employee (5 CFR 2635.403(c)).

The financial interests of the following persons are considered to the same extent as if they were the employee's own interests: (5 CFR 2635.402(b) (2))

- Employee's spouse
- Employee's minor child
- Employee's general partner in a business
- An organization in which the employee serves as officer, director, trustee, general partner, or employee
- Any person with whom the employee is negotiating or has an arrangement concerning prospective employment

2.8 **Gift.** Any gratuity, favor, discount, entertainment, hospitality, loan, forbearance, or other item having monetary value that is not available to the general public. This includes services as well as gifts of training, transportation, local travel, lodgings and meals, whether provided in-kind, by purchase of a ticket, payment in advance, or reimbursement after the expense has been incurred.

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

**Individually-identifiable health information** refers to a subset of health information, including demographic information collected from an individual, that is (VHA Handbook 1605.1):

- Created or received by a health care provider, health plan, or health care clearinghouse;

- Relates to the past, present, or future condition of an individual and provision of or payment for health care; *and*
- Identifies the individual or a reasonable basis exists to believe the information can be used to identify the individual. *NOTE: Individually-identifiable health information does not have to be retrieved by name or other unique identifier to be covered by VHA Handbook 1605.1.*

- 2.10 **Identifiable Biospecimen.** An identifiable biospecimen is a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimens.
- 2.11 **Interaction.** Interaction includes communication or interpersonal contact between investigator and subject.
- 2.12 **Investigational Device.** An investigational device is a device that is an object of an investigation. (21 CFR 812.3(g)).
- 2.13 **Investigational Device Exemption (IDE).** An application to FDA that allows an investigational significant risk device to be used in a clinical investigation to collect safety and effectiveness data. If the device is a non-significant device, it is considered to have an approved application for IDE after IRB approval is obtained. (21 CFR 812)
- 2.14 **Intervention.** Intervention includes both physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.
- 2.15 **Investigator.** Any individual who conducts research including, but not limited to, the Principal Investigator (PI), sub-investigator or co-investigator, and Site Investigator or Local Site Investigator (LSI). All VA investigators on a VA research study or program must hold a VA appointment. (VHA Handbook 1200.05)
- 2.15.1 **Principal Investigator (PI).** The PI is a qualified person who directs a research study or program. The PI oversees scientific, technical, and day-to-day management of the research. If a study is conducted by a team of individuals, the PI is the responsible leader of that team.
- 2.15.2 **Sub-Investigator or Co-Investigator.** A qualified person designated by the PI or LSI to perform critical research procedures and/or to make important research-related decisions. Both terms are interchangeable. These investigators are key personnel on a research study or program.
- 2.15.3 **VA Investigator.** Any individual who conducts research while acting under a VA appointment, including full and part-time employees, without compensation (WOC) employees, or individuals appointed or detailed to VA under the Intergovernmental Personnel Act (IPA of 1970 (5 U.S.C. 3371 et seq.)). Individuals working under a contract with VA cannot conduct research as VA investigators under a WOC appointment while simultaneously working as a contractor.
- 2.16 **Legally Authorized Representative.** A legally authorized representative (LAR) is an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research. If there is no applicable law

addressing this issue, LAR means an individual recognized by institutional policy as acceptable for providing consent in the non-research context on behalf of the prospective subject to the subject's participation in the procedure(s) involved in the research. (VHA Handbook 1200.05)

- 2.17 **Minimal Risk.** Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. (VHA Handbook 1200.05)
- 2.18 **Neonate.** Neonate means a newborn within the first 4 weeks of birth.
- 2.19 **Pregnancy.** Pregnancy encompasses the period of time from implantation until delivery. A woman is assumed to be pregnant if she exhibits any of the pertinent presumptive signs of pregnancy, such as missed menses, until the results of a pregnancy test are negative or until delivery. (VHA Handbook 1200.05)
- 2.20 **Prisoner.** Any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing. (45 CFR 46.303c)
- 2.21 **Private Information.** Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (e.g., a medical record). (See 38 CFR 16.102(e)(4)).
- 2.22 **Research Protocol.** A research protocol details the aims and objectives of a research study, scientific rationale, the methods used to carry out the research, and how data will be analyzed. For human subjects research it also entails how subjects will be accessed/recruited, any foreseeable risks, and how these risks will be mitigated. ***NOTE: The protocol for social or behavioral research is sometimes referred to as the Research Plan or Research Purpose and Methodology.***
- 2.23 **Significant Risk Device.** An investigational device that 1) is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject; 2) is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health safety, or welfare of a subject; 3) is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or 4) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject. (21 CFR 812.3 (m))
- 2.24 **Test Article.** Any drug for human use, biological product for human use, medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the Food, Drug, & Cosmetic Act or under sections 351 or 354-360F of the Public Health Service Act. (21 CFR 50.3(j))



### 3 RESPONSIBILITY

- 3.1 Principal Investigator /Study Chair (PI/SC) – The PI/SC is responsible for the overall conduct of the project and for ensuring that implementation of the project is in compliance with VA and other federal requirements for the protection of human subjects, as well as local VA policies and procedures. For the purposes of this SOP, the PI/SC or designee is responsible for the following:
- 3.1.1 Giving priority to the protection of research subjects, upholding professional and ethical standards and practice, and adhering to all applicable VA and other federal requirements as specified in VHA Directive 1200.05.
  - 3.1.2 Holding a current VA appointment to conduct research and having the appropriate training, education, expertise, and credentials to conduct the research. PIs must also ensure that all research staff are qualified, including but not limited to appropriate training education, expertise, and credentials, to perform research procedures assigned them. All investigators and staff working on a project must be credentialed and privileged as required by current local and VA requirements. PIs must ensure that investigators and other staff only perform those activities in a research study for which they have the relevant credentials and privileges.
  - 3.1.3 Investigators must be identified on the IRB application and must provide credentials, conflict of interest statements, and any other documentation required by the VA Central IRB or local facilities. All investigators on the study must disclose to the VA Central IRB any potential, actual, apparent, or perceived conflict of interest of a financial, professional, or personal nature that may affect any aspect of the research, and comply with all applicable VA and other Federal requirements regarding conflict of interest.
  - 3.1.4 Developing and submitting a research protocol that is scientifically valid and ethical, describes the research objectives, background, and methodology; and is relevant to the health or welfare of the Veteran population. When applicable, the protocol must contain the following safety measures: (1) the type of safety information to be collected, including adverse events (AEs), (2) frequency of safety data collection: (3) frequency or periodicity of review of cumulative safety data; (4) statistical tests for analyzing the safety data to determine if harm is occurring, and (5) conditions that trigger an immediate suspension of the research.
  - 3.1.5 For all non-exempt human subjects research, submitting the protocol for initial review and obtaining written approval from the VA Central IRB, other applicable committees, and from the local R&D Committee that the research is approved. The investigator must receive written notice from the ACOS/R&D at a specific site before initiating research at that site.
  - 3.1.6 During the recruitment process, making initial contact with potential subjects in person or by letter prior to initiating any telephone contact, unless there is written documentation that the subject is willing to be contacted by telephone about the study in question or a specific kind of research as outlined in the study.

