Part I - Overview Information

Department of Veterans Affairs

Participating Organizations

Veterans Health Administration, Office of Research and Development (VA-ORD)

Components of Participating Organizations

Rehabilitation Research and Development (RR&D) Service, VA-ORD

Title: RR&D SCI Translational Collaborative Consortium – Tool and Model Development

Announcement Type

New

Update: There are no updates relating to this announcement.

NOTICE: Applications submitted in response to this Request for Applications (RFA) must be submitted electronically through Grants.gov (http://www.grants.gov) using the Adobe-compatible version of the SF424 Research and Related (R&R) forms.

This RFA must be used in conjunction with the VA version of the SF424 (R&R) Application Guide available on the VA-ORD **Intranet** site at http://vaww.research.va.gov/funding/electronic-submission.cfm. **NOTE: The instructions in this RFA may differ from, and supersede, the general instructions contained in the VA-SF424 Application Guide.**

Request for Applications (RFA) Number: RX-13-007

For Assistance downloading this or any Grants.gov application package, please contact Grants.gov Customer Support at http://grants.gov/CustomerSupport.

Catalog of Federal Domestic Assistance Number(s)

Not Applicable

Key Dates

Release/Posted Date: September 13, 2012

Letter of Intent Receipt Date(s): Standard dates apply; please see Table 4 in Part II, Section IV.

Opening (earliest submission) Date(s): Standard dates apply; please see Table 4 in Part II, Section IV.

Application Deadline(s): Standard dates apply (see Table 4 in Part II, Section IV).
All new or changed/corrected applications must meet 2 separate deadlines:

1. **Submission and acceptance in Grants.gov on or before 6 p.m. (local time) of the Last Possible Submission Date (submission deadline) in Table 4.**

   AND

2. **Verification by eRA Commons on or before the Verification Deadline in Table 4.**

Applications that miss either deadline will not be accepted for review.

NOTE: Applications accepted by eRA Commons with no errors (with or without warnings) are provided a two-business day examination window to check for errors. The application is automatically verified on the third business day if it is not explicitly rejected (withdrawn) by the signing official (SO) during the 2-day examination window.

Once verified, an application is considered final and no other version will be accepted for review. It is the responsibility of the PD/PI and AOR/SO to check for errors during the 2-day examination window. Do not submit a Changed/Corrected application without "rejecting" (withdrawing) the previous successfully submitted application. If multiple versions are submitted and become verified, all versions may be returned without review.

It is strongly recommended that submissions to Grants.gov be completed by the Down to the Wire Deadline in Table 4 to ensure sufficient time to correct any errors that may be identified by either Grants.gov or eRA Commons.

Any application submitted to Grants.gov after the "Last Possible Submission Date" in Table 4 will cause the verification deadline to be missed; late applications will not be accepted for review.

Peer Review Date(s): Standard dates apply; please see Table 4 in Part II, Section IV.

Earliest Anticipated Start Date(s): Standard dates apply; please Table 4 in Part II, Section IV.

Additional Information: Not Applicable

Expiration Date: December 31, 2020

Additional Overview Content

Executive Summary

This Funding Opportunity Announcement (FOA) will use the non-U.S. Department of Health & Human Services (HHS) Research Project (I21) award mechanism.

- **Purpose.** The Spinal Cord Injury (SCI) Translational Collaborative Consortium (SCI TCC) is an intramural Service Directed Research Program directed towards the development of high-risk, high impact therapies to treat SCI. There are two teams of researchers who lead the consortium. The purpose of this funding announcement is to solicit new applications from VA researchers to support and join the consortium by providing consortium leaders with technological developments that could be developed into novel treatments for SCI. This includes the development of in vitro assays, animal models, bioengineered scaffolds, electrodes and small molecule delivery systems, diagnostics (e.g. imaging), diagnostic imaging tools (e.g. ligands, imaging coils), the identification of biomarkers, and the development of "humanized" outcome measures that can be utilized by the teams. This RFA is specifically directed at **two-year pilot projects.**

  Applications electronically submitted to RR&D through Grants.gov will be peer-reviewed by Scientific Review Group (SRGs) to provide the Director of RR&D with evaluations of the quality of the research proposed and make recommendations on scientific merit, budgets, and funding durations.

- **Mechanism of Support.** This Request for Applications will use the Pilot Project Award (I21) mechanism for investigator-initiated VA research.

- **Funds Available and Anticipated Number of Awards.** Availability of funds is dependent on Congressional appropriation.

- **Eligible Institutions/Organizations.** All VA medical centers with an active research program are eligible. Each VA medical center must be registered as an applicant organization in Grants.gov and eRA Commons before any applications can be submitted.

- **Eligible Project Directors/Principal Investigators (PD/PIs).** The Merit Review Award Program is an intramural program and only funds research conducted by VA-ORD investigators at VA medical centers or VA-approved sites. See Section III.1 for eligibility information.

- **Number of Applications and Funded Awards.** An investigator may submit more than one application to RR&D in any given review cycle; however, an application that is submitted to RR&D may not be submitted concurrently to any other component of VA-ORD (i.e., Biomedical Laboratory Research and Development (BLR&D) Service, Clinical Science Research and Development (CSR&D) Service, or Health Services Research and Development (HSR&D) Service). RR&D will not accept or review an application from an applicant who has an overdue Final Report. Applicants may receive funding for more than one RR&D project.

- **Resubmissions.** For applications that have been reviewed, but not selected for funding, VA-ORD allows the submission of up to two revised (Resubmission) applications. All resubmission applications must include a brief Introduction that addresses the concerns raised in the previous review.

