

## Durham VAMC: Research Protocol Guidance

**EXPEDITED REVIEW OF RESEARCH:** In contrast to a convened IRB review process where all members of the IRB review the proposed research, an expedited review is a review conducted by only one designated member of the IRB (usually an IRB Co-Chair). An expedited review is not necessarily faster than a convened review. Research reviewed by the expedited procedure must meet the same standards for approval as research reviewed by the convened IRB. For more information on expedited reviews and what types of research are eligible for expedited review, see Appendix A.

**SINGLE SITE STUDY:** If the research will be conducted only at the Durham VAMC and there are no other participating sites, submit a protocol that provides details for each of the required protocol elements in the “Required Protocol Elements” section of this document.

**RECRUITMENT STUDY:** The Durham VAMC IRB can only approve research that supports VHA’s mission to advance the health care of our nation’s Veterans. To recruit patients from the Durham VAMC for a non-VA study (e.g., a study approved by and conducted at Duke or UNC), the VA protocol must have strong rationale for Veteran participation and describe the relevance of the research and how the research would benefit the Veteran population. Both the protocol and informed consent form should focus on procedures being conducted at the Durham VAMC (e.g., screening and/or recruiting). The procedures occurring at the other site may be briefly summarized but with a clear indication that the VHA is not responsible for the conduct of that portion or phase of the study.

Include the protocol from the other site for informational purposes; the DVAMC IRB will not critique or approve the other site’s protocol but will consider the relevance and risks to veterans before approving recruitment from the Durham VAMC.

Plans for protecting privacy and information security are crucial. Be specific about what information will be provided to the non-VA site and how data will be transferred. Also indicate if the VA PI will participate in data analysis or manuscript preparation.

*NOTE: This guidance does not preclude Durham VAMC clinicians, in the normal course of their clinical duties, from discussing specific research studies with their patients where appropriate, and referring them to a non-VA investigator for more information about a non-VA study. However, Durham VAMC personnel should not provide the non-VA investigator with the names or contact information of Veterans who might be eligible for the study. Instead, the Durham VAMC clinician should provide the Veteran with the contact information for the non-VA investigator so the Veteran may initiate contact if he/she is interested in participating in the non-VA study. Durham VAMC personnel should not provide the non-VA investigator with protected health information (PHI) about Veterans who choose to participate in non-VA studies without a signed release form, **and** a signed HIPAA authorization, **and** adherence to local requirements for the release of medical information.*

## Durham VAMC: Research Protocol Guidance

**MULTI-SITE STUDY:** If the research will be conducted at the Durham VAMC but Durham is one of many sites, there should one “original” or “parent” protocol, usually created by the study sponsor or lead investigator. This must be submitted for IRB review. In addition, there should also be a brief Durham VAMC-specific protocol (“local protocol”) that adequately addresses:

- Any aspect(s) of the original/parent protocol that will not be conducted at the Durham VAMC.
- Any alteration(s) of procedure(s) in the original/parent protocol and how the alteration affects the local risk/benefit ratio.
- Role of individual(s) (i.e., Co-Investigator or usual-care clinician) performing procedure(s) involving clinical care. Describe any special training required as appropriate for non-clinicians.
- Handling of adverse events, data storage, information security, and privacy/confidentiality issues.
- Procedures for indentifying, recruiting, enrolling, and following subjects (as appropriate) at the Durham VAMC.
- Any other issues specific to the Durham VAMC that are not stated in the original protocol, such as process of subject compensation or information regarding usual care.

These items should be addressed in addition to the required elements described in the “Required Protocol Elements” section of this document.

In the local protocol, for ALL of the required elements:

- Specify the page(s) of the original/parent protocol on which this information is located, and
- State that the local protocol does not differ from the original/parent protocol regarding this element—**OR**—note any exceptions.

### **REQUIRED PROTOCOL ELEMENTS**

#### **General Information**

- The protocol should have the following items clearly accessible, either on a cover page or as running headers or footers:
  - Protocol Title
  - Name of Principal Investigator/Local Site Investigator
  - Protocol Version and Date
- All protocol pages should be numbered.
- The protocol should indicate if the local PI a clinician or non-clinician.
  - If the PI is a non-clinician and medical procedures are being performed, the protocol must have provisions for enlisting the services of a clinician with appropriate expertise and privileges to perform duties that may include: medical procedures, reviewing data for safety concerns, reviewing adverse events and new study findings, and making required decisions to protect the health of the subject. If not applicable, state why.