- 3.1.6.1 If existing information from sources such as a medical records or database (research or non-research) are to be used to identify human subjects, the PI/SC must request and have approved as part of the application a waiver of HIPAA authorization and either a waiver of informed consent for this activity or IRB approval to use identifiable information or identifiable biospecimens for screening and recruitment purposes.
- 3.1.6.2 Any initial contact by letter or telephone must provide a telephone number or other means that the potential subject can use to verify that the study constitutes VA research and, if a contractor makes initial contact, the VA investigator must sign the letter. This does not apply when a Veteran calls in response to an advertisement.
- 3.1.7 Obtaining and documenting legally effective informed consent of the subject or the subject's LAR prospectively that is in alignment with ethical principles that govern informed consent for research. The only exceptions are if the IRB determines the research is exempt; or it approves a waiver of the informed consent process; or approves a waiver of the signed informed consent document; or approves access to identifiable information or identifiable biospecimens for screening and recruitment purposes.
- 3.1.7.1 If the investigator does not personally obtain informed consent, the investigator must delegate this responsibility in writing to research staff sufficiently knowledgeable about the protocol and related concerns to answer questions from prospective subjects and about the ethical basis of the informed consent process and protocol.
- 3.1.7.2 If the investigator contracts with a 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 humans subjects research, the firm must have its own IRB oversight of the activity and the Privacy Officer must determine that there is appropriate authority to allow the disclosure of individual names and other information to the contracted firm.
- 3.1.7.3 The investigator must develop an informed consent form, if not requesting a waiver of informed consent, containing all required basic elements, as well as any additional elements as applicable, for the subject populations that will be enrolled. The investigator must also ensure that informed consent is appropriately documented using the most current version of the informed consent form unless a waiver of documentation has been requested and approved by the IRB. Additionally, the investigator must ensure that all original or digitized signed and dated informed consent documents are maintained in the investigator's research files, readily retrievable, and secure.
- 3.1.8 Obtaining a HIPAA authorization or an approved waiver of HIPAA authorization form prior to the use and/or disclosure of the subject's protected health information (PHI). PHI cannot be used or disclosed without prior authorization or a waiver of authorization unless the PHI constitutes a limited data set and there is an appropriate data use agreement (DUA). The information in the written authorization or approved waiver of authorization or DUA for use or disclosure of a limited data set must not contradict any provisions of the protocol and informed consent documents.

- 3.1.9 Conducting VA human subject research involving test articles, such as investigational drugs and devices, in accordance with all applicable VA policies and other federal requirements including, but not limited to VHA Directive 1200.05, VHA Directive 1108.04, Investigational Drugs and Supplies, and applicable FDA regulations. The PI/SC must submit documentation to the VA Central IRB of verification that an Investigational New Drug (IND) application was submitted to FDA for drug studies and that it is active (i.e., FDA has not put it on hold); and/or that an Investigational New Device Exemption (IDE) application has been approved for all significant risk devices. The storage and security procedures for test articles used in research must be included in the IRB application or protocol and reviewed and approved by the IRB. In addition, a model VA Form 10-9012 must be submitted for each study drug that will be prescribed that can be used by LSIs as a template when submitting LSI Applications.
- 3.1.10 Ensuring all applicable requirements regarding the use of vulnerable subjects as specified in VHA Directive 1200.05 and other applicable federal regulations, to include but not limited to pregnant women, children, prisoners, and impaired decision-making individuals, are included as part of the IRB application and reviewed and approved by the IRB prior to using such populations in the research.
- 3.2 Local Site Investigator (LSI) –The LSI is responsible for all aspects of the research project conducted at the local site in accordance with paragraph VHA Directive 1200.05 and for ensuring compliance at that site with all VA and other requirements for the conduct of human research. For the purposes of this SOP, the LSI is responsible for the following:
- 3.2.1 All of the responsibilities as described in paragraphs 3.1.1 through 3.1.3 and 3.1.5 through 3.1.10 of this SOP for research conducted at the local site. The only responsibility that the LSI does not have is submission of the protocol. For multi-site studies overseen by the VA Central IRB, this is the sole responsibility of the PI/SC study team.
- 3.2.2 The LSI recruits the local site project team and prepares the LSI Application for the specific participating local site. The LSI must provide a rationale for any differences between the PI/SC and LSI application. The LSI is responsible for ensuring that the research project at that site does not begin until all required approvals have been received as stated in paragraph 3.1.5.
- 3.3 Project Team Members – All project team members at each participating local site, including the PI/SC and LSIs, are responsible for following the project plan, identifying any conflicts of interest, maintaining research records in accordance with VHA Handbook 1200.05, and adhering to all VA and other requirements regarding the conduct of human research. They are also responsible for remaining current on all VA required training on the protection of human research participants, as well as VA data security and privacy requirements.
- 3.4 Associate Chief of Staff for Research and Development (ACOS/R&D) – For the purposes of this SOP, the ACOS/R&D is responsible for reviewing the PI/SC New Project Application, or the LSI New Project Application as applicable, prior to submission to the VA Central IRB and for certifying the following on behalf of the local site:



- The PI/SC, or LSI as applicable, and the rest of the project team have the experience and training needed to conduct the project;
- All the site project team members have been appropriately credentialed and privileged and they have completed required VA training in the protection of human research participants and, if applicable, Good Clinical Practices;
- If applicable, that the local facility has reviewed or is in the process of reviewing any potential conflicts of interest of local site project team members and the results of the review have been, or will be, forwarded to the VA Central IRB;
- The facility and the PI/SC and/or LSI, as applicable, have the resources to support the functions and operations of the project as described;
- The project will not begin at the local participating facility until the PI/SC, or LSI as applicable, has received written approval to initiate the study in accordance with VHA Directive 1200.01.

3.5 VA Central IRB – The VA Central IRB is responsible for fulfilling all responsibilities and performing all review functions of an IRB of record as specified in VHA Handbook 1200.05 for all projects it receives for review. Once a project is approved, the VA Central IRB is responsible for overseeing the project and conducting continuing review as required and applicable.

3.6 VA Central IRB Administrator – For the purposes of this SOP, the VA Central IRB Administrator is responsible for the following:

- Serving as the initial point of contact for study teams for submitting projects to the VA Central IRB for review.
- Working with the PI/SC and local site project teams to educate them on new project application requirements and procedures
- Ensuring that the participating local sites for a new project have entered into an MOU with the VHACO and listed the VA Central IRB as an IRB of record on their FWA
- Assigning new projects upon receipt to a VA Central IRB Manager and coordinating the workload to ensure that it is evenly distributed among the VA Central IRB Managers
- Offering the study teams the opportunity for a courtesy pre-review and overseeing the pre-review process

## 4 PROCEDURE

### 4.1 Acceptance of a Study for Review and Optional Courtesy Review Process.

4.1.1 The VA Central IRB Administrator serves as the main point of contact for the VA Central IRB for study teams seeking to submit a new study for review. The VA Central IRB Administrator should be contacted prior to the study team completing any submission forms. Contact can be by phone or by e-mail.