  Resubmission applications that were **previously submitted electronically** must be **marked as "Resubmission" in Box 8** on the SF424 (R&R) Cover Component and the Introduction to the revised Application submitted as an attachment named 01_VA_Intro.pdf. See Section 1 "Introduction to Application" in Table 2 for further details. In Box 4a (Federal Identifier) of the Cover Component, enter only the 2-letter R&D Service designation and serial number of the previously assigned application/award number (e.g., RX123456); **do not** include any other portion of the number (e.g., 1 I21, -A1 or –A2).

  See the VA F-424 Application Guide for instructions on submitting a **Changed/Corrected Resubmission** application. Failure to follow these instructions may result in the application being removed from review.

- **Renewals.** Pilot Awards are **not** renewable.
- **Number of PD/PIs.** Only one PD/PI may be designated in the application.
- **Application Materials.** See Section IV.1 for application materials.
- **General Information.** For general information on SF424 (R&R) Application and Electronic Submission to VA-ORD, see http://vaww.research.va.gov/funding/electronic-submission.cfm.

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Part II - Full Text of Announcement

Section I. Funding Opportunity Description

1. Research Objectives

Background: The Spinal Cord Injury Translational Collaborative Consortium is a team-oriented approach to develop therapies to treat spinal cord injury (SCI). Two research teams will lead the consortium in the development of novel therapies towards this goal. One team will focus on the screening of genes following injury while the other team will focus on remyelination and functional imaging strategies using PET. This RFA requests applications for pilot projects intended to develop assays, animal models, devices or technologies for the delivery of therapeutics, development of "humanized" outcome measures, bioengineered scaffolds to support cell transplantation, identification of biomarkers of regeneration/sprouting, biocompatible electrodes and tools that support imaging of the spinal cord. Successful projects will be incorporated into therapies to be tested by the lead teams.

"Axonal Regeneration after SCI": This project will identify, test and support potential clinical development of new strategies for axonal regeneration in the adult central nervous system. This work is planned as a collaborative effort among several laboratories. Work will begin by discovering which genes are most important in supporting nerve regeneration, using gene array studies in targeted CNS regeneration models. Newly identified genes will then be tested in an in vitro neurite outgrowth assay using PNS and CNS neurons. The most potent candidates will be translated into an animal model of CNS axonal regeneration, using spinal cord injury as a test system. In addition to testing individual gene candidates, combination treatment of these most promising approaches to axon regeneration will be tested to determine whether combination therapies are more effective than solitary therapies. The lead candidates from these animal studies may then undergo testing in non-human primate models as a prelude to potential human clinical trials in spinal cord repair.

"Remyelination and Imaging of the Injured Spinal Cord": This project will focus on remyelinating injured and regenerating axons by transplantation of human mesenchymal cells (hMSCs) and functional imaging strategies using PET. Transplantation of a number of cell types including hMSCs leads to improved functional outcome in spinal cord injury (SCI). The transplanted cells can produce trophic factors to provide for neuroprotection, stimulation of local axonal sprouting and they can either remyelinate axons directly or stimulate endogenous remyelination. Moreover, small molecule infusion to block growth inhibitory proteins has been demonstrated to increase axonal growth responses and improve behavioral responses. An important component of the program will be to utilize Positron Emission Tomography (PET) to visualize the raphespinal pathway; a pathway important in locomotion and one that shows plasticity after SCI. Ligands for serotonin reuptake sites are available, and [^{11}C]AFM shows highly selective binding to serotonin transporters (5HTT) in vivo. Raphespinal axons using PET imaging at various times post-SCI in this existing non-human primate (NHP) SCI group will be

studied. A second component of the studies involves overcoming inhibition of regeneration by blocking the Nogo-66 receptor. The efficacy of a soluble human Nogo 66 inhibitor (NgR1(310)ecto-Fc) in combination with intravenous delivery of hMSCs in functional recovery of dexterous hand movements in a C5/C6 spinal cord hemisection in the NHP will be examined. There will be validation of the use of PET imaging for raphespinal tract sprouting initially in rodents and in the NHP. The ultimate objective is to develop novel therapeutic approaches with novel in vivo imaging methodologies of axonal regeneration that could be applied to human clinical studies in SCI.

Scope of the Program: This RFA is directed at the development of novel tools and technologies that will **assist** the lead teams in therapy development. No basic/mechanistic Aims may be included in the research plan.

Non-exempt human studies are outside of the scope and usually may not be included. RR&D does recognize that in some cases human studies are required during the pre-clinical development of tools (e.g. imaging) to identify a patient population that is appropriate for future interventional studies. In these circumstances applications that involve human subjects may be submitted if the proposal does not include clinical interventions. The proposed research must include safely monitoring study participants and must be performed appropriately within the time constraints of the two-year award term.

This RFA is intended to encourage projects that provide tools and resources for therapy development that can be utilized by the research teams.