# Durham VAMC: Research Protocol Guidance

## **Purpose**

Provide a general description of purpose of the study.

## **Background and Significance**

Include a discussion of important literature or data that are relevant to the study and that provide background for the study; provide applicable clinical, epidemiological or public health background or context of the study; state the importance of the study to the VA's mission and any relevant treatment issues or controversies, etc.

## **Design**

Describe of the type/design of study to be conducted (e.g., placebo-controlled, double-mask, parallel design, open-label, dose escalation, instrument validation, focus group, etc.). Include variables, measures, objectives, endpoints, or outcomes, as applicable.

## **Risk/Benefit Assessment**

Describe how risks and discomforts will be minimized. Consider physical, psychological, legal, economic, social, and genetic risks.

## **Selection of Subjects**

The protocol should have a clear set of inclusion and exclusion criteria (bulleted or numbered lists are preferred). Indicate how potential subjects will be identified. Indicate the number of subjects that will be enrolled over all sites (if applicable) and how many subjects will be enrolled at Durham. It may be helpful to state that you will screen/consent individuals until you meet the desired sample size of X subjects. Describe safeguards for vulnerable populations or those subjects who may be susceptible to coercion or undue influence.

## **Subject Recruitment**

Provide a plan for just, fair, and equitable recruitment and selection of subjects. All studies (prospective, retrospective, data/sample repositories, etc.) must describe subject recruitment. If subjects are contacted about the study, include specifics of how this contact will be made. This is typically not well described in original/parent protocols for multi-site studies but is necessary for IRB approval.

## **Consent Process**

Describe the consent process. Indicate whether the study will utilize a waiver of informed consent or a waiver of documented informed consent (e.g., verbal consent but no signed consent document).

## **Study Interventions**

Describe study related treatment (the use of a table of procedures/evaluations may be helpful). If the protocol involves "usual care," the protocol must clearly differentiate the research intervention(s) from "usual care" (whether the "usual care" is limited to one "arm" of the study or is being delivered to all study subjects). Also, the protocol must clearly designate the individual or entity (e.g., the appropriate research personnel

# Durham VAMC: Research Protocol Guidance

versus the subject's health care provider) responsible for relevant aspects of both the research and the usual care.

Note: To decrease the number of protocol deviations, describe and, if applicable, provide a plan to manage any foreseeable issues regarding study conduct (e.g., expected lost equipment or expected missed or out of window visits).

## Adverse Events

Given the study population, disease/illness/condition state being studied, and drug information (as applicable); describe common foreseeable adverse events (i.e., the "expected" or "anticipated" adverse events or serious adverse events). The protocol should state that all adverse events will be reported per Durham VAMC requirements.

## Costs and/or Payments to Subjects

If applicable, add any research-related costs to subjects. Describe what payments or other compensations are provided, how they will be made, and what situations may result in partial payment.

## Data and Safety Monitoring

Future Data Use: If the data may be reused in other studies, the protocol must:

- (1) Describe the research data repository in which the data is to be stored, or, if data repository created through another IRB-approved protocol, identify by title and PI, and then briefly summarize relevant points from that protocol.
- (2) Provide for informed consent and a HIPAA authorization that includes language on the uses and disclosures of the data as defined in the protocol as well as information on how privacy and confidentiality will be maintained and how the data will be secured, **OR** request a waiver or alteration of informed consent and HIPAA authorization. The waiver request must address how the future data use will not affect the rights or privacy of the subjects.

Prospective Studies: Describe the data and safety monitoring plan for prospective studies. (Some studies may not have appreciable safety risks.) This plan must include, but is not limited to, the following:

- (1) What safety information will be collected including SAEs
- (2) How the safety information will be collected (e.g., with case report forms, at study visits, by telephone calls with subjects);
- (3) The frequency of data collection including when safety data collection starts;
- (4) The frequency or periodicity of review of cumulative safety data;
- (5) If not using a DMC, and if applicable, statistical tests for analyzing the safety data to determine if harm is occurring;
- (6) Provisions for the oversight of safety data (e.g., by a DMC); and
- (7) Conditions that trigger an immediate suspension of the research, if applicable.