4.1.2 Multi-site clinical trials funded by the VA Office of Research and Development (ORD) and VHA Central Office (VHACO) will generally be accepted for review unless the VA Central IRB Administrator determines they would be more suitable for review by another IRB of record for the local site. Other studies will be considered for acceptance for review on a case-by-case basis. The VA Central IRB Administrator will consult with the VA Central IRB Co-Chairs regarding these non-VA funded studies and study teams may be asked to submit an abstract of the protocol for review. The following factors will be considered prior to accepting a non-VA funded study for review:

- Number of VA sites
- Type of study (Clinical Trial, Database Study, etc.)
- Relevance to Veterans
- Workload and time constraints

4.1.3 Upon an acceptance or non-acceptance decision being rendered, the VA Central IRB Administrator will document the decision in writing by sending an e-mail to the point of contact for the study team. If the study was not accepted for review, the reason for the non-acceptance will be included in the e-mail.

4.1.4 If the study is accepted for review, the VA Central IRB Administrator will offer the study team the option to have a courtesy pre-review performed. The study team will be advised that the courtesy pre-review is not a determination of the VA Central IRB and is performed by VA Central IRB administrative staff member or other personnel within the Office for Research Protections, Policy, and Education (ORPP&E) who will point out any regulatory or VA policy issues and make suggestions for clarifications.

4.1.4.1 If the study team elects this option, it may submit draft unsigned documents for review. The minimum documents required to do a pre-review are the protocol and draft VA Central IRB Form 108, PI/SC New Project Application (**Attachment 1**) or VA Central IRB Form 108-NSI, PI/SC New Project Application – No Subject Intervention (**Attachment 2**.) Other draft VA Central IRB forms can be submitted as desired by the study team. The study team will be advised not to submit any CVs, bio sketches, case report forms, or conflict of interest forms at this time.

4.1.4.2 Draft documents may be submitted via encrypted e-mail to the VA Central IRB Administrator or a folder may be set up on the VA Central IRB secure SharePoint site and the study team sent the link. If using the SharePoint site to submit the documents, the study team must send an e-mail informing the VA Central IRB Administrator that the documents are available for review.

4.1.4.3 Once the VA Central IRB Administrator receives notice that a pre-review was submitted, the pre-review is logged into the VA Central IRB Access Database and assigned to a VA Central IRB administrative staff member or an OP&E staff member to perform the review. The review will generally be conducted within ten working days of receipt. The results of the review will be sent to the study team via e-

mail with a reminder that the review was a courtesy review and not a determination of the VA Central IRB.

4.1.4.4 The VA Central IRB Administrator will ensure the VA Central IRB tracking database is updated and that the documents review, along with the pre-review results, are filed in the pre-review folders by applicable year and investigator on the VA Central IRB shared drive.

4.1.5 Once a study is accepted for review, the VA Central IRB Administrator will briefly explain submission procedures and advise the study team to use the most current version of the VA Central IRB forms for their submission, which are available on the VA Central IRB website. The VA Central IRB Administrator will remain the study team's main point of contact until the study team is ready to make an official submission.

4.1.6 The VA Central IRB Administrator may also offer to schedule an optional webinar to review the VA Central IRB application process and the various application forms, as well as providing a forum for investigator questions. This is recommended when there are a large number of sites that will be participating.

#### 4.2 Completion of PI/SC New Project Application.

4.2.1 The PI/SC must submit VA Central IRB Form 108, Principal Investigator/Study Chair New Project Application or VA Central IRB Form 108-NSI and all associated documents depending upon the design of the study.

4.2.2 For some projects, there may be one or more Co-PI/SCs designated. For these projects, one of the Co-PI/SCs must complete VA Central IRB Form 108 and the other Co-PI/SC(s) must complete VA Central IRB Form 108a (**Attachment 3**), Co-PI/SC New Project Application Supplement, and submit this form with the VA Central IRB Form 108, as part of the application package. If the Co-PI is a DOE employee, the VA Central IRB Form 108a (DOE) (**Attachment 4**) must be completed.

4.2.3 For all Office of Research and Development Cooperative Studies Program (CSP) projects and for all other studies that use a Coordinating Center to assist in the management of the multi-site study, a VA Central IRB 108b, Coordinating Center PI/SC New Project Application Supplement (**Attachment 5**), must be completed and submitted with the PI/SC New Project Application.

4.2.4 The latest version of the grant application or protocol must be submitted with the version date clearly indicated on the first page. The VA Central IRB has an optional Protocol Template (**Attachment 6**) that can be used by study teams in development of a protocol. If there is an existing protocol, the PI/SC must ensure that all elements indicated on the VA Central IRB Protocol template are adequately addressed in the existing protocol. If not, and the protocol is from a non-VA sponsor, any issues not adequately addressed must be detailed in the VA Central IRB Form 108.

4.2.5 Depending upon the study design, additional forms may be required. The VA Central IRB Form 108 is self-explanatory and indicates when additional forms must be completed and submitted

relating to investigator qualifications; conflict of interest requirements; informed consent documents; requests for informed consent and/or HIPAA waivers; and requests for using pregnant women or prisoners. These additional requirements will be detailed in subsequent paragraphs.

4.2.6 The PI/SC should thoroughly review all application instructions and complete all required forms in order to ensure timely processing of the project by the VA Central IRB. The PI/SC is encouraged to contact the VA Central IRB Administrator throughout the process of completing the VA Central IRB Form 108 and any other required forms, with questions or concerns.

#### 4.3 Investigator Qualifications and Conflict of Interest Requirements.

4.3.1 All study team members serving in an investigator role (PI/SC, Co-PI/SC, Sub-I, Co-I) must submit a recent bio sketch (merit review or NIH format) or a curriculum vitae (CV) that indicates sufficient research experience for the role they will be serving in the study.

4.3.1.1 If the investigator is new or does not have sufficient experience, a mentorship plan should also be submitted. This plan must include regular meetings with an experienced mentor and what these meetings will entail. If the mentor will have access to protected health information (PHI) the mentor should also be listed on the VA Central IRB Form 108 as a study team member.

4.3.1.2 If an investigator has sufficient clinical experience but is new to the VA, a mentorship plan must also be submitted. This can include a statement by the local ACOS/R&D or other experienced VA investigator that he/she will be available to mentor the PI/SC on VA requirements.

4.3.2 All VA investigators, whether compensated or uncompensated, whether part-time or full-time, must comply with all VA and other requirements relating to conflict of interest. For each project submitted for review, the Principal Investigator/Study Chair (PI/SC), Co-PI/SC, investigators, and any other study personnel identified as serving in an “investigator” role are required to disclose any perceived or actual conflicts of interest. These conflicts can be financial or another type of conflict, such as personal or business relationships. All such conflicts must be appropriately disclosed and managed or resolved so they do not negatively impact human research participants.