Possible goals of such projects include, but are not limited to:

- Development of assays that permit the preliminary screening of candidate therapeutics (i.e. promotion and inhibition of axon outgrowth). These include biochemical, cellular and modified model organisms as well as electrophysiological or behavioral recording devices. Assays that can be used for high throughput screening are particularly encouraged.
- Development of animal models that permit further evaluation of candidate therapeutics and/or toxicology studies. Examples include genetically modified animals and models that recapitulate critical features of SCI, that is, models that mimic severe contusion injury to the cervical spine.
- Development of tools and technologies that can be used to enhance therapy development. Examples include novel gene therapy vectors, genetically modified cells, in-dwelling drug delivery devices, biodegradable drug delivery systems, bioscaffolds, microstimulators and microelectronic recording devices. These tools or technologies should overcome existing obstacles to treatment and be capable of being directly applied to repair, or stimulate the repair of the injured spinal cord to, or adapted for, the delivery of potential therapeutics.
- Development of novel imaging techniques and imaging tools that will provide non-invasive visualization of regenerating fibers. Possible techniques and tools include

DTI/fMRI, myelin water imaging, PET, novel PET ligands, and imaging coils. In addition, imaging methods that would assist in the placement of microinjection devices for the delivery of cells, drug delivery systems and gene therapy is also encouraged.

- Development of "humanized" outcome measures for non-human primates. Examples include clinically relevant functional outcomes that can be tested in non-human primates (e.g. Arm Motor Activities Test). Non-human primates will be trained to perform similar tasks that will be tested in human patients to ensure clinical relevance of the task.
- Development of microinjection devices for the delivery of cell, gene therapy and biopolymer drug delivery systems.

This RFA encourages use of the core measures of the NINDS Common Data Elements appropriate for the outcome measures used in the research plan (see: http://www.commondataelements.ninds.nih.gov.) For studies addressing pain outcomes, please refer to the NIH PROMIS site (http://www.nihpromis.org/) for data elements.

Investigators are strongly encouraged to consult VA RR&D program staff to determine if the technology or tool falls within the mission of the SCI Translational Collaborative Consortium. This early contact will also provide an opportunity to clarify the applicant's understanding of program goals and guidelines, including the scope of projects within the program.

Applications electronically submitted to RR&D through Grants.gov will be peer-reviewed by Scientific Review Groups (SRGs) to provide the Director of RR&D with evaluations of the quality of the research proposed and make recommendations on scientific merit, budgets, and funding durations (please see RR&D VHA Handbook 1203.1 for additional information regarding the Merit Award Program).

Section II. Award Information

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1. Mechanism of Support

This Request for Applications (RFA) will use the Pilot Project Award (I21) mechanism for investigator-initiated VA research.

This RFA uses "Just-in-Time" information concepts.

2. Funds Available

Budget of Merit Review Awards: Because the nature and scope of the proposed research will vary from application to application, it is anticipated that the size of each award will also vary. Proposed budgets in excess of $100,000/year must be discussed with Dr. Audrey Kusiak, RR&D Scientific Program Manager, at 202-443-5465 or audrey.kusiak@va.gov prior to submission.

Duration of Merit Awards: Pilot study proposals responsive to this RFA will be funded for **up to two years**. A pilot proposal is a new study to establish feasibility or to develop data, a technique, tool, concept or procedure, which is preliminary to undertaking a full Merit Review project.
Cost-of-living adjustments (maximum of 3% per year) may be included for all VA-salaried personnel. Cost-of-living adjustments are not permitted for any other budget category or for personnel on an IPA. Cost-of-living adjustments may not be used to exceed the annual budget caps.

Note: RR&D will no longer provide funds to support travel to scientific meetings. Only travel costs for accomplishing any part of the proposed specific aims should be included in the budget.

Section III. Eligibility Information

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1. Eligible Applicants

1.A. Eligible Institutions

Applications may be submitted from any VA medical center with an active research program. **Documentation of support for the application from the Medical Center Director must be included as a separate attachment.** Applications submitted without such documentation may be administratively withdrawn. See Item 8 "Director's Letter" in Table 2 for details on meeting this requirement. A separate approval letter from the R&D Committee is no longer required for submission.

1.B. Eligible Individuals

Determinations regarding eligibility are made by individual services within VA-ORD. The general policy for eligibility to receive research support from VA-ORD is described in VHA Handbook 1200.15.

The RR&D Merit Review Award Program is an intramural program to fund research conducted by VA-salaried investigators at VA medical centers or VA-approved sites. Each application must have at least one PD/PI who is eligible to submit an application

To be eligible to submit a Merit Review application to RR&D, the PD/PI must have at least a 5/8ths time VA appointment **at the time the award is funded** (refer to VHA Handbook 1200.15)**.** Additionally, the PD/PI shall hold a MD, PhD, or equivalent doctoral degree in a medical, biological, or behavioral science.

2. Cost Sharing or Matching

Not Applicable

3. Other—Special Criteria

3. A. Location of Research Space

It is expected that the PD/PI and VA co-investigators will perform all of the funded research in VA space or VA leased space. If any portion of the proposed work will be carried out in laboratory space assigned to (i.e., controlled by) a PD/PI or VA co-investigator/collaborator at any other location(s), a waiver to perform the research off-site must be obtained **prior to submitting the application** (refer to VHA Handbook 1200.16).

Standard due dates apply; please see Table 4 in Part II, Section IV. Guidelines for submitting an application for an off-site waiver are described in the VHA Handbook 1200.16, VA Off-site Research Handbook. A copy of the approval letter for the off-site waiver must be included in the Letters of Support.

Although the use of VA leased space does not require an off-site waiver, VA-ORD must approve a plan for local VA oversight of the research activities performed in the leased space (refer to VHA Handbook 1200.16).

All performance sites (VA and non-VA) must be included in the Project/Performance Site Locations component of the SF424 application package.

3. B. Duplicate Submissions

An application submitted to RR&D may not be concurrently submitted to any other VA-ORD Service (BLR&D, CSR&D, or HSR&D).