**NOTE:** *The data and safety monitoring plan may vary depending on the potential risks, complexity, and nature of the study. The use of an independent DMC needs to be considered if there are multiple clinical sites, the study is blinded, interventions are high-*

# Durham VAMC: Research Protocol Guidance

*risk, vulnerable populations are included, or when required by the funding organization, FDA, sponsor, or other relevant entity.*

**Retrospective Studies:** Describe the safety and monitoring plan for retrospective studies, including studies involving pre-existing data and biological specimens. When applicable, the plan needs to include, but is not limited to, the following:

- (1) A discussion with the subject of potential study outcomes that may have an effect on the subject's health or well-being; and
- (2) A procedure to determine when and how to notify individual subjects or their health care providers of findings that may affect the subjects' health.

## **Privacy and Confidentiality**

Describe privacy and confidentiality protections. The description needs to be sufficiently specific for the IRB to understand how the procedures protect the subject's privacy and the confidentiality of the data. These procedures must be in compliance with all applicable VA and federal requirements.

## **Information Security**

Describe a plan for information security. The plan must clearly identify and include, but not be limited to:

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

If you are sending or providing data to external sites or other facilities, provide a detailed list of what items and/or data will be included in the data transfer.

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

# Durham VAMC: Research Protocol Guidance

## **Data Analysis and Statistical Considerations**

Describe statistical tests and provide a detailed analysis plan for the protocol. Describe the interim analysis plan, if applicable.

## **References**

Provide references, if applicable.

# Durham VAMC: Research Protocol Guidance

## Appendix A: Expedited Review of Research

The categories of research that may be reviewed by the IRB through the expedited review procedure include research activities that present no more than minimal risk to human subjects **AND** involve procedures listed in one or more of the specific categories listed below.

The expedited review procedure is not to be used when identification of the subjects or their responses would reasonably place them at risk of criminal or civil liability; be damaging to the subjects' financial standing, employability, insurability, or reputation; or be stigmatizing, unless reasonable and appropriate protections are implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal. The IRB must apply the standard requirements for informed consent (or its waiver, alteration, or exception) to all studies that undergo expedited review.

<b>EXPEDITE CATEGORIES</b>
<p><b>1-Drugs and Devices:</b> One of the following must be met:</p> <ul style="list-style-type: none"><li>(1) The research is on drugs for which an IND application is not required.</li><li>(2) The research is on medical devices for which an investigational device exemption (IDE) application is not required; or the medical device is cleared or approved for marketing, and the medical device is being used in accordance with its cleared or approved labeling.</li></ul>
<p><b>2-Blood Samples:</b> Collected by finger / heel / ear stick or venipuncture:</p> <ul style="list-style-type: none"><li>(1) From healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 milliliters (ml) in an 8-week period, and collection may not occur more frequently than two times per week; or</li><li>(2) From other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kilogram (kg) in an 8-week period, and collection may not occur more frequently than two times per week.</li></ul>
<p><b>3-Noninvasive Collection of Biological Specimens:</b> Collected prospectively for research purposes by noninvasive means:</p> <ul style="list-style-type: none"><li>(1) Hair and nail clippings in a non-disfiguring manner.</li><li>(2) Deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction.</li><li>(3) Permanent teeth if routine patient care indicates a need for extraction.</li><li>(4) Excreta and external secretions (including sweat).</li><li>(5) Uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue.</li><li>(6) Placenta removed at delivery.</li><li>(7) Amniotic fluid obtained at the time of rupture of the membrane prior to, or during, labor.</li><li>(8) Supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques.</li><li>(9) Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings.</li><li>(10) Sputum collected after saline mist nebulization.</li></ul>

# Durham VAMC: Research Protocol Guidance

## EXPEDITE CATEGORIES

**4-Noninvasive Collection of Data:** Data must be collected through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves.

(1) Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy.

(2) Weighing the subject.

(3) Testing sensory acuity.

(4) Magnetic resonance imaging (MRI).

(5) Electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, Doppler blood flow, and echocardiography.

(6) Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing, where appropriate, given the age, weight, and health of the individual.

**5-Collected Material:** Research involves:

(1) Materials (data, documents, records, or specimens) that have been collected for any purpose, including previous research; or

(2) Materials (data, documents, records, or specimens) that will be collected solely for nonresearch purposes (such as medical treatment or diagnosis).

**6-Collection of Data From Voice, Video, or Photographs:** Research involves collection of data from voice, video, or photographs.

**7-Group Characteristics, Surveys, Interviews, and Quality Assurance:** Research must be on individual or group characteristics or behavior (including, but not limited to: research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior), or will employ survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. **NOTE:** *Some research in this category may be exempt from the VA regulations for the protection of human subjects (38 CFR 16.101(b)(2) and (b)(3)). This listing refers only to research that is not exempt.*