4.3.2.1 All investigators or other personnel associated with a project to be reviewed by the VA Central IRB must complete a financial disclosure form and have it reviewed by their local VA facility in accordance with the local VA facility policies and procedures. In the event that the local facility cannot do this review, such as if the FCOI reviews are done by the local affiliate IRB, the investigator completes OGE Form 450 Alternative-VA, Research Financial Conflict of Interest Statement, and it must be submitted to the VA Central IRB with the VA Central IRB Form 108. This form must contain the specific title of the project being submitted and it must be signed and dated within one year of submission.

4.3.2.2 For those investigators whose local facilities have a Conflict of Interest Committee or Conflict of Interest Official who performs such reviews at the local site, a memorandum listing all investigators from the site and whether each investigator had a conflict or not will be accepted in lieu of the OGE Form 450 Alternative-VA. If there was a conflict, the conflict must be indicated as well as the management plan and/or resolution that was agreed upon by the investigator, local site, and the Office of General Counsel.

4.4. Informed Consent Requirements. Informed consent involves following core general principles when obtaining consent and providing participants core basic elements that must be part of every consent. Other, additional elements may be required based on study design and/or study populations used.

4.4.1 General Principles. The following are general principles when obtaining informed consent:

- 4.4.1.2 It is the policy of the VA Central IRB that an investigator may not involve a human being as a participant in non-exempt research that the VA Central IRB oversees unless the investigator or the investigator's designee obtains the informed consent of the participant or the participant's legally authorized representative, unless the requirement for obtaining such consent is waived by the VA Central IRB.
- 4.4.1.2 If someone other than the investigator conducts the interview and obtains consent from a participant or the participant's legally authorized representative, the investigator needs to formally delegate this responsibility in writing, and the person so delegated must have appropriate qualifications and have received appropriate training to perform this activity. Unless otherwise required by the VA Central IRB, the PI/SC or LSI does not have to designate the individuals by name but can designate the position title in the protocol or other study documents, such as the VA Central IRB Form 108 where there is a column for this purpose in the personnel section of the form.
- 4.4.1.3 An investigator can seek consent only under circumstances that provide the prospective participant, or the participant's legally authorized representative (LAR), sufficient opportunity to read the informed consent document and consider whether or not to participate. The investigator must also minimize the possibility of undue influence or coercion. If a participant's legally authorized representative provides surrogate consent, assent must be sought from the participant whenever possible.
- 4.4.1.4 No informed consent, whether oral or written, may include any exculpatory language through which the prospective participant, or the prospective participant's LAR, is made to waive or appear to waive any of the participant's legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence.
- 4.4.1.5 The prospective subject or LAR must be given information that is in a language that is understandable to the subject or LAR. Any scientific and technical terms must be adequately explained. A reading level of 8<sup>th</sup> grade is desirable but higher levels, particularly for VA provider participants, may be accepted by the VA Central IRB as long as the readability is found to be appropriate for the participant population.



4.4.1.6 The prospective subject or LAR must be provided with information that a reasonable person would want to have in order to make an informed decision about whether to participate, and an opportunity to discuss that information. Information must be presented in sufficient detail relating to the research and be organized and presented in such a way that does not merely provide lists of isolated facts, but rather facilitated the prospective subject's or LAR's understanding of the reasons why one might or might not want to participate.

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

4.4.2 Basic Elements of Informed Consent. Except when an informed consent waiver or alteration is requested and granted by the VA Central IRB, the following basic elements of consent must be provided to each prospective participant or the prospective participant's LAR:

- The name of the project, the name of the sponsoring organization, and the name of the Principal Investigator (PI). For multisite studies that involve submission of Local Site Investigator Applications, both the name of the PI and the LSI must be provided on the informed consent documents for a particular site.
- A statement that the project involves research and an explanation of the purpose of the research.
- The expected duration of a participant's active participation, to include long-term follow-up.
- A description of the procedures to be followed, identifying any procedures which are going to be performed solely for research purposes and/or any procedures that are experimental.
- A description of any reasonably foreseeable risks or discomforts to the participant, to include but not limited to, physical, social, legal, economic, psychological, and any privacy risks that may result from the research. Risks of standard care are not to be included and the participant must be advised to discuss these with the participant's health care provider.
- A description of the potential benefits to the participant or to others that may reasonably be expected from the research.
- A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the participant. If the only alternative is not to participate, this element does not need to be included in the consent form.
- A statement describing the extent to which confidentiality of any records identifying the participant will be maintained. If appropriate, a statement that other federal agencies including but not limited to the VHA Office of Research Oversight (ORO), the Office for Human Research Protections (OHRP), and the Government Accountability Office (GAO) may have access to the records. If an FDA-regulated test article is involved, there must be an additional statement indicating the FDA may choose to inspect research records that include the participant's medical records.
- For research involving more than minimal risk, an explanation as to whether any compensation is available and an explanation as to whether any medical treatments are

available if injury occurs; what those treatments consist of; and where further information can be obtained. This includes a statement that VA will provide treatment for any research related injury unless the injury is due to noncompliance by the subject with study procedures or the research is conducted under a contract with an individual or non-VA institution.

- 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 a research-related injury to the subject. The contact(s) must be someone knowledgeable of the specific research project and the contact's name and phone number must be provided to the participant. The VA Central IRB toll free number (877-254-3130) also should be included as a point of contact.
- A statement that participation is voluntary and that refusal to participate will involve no penalty or loss of benefits to which the participant is otherwise entitled and that the participant may discontinue participation at any time without penalty or loss of benefits to which the participant is otherwise entitled.
- For any research involving the collection of identifiable private information or identifiable biospecimens, the following must be included: 1) a statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional consent from the subject or LAR or, if this might be a possibility; **or** 2) a statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.

**4.4.3 Additional Elements of Informed Consent.** When appropriate, one or more of the following additional elements of information shall also be provided to the participant:

- A statement that the particular treatment or procedure may involve currently unforeseeable risks to the participant or to an embryo or fetus if the subject becomes pregnant.
- Any anticipated circumstances under which the participant's participation in the research may be terminated by the investigator without the subject's or the LAR's consent
- Any additional costs to the participant that may result from participation in the research to include a statement that a Veteran participant or their insurance company will not be required to pay for care received that is part of a VA research project but that they will, however, be required to pay any co-payments they would ordinarily be required to pay for any non-research related VA medical care and/or services.
- An explanation of the consequences of a participant's decision to withdraw from the research and the procedures for the orderly termination of participation by the participant.
- A statement that significant new findings developed during the course of the research which may relate to the participant's willingness to continue participation will be provided to the participant to include the procedures for contacting the participants and for confirming their continued participation if applicable.
- The approximate number of subjects to be entered into the study, both over the entire study and at the particular local site at which the subject is enrolling.
- As appropriate, a statement regarding any payment the participant is to receive and how it will be made, to include a description of how payment will be prorated and calculated for participants who withdraw early. If the payment will generate an Internal Revenue Service reporting requirement, this should also be stated.