Section IV. Application and Submission Information

For a completed SF424 (R&R) application package to be submitted, a one-time institutional registration is required for each VA medical center at both:

- Grants.gov (http://www.grants.gov/GetStarted) and
- eRA Commons (http://era.nih.gov/ElectronicReceipt/preparing.htm)

In addition, the PD/PI named in Box 14 on the SF424 (R&R) Cover Component must be individually registered in the NIH eRA Commons.

- In the case of multiple PD/PIs, all PD/PIs must be registered in the eRA Commons prior to the submission of the application.
- A PD/PI who is also an Authorized Organization Representative/Signing Official (AOR/SO) must have separate Commons accounts for each role.
- If the applicant has a PD/PI role and an Internet Assisted Review (IAR) role, however, both roles should exist under one Commons account.
- All PD/PIs at the applicant VA medical center must be affiliated with that organization. PD/PIs located at another VA medical center need not be affiliated with the applicant

organization, but must be affiliated with their own organization to be able to access the Commons.

- This registration/affiliation must be done by the AOR/SO or their designee who is already registered in the Commons.

Both the PD/PI(s) and AOR/SO need separate accounts in the NIH eRA Commons since both are authorized to view the application image.

Note that if a PD/PI is also an NIH peer-reviewer with an Individual DUNS and CCR (Grants.gov) registration, that particular DUNS number and CCR registration are for the individual reviewer only. **That individual DUNS number should not be used on any SF424 (R&R) application submitted in response to this RFA.**

1. Request Application Information

Applicants must download the specific SF424 (R&R) application forms for this RFA through Grants.gov/Apply. Click on the link to "Download a Grant Application Package" and then enter the RFA number from page 1 of this announcement in the middle box labeled "Funding Opportunity Number." **VA-ORD RFA Numbers cannot be found by using the Grants.gov search engine.**

Note: Only the forms package directly attached to a specific RFA can be used to respond to that RFA. You will not be able to use any other SF424 (R&R) forms (e.g., sample forms, forms from another RFA); although some of the "Attachment" files may be useable for more than one RFA.

Adobe Reader 8.1.1 or higher **is required to open and work on the SF424 (R&R) application forms for this RFA**; version 9.0 or higher is strongly recommended. The full version of Adobe Acrobat is not required (**see the VA SF-424 Application Guide for further information on the use of Adobe Reader and Adobe Acrobat**).

For further assistance downloading the package, contact Grants.gov Customer Support at http://grants.gov/CustomerSupport.

2. Content and Form of Application Submission

Prepare all applications using the SF424 (R &R) application forms for this RFA in accordance with the VA Application Guide SF424 (R&R) found at http://vaww.research.va.gov/funding/electronic-submission.cfm.

The SF424 (R&R) application has several components. Some components are required, others are optional. The forms package associated with this RFA in Grants.gov/Apply includes all applicable components, required and optional. A completed application in response to this RFA includes the data in the following components:

Table 1. Components of a VA-ORD Application

Document	Required	Optional	Instructions*
SF424 (R&R) Cover Component (Applicant Information, Project Title, etc)	✔		Section 4.2
SF424 (R&R) Other Project Information (Abstract, Relevance, Introduction to Revised Application, Specific Aims, Research Plan, Progress Report Publications, Human Subjects, Vertebrate Animals, Biohazards, Letters of Support, Appendices)	✔		Section 4.3
SF424 (R&R) Project/Performance Site Locations	✔		Section 4.4
SF424 (R&R) Senior / Key Person Profile(s) (Biosketches and Current & Pending Support)	✔		Section 4.5
SF424 (R&R) Budget†	✔		Section 4.6
SF424 (R&R) Subaward Budget Attachment Form‡		✔	Section 4.7

*Sections refer to the VA Application Guide SF424 (R&R) found at http://vaww.research.va.gov/funding/electronic-submission.cfm

† Application packages for VA-ORD funding opportunities include only the SF424 (R&R) Budget; modular budgets are not accepted. A budget component must always be submitted.

‡ Subaward Budgets are currently not being accepted for multi-site Merit Review applications. All requested funds must be listed in the main Budget, with a separate explanation and justification for each site on the Budget Justification.

Guidance specific for this RFA:

The instructions in this RFA may differ from, and supersede, the general instructions contained in the VA-SF424 Application Guide.

Unless otherwise noted in this RFA, all instructions contained in the VA-SF424 Application Guide must be followed. Failure to follow instructions may cause delays in submission or withdrawal of applications from review.

SF424 Other Project Information Component

Table 2 below contains descriptions of the required content of the separate files that must be attached to Item 12 "Other Attachments" of the SF424 Other Project Information Component (section 4.3 of the VA-SF424 Application Guide). Templates are available on the ORD Intranet at http://vaww.research.va.gov/funding/electronic-submission.cfm.

For creation of attachments and format specifications, see SF424 Application Guide, Part I, Section 2.3.2 Creating PDFs for Text Attachments and Section 2.6 Format Specifications for Text (PDF) Attachments.