- A clear statement concerning any conflict of interest by investigators involved with the project or the institution at which the research will be performed that has not been resolved or eliminated.
- For research involving the use photography, video, and/or other audio recordings for research purposes, a statement that describes any photographs, videos, 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 they will be disclosed outside the VA. If these items are taken while a participant is an inpatient or an outpatient and the items will be filed in the participant's medical record, a VA Form 10-3203, Consent for Use of Picture and/or Voice must be used for this purpose and model document also submitted for review.
- A statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit.
- A statement whether clinically relevant research results and/or aggregate results will be disclosed to subjects, and if so, under what conditions.
- A statement whether research involving the use of biospecimens will include, if known, or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen.
- If the data and/or biospecimens collected on the subject will be banked and used for future research, the name and location(s) at which the data and/or specimens will be stored, who will have access to the data and/or specimens (by name or role), the types of specimens to be stored, and whether this is optional component of the research.
- Studies involving genetic analysis will contain language pertaining to the Genetic Information Non-Discrimination Act (GINA) as approved by the VA Office of General Counsel.
- If the study is a clinical trial, there must be a statement that one IRB-approved consent form used to enroll subjects, unless the IRB waived documentation of informed consent, will be posted after the clinical trial is closed to recruitment at all sites to either <https://clinicaltrials.gov> or a docket folder on <https://Regulations.gov>.
- If the study is protected by a Certificate of Confidentiality, 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 this will be the case and for studies in which the IRB requires a written informed consent, the informed consent document approved by the IRB must include a statement that the study has a Certificate of Confidentiality.

4.4.4 Documentation of Informed Consent. Except if a waiver is approved by the VA Central IRB, informed consent must be documented by the use of a written consent form approved by the VA Central IRB and signed and dated by the subject or the subject's LAR. A physical or electronic copy must be provided or made available to the person who signed the form and the original kept in the project files. A copy should also be filed in the subject's medical record if the research intervention is taking place at a VA facility as part of a documented encounter. The study team should also follow all local VA medical facility requirements for documenting the subject's participation in a project.

4.4.4.1 The VA Central IRB requires the use of one of two VA Central IRB informed consent templates to ensure inclusion of all of the above requirements as applicable. Depending upon study design, the Combined VA Central IRB Informed Consent and HIPAA

Authorization Template ([Attachment 7](#)) or the VA Central IRB Informed Consent Only Template ([Attachment 8](#)) can be used. Detailed instructions for completion and submission of these forms are included within the form themselves. The PI submits model informed consent documents, leaving blank site-specific information to be filled in by local participating sites as part of the LSI Application process. Generally, only site-specific contact information should be left blank as the informed consent forms across all sites should be as uniform as possible.

4.4.4.2 If informed consent is being obtained from the participant’s legally authorized representative (LAR), the LAR must be informed of his/her role and obligation to protect the participant and to act in what the LAR determines to be the participant’s best interest. All information that would have ordinarily been provided to the subject must be provided to the LAR so that he/she can make a fully informed decision.

4.4.4.3 The use of a witness signature is optional. The VA Central IRB may still require the signature of a witness based upon the study design and/or the population being targeted for the research. The sole role of a witness is usually to witness the participant’s or the participant’s legally authorized representative’s signature on the consent form. If required by the VA Central IRB or a sponsor, the witness can witness the entire informed consent process. If this is done, the witness is attesting that the information was accurately relayed, the participant had the opportunity to ask and have questions answered, and that consent was given freely. The witness can be a member of the study team but cannot be the member that obtained the informed consent.

4.4.5 Withdrawal or Termination of Consent. As part of the informed consent process, investigators should ensure that participants are informed that, if they later wish to withdraw consent or they are terminated from the project for some reason, the following applies:

4.4.5.1 That the data collected on the participant to the point of withdrawal remains part of the study database and may not be removed. The consent document cannot give the participant the option of having data removed.

4.4.5.2 An investigator may ask a participant who is withdrawing whether the participant wishes to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the participant would distinguish between study-related interventions and continued follow-up of associated clinical outcome information, such as medical course or laboratory results obtained through noninvasive chart review, and address the maintenance of privacy and confidentiality of the participant's information.

4.4.5.3 If a participant withdraws from the interventional portion of the study, but agrees to continued follow-up of associated clinical outcome information, the investigator must obtain the participant’s informed consent for this limited participation in the study (assuming such a situation was not described in the original informed consent form). VA Central IRB approval of this limited informed consent documents would be required.

4.4.5.4 If a participant withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, the investigator must not access the participant's medical record or other confidential records requiring the participant's consent. However, an investigator may review study data related to the participant collected prior to the participant's withdrawal from the study, and may consult public records, such as those establishing survival status.

4.4.6 Waiver of Documentation of Informed Consent. Investigators may request a waiver of the requirement to obtain a signed informed consent document. To do this, they must complete VA Central IRB Form 112b, Request for Waiver of Documentation of Informed Consent ([Attachment 9](#)), and submit as part of the PI/SC Application.

4.4.6.1 In order to request this waiver, the research for which the waiver is being requested must meet one of the following criteria:

- The research involves no more than minimal risk of harm to participants and involves no procedures for which written consent is normally required outside of the research context; *or*,
- The only record linking the participant and the research would be the consent document and the principal risk to the participant would be potential harm resulting from a breach of confidentiality. Each participant will be asked whether he/she wants documentation linking him/her with the research and the participant's wishes will govern; *or*,
- For studies subject to the 2018 requirements, if the subjects or LARs are members of a distinct cultural group or community in which signing an informed consent form is not the norm, that the research presents no more than minimal risk of harm to subjects and provided that there is an appropriate alternative mechanism for documenting the informed consent.

4.4.6.2 Even if a waiver of the requirement to obtain a signed consent form is granted, the VA Central IRB may still require other conditions of the investigator, such as providing subjects with an information sheet or other documentation about the research. The VA Central IRB may require the use of the VA Central IRB Information Sheet Template ([Attachment 10](#)) to be used. This sheet can serve to guide the investigator in ensuring that all elements required for informed consent are covered in the information given.

4.4.7 Waiver of Informed Consent. An investigator may request a waiver, alteration, or omission of the elements of informed consent by completing VA Central IRB Form 112a ([Attachment 11](#)).

4.4.7.1 For research involving public benefit and services programs conducted by or subject to the approval of State or local officials, the research could not practicably be carried out without the waiver or alteration and it must be designed to study, evaluate, or otherwise examine one or more of the following:



- Public benefit or service programs
- Procedures for obtaining benefits or services under those programs
- Possible changes in or alternatives to those programs or procedures
- Possible changes in methods or levels of payment for benefits or services under those programs

4.4.7.2 For all other studies, **all** the following criteria must be met for granting of the waiver or alteration:

- The research involves no more than minimal risk to the subjects,
- The research could not practicably be carried out with the requested waiver or alteration,
- The waiver or alteration will not adversely affect the rights and welfare of the subjects,
- Whenever appropriate, the subject or LAR will be provided with additional pertinent information after participation, **and**
- For studies subject to the 2018 requirements, if the research involves using identifiable private information or biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format.

If requesting a waiver or alteration for only specified portions of the study, each portion must meet the above approval criteria and each be fully described on the VA Central IRB Form 112a. Only one VA Central IRB Form 112a should be submitted per study by the PI/SC. Local site Investigators do not have to submit separate waivers unless they are requesting a waiver in addition to the waiver approved by the VA Central IRB as part of the PI/SC Application.

4.4.7.3 For studies subject to the 2018 requirements in which an investigator obtains identifiable information and biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective subjects without the informed consent of the prospective subject or the subject's LAR submission of an informed consent waiver is no longer required if either of the following conditions is met:

- The investigator will obtain information through oral or written communication with the prospective subject or LAR; **or**
- The investigator will obtain identifiable private information through or identifiable biospecimens by accessing records or stored identifiable biospecimens.

If one of the above criteria is met, the VA Central IRB 112a does not need to be submitted for this activity. However, a waiver of HIPAA authorization must still be submitted and approved.

4.5 HIPAA Requirements. A written HIPAA authorization signed by the individual to whom the information or record pertains is required when VA health care facilities utilize individually-

identifiable health information for a purpose other than treatment, payment or health care operations. Research is considered an other purpose.

- 4.5.1 The HIPAA authorization can be part of the informed consent document. The VA Central IRB Combined Informed Consent and HIPAA Authorization should be used when combining these documents as it contains all the elements required in a HIPAA authorization.
- 4.5.2 When a study team elects not to combine the informed consent and HIPAA authorization into one document, the VA Central IRB requires use of VHA Form 10-0493, Authorization for Use and Release of Individually Identifiable Health Information for Veterans Health Administration (VHA) Research. The PI/SC should prepare a model form with all but the site-specific information completed and submit it as part of the PI/SC Application. The use of VA Form 10-10116, Revocation of Authorization for Use and Release of Individually Identifiable Health Information for Veterans Health Administration (VHA) Research is optional but recommended.
- 4.5.2.1 The VA Central IRB highly recommends separate informed consent and HIPAA authorization forms when enrolling impaired decision-making individuals to ensure the appropriate individual signs the HIPAA authorization since this must be a person who has durable medical power of attorney or is a court-appointed guardian. If the study team elects not to have a separate authorization when enrolling impaired decision-making subjects, it must provide the VA Central IRB its plan for ensuring that only authorized individuals sign the combined document.
- 4.5.2.2 In studies in which there are optional components, such as data or tissue banking, a separate HIPAA authorization form and informed consent document should also be used to ensure appropriate authorizations are made, particularly for any optional banking component of the study.
- 4.5.3 Waiver of HIPAA authorization. The PI/SC may also request a waiver of the requirement to obtain the HIPAA authorization by submitting a VA Central IRB Form 103, Request for Waiver of HIPAA Authorization Requirement (**Attachment 12**). The PI/SC needs to provide sufficient detail on the VA Central IRB Form 103 to ensure the IRB has the information it needs to make a determination regarding whether the waiver meets the required IRB approval criteria, which can be found on the form for reference.
- 4.5.3.1 Investigators may submit a waiver for only certain phases of the study or for the entire study. If requesting access to identifiable data for the purposes of screening, recruiting, or determining eligibility, submission of a VA Central IRB Form 103 is required.
- 4.5.3.2 If the PI/SC submits a VA Central IRB Form 103 and it is approved, the LSIs do not need to submit any additional VA Central IRB Forms 103 to request a waiver of the same issues with their local applications. Only one VA Central IRB Form 103 should be submitted per study. LSIs may submit a site-specific VA Central IRB

Form 103 if they are requesting a waiver for a purpose or from a database not specified in the PI/SC submitted waiver.

- 4.6 Use of Vulnerable Populations in Research. Pregnant women, human fetuses, neonates, children, and prisoners are considered vulnerable per statute and statutory safeguards must be in place for their use. Other vulnerable populations can be used in research if the VA Central IRB determines sufficient safeguards exist.
- 4.6.1 Pregnant Women, Human Fetuses, and Neonates. Women who are known to be pregnant, their fetuses, and neonates may be involved in research if statutory conditions are met and if permitted per VHA Directive 1200.05. The local VA medical facility Director must also certify 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.
- 4.6.1.1 VA investigators cannot conduct interventions that include neonates while on official VA duty, at VA facilities, or at VA-approved off-site facilities. VA researchers 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.
- 4.6.1.2 Research that involves provision of in vitro fertilization services can be conducted by VA investigators while on official VA duty, at VA facilities, or at VA-approved off-site facilities. Prospective and retrospective studies that enroll or include pregnant subjects who conceived through in vitro fertilization or other artificial reproductive technologies are also permitted.
- 4.6.1.3 Research in which the focus is either a fetus, either in-utero or ex-utero, can be conducted by VA investigators while on official VA duty, at VA facilities, or at VA-approved off-site facilities. Use of human fetal tissue cells and human stem cells is governed by the policy set by NIH for recipients of NIH funding.
- 4.6.1.4 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 cannot be conducted by VA investigators at VA facilities, or at VA approved off-site facilities.
- 4.6.1.5 If a research project involves the use of Pregnant Women, Human Fetuses, or Neonates a VA Central IRB Form 110a, Vulnerable Population Supplement (Pregnant Women, Human Fetuses, and Neonates) (**Attachment 13**) must be completed and submitted by the PI/SC, along with the VA Central IRB Form 108. The VA Central IRB Form 110a includes the ethical and scientific criteria which must be met when using and enrolling this population.

4.6.2 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) in the VA Office of Research and Development (ORD). This request must be submitted electronically and meet the requirements as specified in VHA Directive 1200.05, paragraph 20.

4.6.2.1 Included in these requirements is that the following documents be provided after approval by the VA Central IRB:

- A copy of the IRB approval letter specifically documenting the IRB's review determinations according to 45 CR 46.305a
- A copy of the IRB minutes approving the research with documentation that at least one member of the IRB included a prisoner or a prisoner representative for the review of the research
- A copy of the IRB-approved research study
- A copy of the IRB-approved informed consent document or HIPAA authorization (a combined informed consent document and HIPAA authorization will meet this requirement as well.)

4.6.2.2 In order for the VA Central IRB to complete the required review and provide the necessary documentation, the PI/SC must complete and submit a VA Central IRB Form 110b, Vulnerable Population Supplement (Prisoners) (**Attachment 14.**) This form contains all the criteria the VA Central IRB will use when evaluating a request to conduct research using prisoners.