Note: The file names indicated in boldface, italic type in the table below are ***mandatory*** *and may not be changed (unless specifically indicated in the table below). Altered file names will cause warnings to be generated and may result in parts of your application being excluded from the final electronic image that the reviewers receive or for the sections to appear in the wrong order. There are no spaces in the required filenames, only the underscore character.*

Table 2: Other Project Information Component Attachments for Item 12

Attachment and ***Required File Name***	**Instructions**	**Page Limit**
1. Introduction to Application (for Resubmission only) ***01_VA_Intro.pdf***	This attachment must be included for "Resubmissions" of applications **previously submitted through Grants.gov.** Information on resubmission applications can be found in the Executive Summary.	**3**
2. Specific Aims ***02_VA_Specific_Aims.pdf***	State concisely the goals of the proposed research and summarize the expected outcome(s), including the impact that the results of the proposed research will exert on the research field(s) involved. List succinctly the specific objectives of the research proposed, e.g., to test a stated hypothesis, create a novel design, solve a specific problem, challenge an existing paradigm or clinical practice, address a critical barrier to progress in the field, or develop new technology.	**1**
2a. Research Plan ***02a_VA_Research_Plan.pdf***	The Research Plan must include sufficient information needed for evaluation of the project, independent of any other document (e.g., previous application). Be specific and informative. In general, the Research Plan should include the following sections: **Background and Significance** Briefly sketch the background leading to the present application, critically evaluate existing knowledge (i.e., published literature, clinical trials, etc.), and specifically identify the gaps that the project is intended to fill. State concisely the importance and health relevance of the research described in this application by relating the specific aims to the broad, long-term objectives. If the aims of the application are achieved, state how scientific knowledge or clinical	**9** **Total**

Attachment and *Required File Name*	Instructions	Page Limit
2a. Research Plan (cont)	practice will be advanced. Describe the effect of these studies on the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field. Use of drugs should be detailed, including pharmacological and toxicological data as appropriate. For clinical trials, include references to preliminary findings, meta-analysis studies, or other supporting data, if appropriate. **Preliminary Studies** Use this section to provide an account of the PD/PI's preliminary studies pertinent to this application, including his/her preliminary experience with and outreach to the proposed racial/ethnic group members, when relevant. This information will also help to establish the experience and competence of the investigator to pursue the proposed project. For epidemiology research applications, pilot data demonstrating feasibility of obtaining samples and/or data needed for the project must be included, if applicable. Scientific Review Groups generally view preliminary data as an essential part of a research application. Preliminary data often aid the reviewers in assessing the likelihood of the success of the proposed project. **Research Design and Methods** Describe the research design conceptual or clinical framework, procedures, and analyses to be used to accomplish the specific aims of the project. Include how the data will be collected, analyzed, and interpreted. Describe any new methodology and its advantage over existing methodologies. Describe any novel concepts, approaches, tools, or technologies for the proposed studies. Discuss the potential difficulties and limitations of the proposed procedures and alternative approaches to achieve the aims. As part of this section, provide a tentative sequence or timetable for the project. Point out any procedures, situations, or materials that may be hazardous to personnel and the precautions to be exercised. Clearly identify all animal models, cell lines and/or sources of tissue to be used. For epidemiology research applications this section must include: • Description of various comparison groups.	

Attachment and ***Required File Name***	**Instructions**	**Page Limit**
2a. Research Plan (cont)	• Subjects recruitment strategies, if applicable, including control groups. The criteria to be used for subject selection, the criteria for assignments to various study groups, and the number of subjects expected to be recruited each year until the conclusion of the study **should be clearly detailed.** Data describing subject population inclusion/ exclusion criteria at recruiting sites, including number of subjects available, should be provided as evidence of feasibility. • The statistical analysis plan including the statistical approach to the questions being investigated, calculations of sample size, and other comparative measurements should be described. The application also needs to detail how various data measures will be categorized and assessed.	
3. Progress Report ***03_VA_Prog_Report_Pubs.pdf***	Not applicable for applications in response to this RFA.	None
4. Human Subjects ***04_VA_Human_Subjects.pdf*** **All applications requiring an IRB decision on exempt status (even if the decision has already been made) must indicate "Yes" for use of human subjects.**	**This attachment is required if you checked "Yes" for Question 1 on the Other Project Information Component (Are Human Subjects Involved?) A Human Subjects attachment is required for all use of tissue bank or excess pathology material.** This section covers the information regarding the Protection of Human Subjects. In this attachment, the following four headings should be used and fully described. Refer to Parts II and III of the VA Application Guide SF424 (R&R). 1. Risk to Subjects • *Human Subjects Involvement and Characteristics*. Describe the proposed involvement of human subjects in the work outlined. Describe the characteristics of the subject population, including their anticipated number, age range, and health status. Identify the criteria for inclusion or exclusion of any subpopulation. Explain the rationale for the involvement of special classes of subjects, such as pregnant women, prisoners, institutionalized individuals, or others who may be considered vulnerable populations. **Indicate whether all subjects recruited for the study will be Veterans or whether non-Veterans will also be included. Justification must be provided for recruitment of non-Veteran subjects.**	None

4. Human Subjects (cont)	• *Sources of Materials*. Identify the sources of research material obtained from individually identifiable living human subjects in the form of specimens, records, or data. Indicate whether the material or data will be obtained specifically for research purposes, or whether use will be made of existing specimens, records, or data. **Justification must be provided for use of biological samples from non-Veteran subjects.** • *Potential Risks*. Describe the potential risks to subjects (physical, psychological, social, legal, or other) and assess their likelihood and seriousness to the subjects. 2. Adequacy of Protection from Risk • *Recruitment and Informed Consent***.** Describe plans for the recruitment of subjects and the process for obtaining informed consent. Include a description of the circumstances under which consent will be sought and obtained, who will seek it, the nature of the information to be provided to prospective subjects, and the method of documenting consent. ***NOTE:*** *The informed consent document may not be submitted at this time.* • *Protection Against Risk*. Describe the planned procedures for protecting against or minimizing potential risks, including risks to confidentiality and data security, and assess their likely effectiveness. Where appropriate, discuss plans for ensuring necessary medical or professional intervention in the event of adverse effects to the subjects. 3. Potential benefits of research to subjects and others. Discuss the potential benefits of the research to the subjects and others. Discuss why the risks to subjects are reasonable in relation to the anticipated benefits to subjects and others. 4. Importance of knowledge to be gained. Discuss the importance of the knowledge to be gained as a result of the proposed research. Discuss why the risks to subjects are reasonable in relation to the importance of the knowledge that reasonably may be expected to result. In addition, the inclusion of women, minorities and/or children must be addressed. • VA-ORD requires the inclusion of women and minorities, as such any exclusion must be research driven (e.g., prostate-related studies). • Children may not be included in VA-approved research conducted by VA investigators while	