4.6.3 Children. Research involving children must have relevance to the VA and must not present greater than minimal risk to the children. There is no separate supplement to be completed for children. However, the VA Central IRB follows requirements for use of children as specified in 45 CFR 46, Subpart D. Research involving biological specimens or data obtained from children is also considered to be research involving children even if de-identified. Therefore, investigators must carefully consider the following and ensure that each issue below is adequately addressed in the protocol, VA Central IRB Form 108, and/or the informed consent document as applicable.

4.6.3.1 Investigators must indicate if the assent of children will be obtained taking into account the ages, maturity, and psychological state of the children. The PI/SC must also indicate how the assent will be documented.

4.6.3.2 For minimal risks studies as described at 45 CFR 46, Subpart D, paragraphs 46.404 the permission of one parent is sufficient and the informed consent should reflect this when submitted. Other provisions of Subpart D do not apply since the VA does not approved greater than minimal risk in children.

4.6.3.3 The use of children must be adequately justified. The investigator must indicate why children must be included and what benefit is derived to the VA, Veterans, and to children.

4.6.4 **Impaired Decision-Making Capacity.** Individuals with impaired-decision making capacity may be enrolled in VA research studies. If enrolling such individuals, investigators must carefully consider the following and ensure that each issue below is adequately addressed in the protocol, VA Central IRB Form 108, and/or the informed consent document as applicable.

4.6.4.1 Informed consent must be obtained from the subject's LAR. This should be reflected in the informed consent. Due to more stringent HIPAA requirements on who can sign a HIPAA authorization for impaired decision-making subjects, it is highly recommended that the VA Central IRB Informed Consent Only Template and a separate VA Form 10-0493 be used.

4.6.4.2 Investigators must indicate if assent will be obtained from the subjects and if so, how will this be documented. If not, the investigator should indicate why not. The investigator should also indicate that any dissent displayed by the prospective participant will be respected.

4.6.4.3 Investigators should indicate what, if any, additional safeguards will be in place to protect this vulnerable population.

4.6.4.4 Study documents must also describe how a participant's representatives will be informed regarding their roles and obligations to protected impaired decision-making participants and that the representatives must consider what the participant would have wanted or what is in the participant's best interest, not their own

4.6.4.5 If an individual has fluctuating or temporarily impaired decision-making capacity and is enrolled in the study through an LAR, if the individual regains capacity the study team must consent the individual before continuing the individual's participant in the study.

4.6.4.6 Investigators must follow state and local laws, as well as VA policy, when determining whether a subject has decision-making capacity. How this will be done should also be documented in the study documents.

4.7 **Other New Project Application Issues to Consider.** When completing the VA Central IRB 108, protocol, informed consent documents, and other associated forms as part of the PI/SC New Project Application, there are a number of other issues that PI/SC study teams might also have to consider as follows:

4.7.1 **Students and Employees.** Anyone with an employment or academic relationship to the VA will be informed that their participation in the project, or refusal to do so, will in no way influence their employment, ratings, or subsequent recommendations. The involvement of students or employees in the project requires a disclosure in the informed consent form acknowledging that refusal to participate will have no influence on their academic progress or employment status.

4.7.2 **Participants Who Cannot Sign the Informed Consent Document.** If the use of illiterate participants is proposed, or participants who are literate but cannot physically sign the consent



document, the investigator will provide details on how the informed consent is going to be obtained.

- 4.7.2.1 For illiterate participants, at a minimum, the investigator will include in the description that the informed consent document is read to the participant and the document then signed by the participant in the signature section by the participant “making their mark.” The VA Central IRB requires a witness to the mark.
- 4.7.2.2 A similar process is followed for potential participants who are literate and mentally capable of giving informed consent but physically unable to sign the form. The VA Central IRB can add additional stipulations depending upon the capabilities of the study population and the research design.
- 4.7.2.3 The investigator must specify if there are any state and local laws that govern how an illiterate subject is to “make their mark” or how a literate person who cannot physically sign the form. This may be different for local participating sites and will need to be reviewed for each submitted Local Site Investigator Application, which are addressed in paragraph 4.9 of this SOP.
- 4.7.3 Non-English-Speaking Participants. Most VA research involves Veterans as subjects. Veterans by the nature of their service are deemed to be proficient in English but exceptions may apply and will be considered by the VA Central IRB as applicable, such as older Veterans residing in Spanish-speaking areas, i.e., Puerto Rico. Care givers and family members participating in research may also not speak English.
- 4.7.3.1 If the involvement of participants who do not speak or read English is proposed a translator will be present to assist in the consent process and act as witness. A professional translator is preferred. In no case should the translator be a family member of the prospective subject.
- 4.7.3.2 Consent documents will be written in a language understandable to the participant population and a certified copy of any translated document forwarded to the VA Central IRB for review prior to enrollment of any participants. The VA Central IRB may use the expedited review procedure in reviewing this document if the English language version has already been approved and the translation is done by a certified translator.
- 4.7.4 Investigator is Participant’s Medical Provider. For projects in which an investigator also serves as one of the potential participant’s health care provider, someone other than the investigator will be designated to obtain the informed consent. Potential participants must be informed in the consent document that refusal to participate will in no way affect their current or future treatment.
- 4.7.5 Terminally Ill Participants. Terminally ill patients may be considered a special class of participants that may be subject to undue influence or coercion based on their lack of alternatives. Investigators must ensure that the nature, magnitude, and probability of the risks and benefits of the research are identified as clearly and as accurately as possible. Accurate

information concerning eligibility for participation, treatment options, and risks and benefits will be conveyed clearly and in a manner that will not either engender false hope or eliminate all hope.

**4.7.6 The Use of Deception in Human Subjects Research.** When a study proposes to use deception as part of the study design, the PI/SC must submit a VA Central IRB Form 112a to request an alteration in the informed consent process. As part of the alteration request, the PI/SC also must provide the following information:

4.7.6.1 Justification for the use of the deception based on the study’s significant prospective scientific, education, or applied value and an explanation as to why equally effective non-deceptive alternative procedures are not feasible.

4.7.6.2 A description of the measures that will be taken at the conclusion of the study to debrief participants and fully explain the nature of the deception, to include allowing participants to withdraw their data, or provide explicit justification for withholding such information. The VA Central IRB has a guidance document on the use of deception (**Attachment 15**) which should be followed as much as possible by the study team in designing their study.

**4.7.7 Participation in Multiple Studies.** Dual enrollment, i.e., enrollment in two or more studies concurrently, may be permitted as long as the dual enrollment:

- Does not adversely affect the rights or well-being of the subject; or
- Is not prohibited by the funding agency (e.g., CSP) or by one or more of the studies.

It is the responsibility of the Principal Investigator or Local Site Investigator to determine if it is appropriate for a subject to be in more than one study concurrently. This may require, especially for clinical studies, contacting the Principal Investigator of the other study to determine appropriateness.

**4.8 Recruitment Materials and Methods.** Recruitment materials should be factual and contain certain basic elements so a prospective subject can determine whether he/she might want to seek additional information about the study. The VA Central IRB allows many types of recruitment methods as long as VA policy does not prohibit their use. Both the VA Central IRB Form 108 and the protocol should contain detailed, step-by-step descriptions of all recruitment methods used.