4. Human Subjects (cont)	on duty, or conducted at VA facilities or approved off-site locations, unless a waiver has been granted by the Chief Research and Development Officer. Refer to Part II of the VA-ORD Application Guide SF424 (R&R). This RFA encourages use of the core measures of the NINDS Common Data Elements appropriate for the outcome measures used in the research plan (see: http://www.commondataelements.ninds.nih.gov.) For studies addressing pain outcomes, please refer to the NIH PROMIS site (http://www.nihpromis.org/) for data elements.	
5. Vertebrate Animals ***05_VA_Animals.pdf***	**An attachment addressing the following five key points is required if you checked the box marked "Yes" for Question 2 on the Other Project Information Component (Are Vertebrate Animals Used?)** When research involving vertebrate animals will take place at other performance site(s), provide this information before discussing the five points. Although there is no specific page limitation, be succinct. 1. Provide a detailed description of the proposed use of the animals. Identify the species, strains, ages, sex, and numbers of animals to be used in the proposed work. 2. Justify the use of animals, the choice of species, and the numbers to be used. If animals are in short supply, costly, or to be used in large numbers, provide an additional rationale for their selection and numbers. 3. Provide information on the veterinary care of the animals involved. 4. Describe the procedures (i.e., use of analgesic, anesthetic, and tranquilizing drugs and/or comfortable restraining devices, where appropriate) for ensuring that discomfort, distress, pain, and injury will be limited to that which is unavoidable in the conduct of scientifically sound research. 5. Describe any method of euthanasia to be used and the reasons for its selection. State whether this method is consistent with the recommendations of the Panel on Euthanasia of the American Veterinary Medical Association; if not, present a clear justification.	None
6. Multiple PD/PI Leadership Plan ***06_VA_Multiple_PI.pdf***	**A leadership plan is required if more than one individual is assigned the role of PD/PI in the Key Personnel and Section A of the Budget Component.** ***Non-VA investigators may not be assigned the PD/PI role. The co-PD/PI or co-PI roles are not recognized by eRA; assigning these roles will not allow inclusion***	None

6. Multiple PD/PI Leadership Plan (cont)	***of the Multiple PD/PI Leadership Plan.*** The governance and organizational structure should be described, including communication plans and procedures for resolving conflicts. The shared administrative, technical, and scientific responsibilities for the project should be delineated for each PD/PI. Reviewers may evaluate the Leadership Plan and include it in their scoring deliberations. Investigators should discuss the inclusion of multiple PD/PIs with appropriate RR&D Service staff prior to submission of their application.	
7. Consortium/Contractual Agreements ***07_VA_Agreements.pdf***	This attachment should only be used to describe **existing** consortium or contractual agreements that are relevant to the proposed research; new agreements to perform a portion of the proposed research will not be considered binding to VA. **Do not include IPAs here.**	None
8. Director's Letter ***08_VA_Director_Letter.pdf*** **The required file name for this attachment may generate a warning message from eRA Commons. This warning can be safely ignored.**	A letter of support from the medical center Director must be submitted as a **separate attachment** and must include the following: • A statement that the Director understands the impact of the proposed research on the facility's organization and that he/she endorses the project. • Where the research will be conducted, if any off-site waivers are included with the application, and that the VA space described in the application and necessary support of the VA facility will be available. • If a clinician PD/PI's appointment is to start at the time of funding, the VA medical center Director's memorandum **must** contain a statement indicating that the PD/PI will be given a VA-paid clinical appointment of at least 5/8ths time. • Director's signature and date (must be within the last year) **Applications submitted without this attachment will not be accepted for review.**	None
8a. R&D Committee Letter ***08a_VA_R_D_Committee_Letter.pdf***	Not applicable for applications in response to this RFA.	None
8b. Letters of Support ***08b_VA_Letters.pdf***	Include endorsement memoranda or letters from all individuals confirming their roles in the project and willingness to fulfill the duties described in the application. **If applicable, include copies of the**	None

8b. Letters of Support (cont) **The required file name for this attachment may generate a warning message from eRA Commons. This warning can be safely ignored.**	**approval letters for eligibility, off-site waivers, and/or exceeding budget caps/duration in this attachment.** All memoranda/letters should be scanned and submitted as a single PDF document. Letters must be dated within the last year. Note: Biosketches are to be included in the Senior/Key Person Section, not in Letters of Support.	None
9. Checklist ***09_VA_Checklist.pdf***	Attach a completed copy of the Electronic Submission Checklist. **Check only those items that have been addressed or are applicable.**	None
10, 11, 12. Appendices ***10_VA_Appendix_1.pdf*** ***11_VA_Appendix_2.pdf*** ***12_VA_Appendix_3.pdf*** (additional attachments as needed: same file name format) **If descriptive text is included in an attachment name before the ".PDF" as described in the examples in bold, you will receive a warning message from eRA Commons concerning the attachment name. This warning can be safely ignored.**	**Do not use Appendices to circumvent the page limitations of the Research Plan.** An application that does not observe the stated page limitations will be administratively withdrawn from review. A summary sheet listing all of the items included in the appendix may be included in the first appendix attachment; this is encouraged but not required. Appendices should be named using the following convention in the following order: • Attachment number, starting with 10, then 11, 12, etc. • Underscore • The phrase "VA_Appendix" • Underscore • Appendix number starting with 1, then 2, 3, etc. • Underscore • Brief description of the contents (e.g., Abbreviations, Accepted Manuscripts, Patents) • ".pdf" See examples below. If the first appendix is a list of abbreviations used in the application, the file should be named: **"10_VA_Appendix_1_Abbreviations.pdf."** **New and resubmission applications may include the following materials in the Appendices.** Similar appendix material should be combined within an attachment. For example, please place all accepted, but not yet published, manuscripts in one attachment. • Applicants may submit up to a total of 3 publications as PDF attachments. They may be of the following types: o Manuscripts and/or abstracts accepted for publication but not yet published. Do not include unpublished theses or abstracts/manuscripts that have been	None

10, 11, 12. Appendices (cont)	submitted but not yet accepted for publication. o Manuscripts and/or abstracts published, but a free, online, publicly available journal link is not available. **Published manuscripts and/or abstracts that have a free, publicly available online journal link should no longer be included in the appendix material.** The URL or PMC submission identification numbers should be included along with the full reference in the Bibliography and References cited section, the Progress Report Publication List section, and/or the Biographical Sketch section. o Patents directly relevant to the project. • Surveys, questionnaires, data collection instruments, clinical protocols, and informed consent documents may be submitted as PDF attachments. • Photographs or color images of gels, micrographs, etc., **are not accepted as Appendix material.** These images must be included in the Research Plan PDF and will count toward the 24-page limit. Images embedded in publications are allowed.	

R&R Budget Component

Budget Guidance

It is RR&D's policy to only reimburse salary commensurate with the actual effort expended on the project by the PI (or other study personnel). Furthermore, salary support may be requested *only* for activities that are <u>uncompensated from other sources.</u> Cost-of-living adjustments (maximum of 3% per year) may be budgeted in out years of a project for VA-salaried personnel (no IPAs); all differences in the operating expenses between years must be fully justified. <u>All dollar fields must be rounded to the nearest whole dollar</u>. The table below summarizes specific guidance for budget categories.

Table 3. Unauthorized Budget Items

Personnel	
Physicians (Title 38)	Salary support is not authorized for any VA physician.
Title 38 Nurses or any Clinician (Hybrid Title 38 occupations with clinical responsibilities)	Salary support is not authorized for any Title 38 nurse or any clinician (Hybrid 38 occupations with clinical responsibilities) in VA unless a waiver has been granted by the CRADO. If waived, salary support is allowed only for services beyond usual care.
Clerical support	Clerical support may not be included as study personnel unless the support provided can be justified as necessary to the conduct of the research.

Summer/Graduate students	Not authorized
IPAs	IPAs provide for salary and fringe benefit reimbursements; they do not allow for "overhead" costs. IPAs may not be used for physicians. IPAs may not be used for any individual assigned the PD/PI role. IPAs must be listed under personnel without a requested salary; list the cost of the IPA in the "Other" section of the budget.
Consultants	Limit of $500 per consultation and $2,500 per annum. Physicians may not be paid as consultants.
Contract for Services	Service contracts are used to obtain a deliverable/product from a company or an institution, e.g. service contract with the University of California for statistical analysis of data. You may not contract for clinical services or identify the individual(s) who will provide the service. A non-VA physician may only perform non-clinical work. A detailed description of the services being contracted for, along with the name and credentials of the person(s) who may be providing the services, should be part of the budget justification.
Equipment	
Computers	Computers (and IT expenditures) should not be listed in the budget. However, do itemize these expenditures in the budget justification.
Furniture	Usually provided by the local facility. Must be justified as necessary for the conduct of this research. Justification must account for disposition of previously funded furniture purchases for projects that are terminated.
Medical Equipment	Usually provided by the local facility. Must be required for the conduct of the research project and not be used as part of routine and customary patient care.
Supplies	
Postage	Not authorized, unless special circumstances require other than ordinary mail
Copying	Not authorized
Books, journals, or reprints	Not authorized
Other	
General Administrative costs	Not authorized
Phone costs	Usually provided by the local facility. Special 800 lines may be approved with strong justification.
Construction	Contact ORD for guidance on construction requests
Professional memberships	Not authorized
Patient Incentives	Small amounts of money can be offered as a reimbursement for time and/or travel to participate in a study. The incentive must not, in and of itself, constitute an incentive and must be consistent with IRB and ethics policies.

Personnel (Section A and B): Starting with the Contact PD/PI, list all personnel involved in the project. In the appropriate columns list their names, role in the research proposed, the calendar months effort each will devote to the project, and whether or not salaries are requested.

Assigned project roles in sections A and B must agree with the project roles assigned in the key Personnel component. Requested salaries are to include fringe benefits (use actual rate for "hired" employees; up to 30% for estimated salaries) for all VA-salaried personnel to be paid from RR&D funds. Secretarial salaries are not allowed. Physicians and dentists and, in most cases, nurses may not receive salaries from the medical research and prosthetics appropriation. Physicians and dentists who are not licensed to practice in the United States may request salary, but they must be clearly identified as such in the budget justification section. PD/PIs cannot be paid through Inter-agency Personnel Act (IPA) agreements.