4.8.1 Texting and use of e-mail is only allowed if the content of the text is free of all PHI. This means that no individually identifiable information can be combined with any medical information, such as the name of the study or the name of a clinic for which an appointment reminder might be sent to a participant. A copy of the proposed text or e-mail must be provided with the application package. MyHealthyVet may be used after participant enrollment and messages within this system can contain PHI. However, MyHealthyVet cannot be used for recruitment at this time.

4.8.2 The use of the opt-out method of recruiting is allowed depending on the study. Investigators may send letters to potential participants and, if the potential participants do not opt-out by calling or sending a return post card or other letter, call the participants after a specified period, usually two weeks to ensure the participants have had time to see the letter. Copies of all recruitment letters, as well as a telephone script must be submitted to the VA Central IRB with the PI/SC New Project Application Package. The VA Central IRB may still decide to only allow an opt-in method.

4.8.3 Recruitment materials should not promise any benefits that might be derived from participating in a study, nor should they make claims of how important the research is, how it will help fellow Veterans, or that it is an historical cutting-edge study. The following are the types of information that are required at a minimum in recruitment materials:

- It must be clear that the study involves “research.”
- A point of contact address or telephone number should be given – not an e-mail unless VA employees are being recruited and then an e-mail address can be provided.
- Duration of the participant’s involvement in the research
- Important inclusion/exclusion criteria
- Purpose of the study
- Whether any payment is offered for participation

4.9 Local ACOS/R&D Sign-Off and Submission of PI/SC Application to the VA Central IRB. Once the PI/SC study team has completed all applicable forms, the application must be checked for completeness and accuracy by the PI/SC or Co-PI/SC and signed.

4.9.1 The application must also be reviewed by the local ACOS/R&D, who must complete and sign a VA Central IRB Form 102, Local ACOS/R&D Application Review Supplement (**Attachment 16**), to indicate to the VA Central IRB that the local site is aware of the project and that local requirements for training credentialing, and conflict of interest review have been met or are in process. The study team must also ensure that all other documents requiring signature of the PI or Co-PI-SC have been signed. All informed consent documents should be submitted in Microsoft Word for ease in editing by the VA Central IRB, as should the VA Central IRB 103.

4.9.2 Once the package is complete, all documents should be uploaded into the Initial Submissions Folder on the VA Central IRB website and an e-mail sent to the general VA Central IRB e-mail address at [vacentralirb@va.gov](mailto:vacentralirb@va.gov) to indicate submission is complete. The VA Central IRB staff will not download the submission until it receives this message. This gives study teams time to load documents and revise them as needed prior to submission. Investigators who did not go through the pre-review process and who do not already have a submission folder set-up should contact the VA Central IRB Administrator. This can be done at any time after the study team receives notice that the VA Central IRB can review the study.

4.10 Application Requirements for Local Site Investigators (LSIs). Local Site Investigator Applications must be submitted for each site that will be engaged in the human subjects research project. This includes the PI/SC site if recruitment of subjects is going to take place at the PI/SC site. If recruitment will not take place at the PI/SC site an LSI Application does not need to be submitted

from the PI/SC site. A PI/SC may also serve as the LSI for his or her home site. If this is the case, the PI/SC also prepares the VA Central IRB Form 104 to include all associated documents, for the specific site. **However, LSI Applications will not be accepted for review until the PI/SC application is approved. During the review process there may be many changes made in the original PI/SC application and these will also need to be reflected in the LSI Application submissions.** For more information on the submission of LSI Applications, see VA Central IRB SOP 104, VA Central IRB Review Requirements for New Project Applications (Expedited and Convened.)

## 5 DOCUMENTATION REQUIREMENTS

- 5.1 Forms used to submit PI/SC New Project Applications are reviewed regularly and updated as needed to ensure they remain current and in accordance with any changes in regulatory or VA requirements. Forms are made available on the VA Central IRB website for study teams to download. Current forms, as well as obsolete copies of outdated forms are also kept on the VA Central IRB shared drive.
- 5.2 Documents are kept in a combination of paper, the VA Central IRB shared drive and the VA Central IRB SharePoint site.

## 6 REFERENCES

- 6.1 38 CFR 16, Department of Veterans Affairs, Protection of Human Subjects
- 6.2 VHA Directive 1200.05, Requirements for the Protection of Human Subjects in Research
- 6.3 VHA Directive 1058.03, Assurance of Protection for Human Subjects in Research
- 6.4 VHA Directive 1108.04, Investigational Drugs and Supplies
- 6.5 45 CFR 46, Department of Health and Human Services, Protection of Human Subjects, Subparts B through D
- 6.6 21 CFR 50, U.S. Food and Drug Administration, Protection of Human Subjects
- 6.7 21 CFR 312, U.S. Food and Drug Administration, Investigational New Drug Application
- 6.8 21 CFR 812, U.S. Food and Drug Administration, Investigational Device Exemptions



## New Project Application Requirements

Document No.: VA-CIRB-SOP-103

Supersedes SOP 104 Aug 28, 2014; SOP 105 July 23, 2014; SOP 106 Oct 24, 2013

Revision Date:  
January 28, 2019

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As the responsible authority delegated by the VHA Central Office Institutional Official for administrative oversight of the VA Central IRB, I have reviewed and approved the contents of this VA Central IRB Standard Operating Procedure.

Marisue Cody, Ph.D.  
Director of Operations  
VHA Human Protections Administrator  
Office of Research and Development

16 attachments

1. VA Central IRB Form 108, Principal Investigator/Study Chair New Project Application
2. VA Central IRB Form 108, Principal Investigator/Study Chair New Project Application (No Subject Interventions)
3. VA Central IRB Form 108a, Co-Principal Investigator/Study Chair New Project Application Supplement
4. VA Central IRB Form 108a (DoE), Co-Principal Investigator//Study Chair New Project Application Supplement – DoE.
5. VA Central IRB Form 108b, Coordinating Center PI/SC New Project Application Supplement
6. VA Central IRB Protocol Template
7. VA Central IRB Combined Informed Consent Template and HIPAA Authorization
8. VA Central IRB Informed Consent Template Only
9. VA Central IRB Form 112b, Request for Waiver of Documentation of Informed Consent
10. VA Central IRB Information Sheet Template (Waiver of Documentaion of Consent)
11. VA Central IRB Form 112a, Request for Waiver or Alterantion of the Informed Consent Process
12. VA Central IRB Form 103, Reqeust for Waiver of HIPAA Authorization
13. VA Central IRB Form 110a, Vulnerable Population Supplement (Pregnant Women, Human Fetuses, and Neonates)
14. VA Central IRB Form 110b, Vulnerable Population Supplement (Prisoners)
15. Use of Deception in Research Handout
16. VA Central IRB Form 102, Local ACOS/R&D Application Review Supplement