Only calendar months should be used in sections A and B of a VA Budget. To calculate calendar months and requested salary for VA-salaried personnel, or personnel with a joint appointment, use the following table **(use only VA hours spent on the project).**

Hours per 40 hour work week spent on the project	Calendar Months	% hours worked per 40 hour work week*
1	0.3	2.5
5	1.5	12.5
10	3.0	25.0
15	4.5	37.5
20	6.0	50.0
25	7.5	62.5
30	9.0	75.0
35	10.5	87.5
40	12	100.0

*Multiply the full VA salary by this amount to determine "requested salary".

If the PD/PI is a clinician, enter the calendar months that indicate the **actual effort** that the investigator will spend on the research project, but do not request salary.

If the PD/PI is a non-clinician, enter the calendar months that indicate the **actual effort** that the investigator will expend for the research described in this application only.

If any participant in the research is a Research Career Scientist or Career Development Awardee, list the calendar months effort the person will devote to the proposed research, but **do not include salary in the budget**.

All co-investigators, collaborators, and technical staff, whether paid or not, are to be listed in the Section A or B.

Individuals paid through a contract for services or an IPA must be listed with their calendar months effort in the personnel section, but no salary may be requested; all costs for such contracts or IPAs should be listed in lines 8-10 of Section F "Other Direct Costs" of the budget.

Equipment Description (Section C): All major equipment is included in this section. Major equipment is defined as an individual item of property that has an acquisition cost of $5,000 or more. Such equipment consists of relatively permanent, fixed assets that are essential to the completion of the proposed research. When feasible, equipment is to be purchased in the first year of the project. RR&D Service will consider equipment requests in years 2–4 only under unusual circumstances, and if properly justified.

Travel (Section D): Travel costs for accomplishing any part of the proposed specific aims should be included in the project budget and clearly justified in the budget justification section. RR&D will no longer provide funds to support travel to scientific meetings.

Other Direct Costs (Section F):

Materials and Supplies (item 1): Expendable items and small equipment (<&5,000 per item) should be requested as Materials and Supplies.

Consultant Services (item 3): A consultant may not receive a fee of more than $2,500 per year. MD consultants may not receive salary compensation.

ADP/Computer Services (item 4): Do not include IT costs in the Merit Review Budget.

Subawards/Consortium/Contractual Costs (item 5): Do not use a subaward component to delineate the budget for another performance site; all costs must be included in the main budget and a site-by-site breakout provided in the Budget Justification. The costs for all existing consortia or contracts must be totaled and included here.

Other Costs (items 8, 9 and 10): List **service contracts for equipment** utilized only for the proposed research. If the equipment is used by multiple research projects, request a proportionate amount of the service contract. List costs for any **personnel to be paid through an IPA**.

Budget Justification (Section K)

All items in the budget must be clearly justified. This is a single justification for all budget years, so include all justification information for all years and all sites in the same file.

Personnel: Fully explain the role and calendar months effort of the PD/PI and all personnel listed under personnel. Indicate Grade and Step for all VA employees and identify anyone paid through an IPA. Physicians and dentists who are not licensed to practice in the United States

and are requesting salary must be clearly identified as such and justified in this section. If the project has more than one performance site, identify the personnel by site.

Equipment: For each item, justification should include a discussion of why the equipment is needed and why similar existing equipment (if any)—whether in the laboratory, common resource equipment, borrowed, or on loan—cannot be used. Include the cost of maintenance. Patient care equipment purchased for use in the research study must be equipment that is not provided in the customary care of patients. If the project has more than one performance site, identify and justify the equipment needed by site.

Travel: Travel costs for accomplishing any part of the proposed specific aims should be clearly justified.

Other Direct Costs: Justify the costs of any items listed under this budget category.

Materials and Supplies: Itemize expendable supplies in separate categories. Explain how the costs for each category of supplies were derived (e.g., based on the PD/PI's expense history in performing similar research). Small (<$5,000) equipment must be justified. If animals are to be purchased, state the species, cost per animal, and number to be purchased in each year. Include the daily and total charges for Animal Research Facility maintenance of all animal subjects required in the research. If the project has more than one performance site, identify the materials and supplies needed by site.

Consultant Services: clearly explain the involvement of each consultant with the proposed research and state the frequency of consultations.

ADP/Computer Services: <u>Do not include IT costs in the Merit Review Budget</u>. However, planned IT expenditures must be itemized in the Budget Justification attachment in "Section F. Other Direct Costs" of the SF424 R&R Budget Component using the Planned IT Expenditures Table format below. Unusual requests should be accompanied by a vendor quote and a strong justification. Shared network charges are not authorized. If the project has more than one performance site, identify planned IT expenditures by site.

Planned IT Expenditures Table				
Category	Type	Amount Year 1	Amount Year 2	Amount Year 3
Hardware	Purchased			
	Leased			
	Services			
Software	Purchased			
	Leased			
	Services			

Telecommunications	Purchased			
	Leased			
	Services			
IT Supplies and Materials	Purchased			
	Leased			
	Services			
IT Personnel (personnel on a 2210 Position Description)				
	TOTAL			

SPECIAL INSTRUCTIONS

Applications Involving a Single Institution: When all PD/PIs are within a single institution, follow the instructions contained in the SF424 (R&R) Application Guide. **Be sure to include all requested funding periods in the Budget Component.**

Applications Involving Multiple Institutions: When multiple VA medical centers are involved, the submitting VA is considered to be the primary performance site. Budget requests for all sites must be "rolled-up" into the main budget. **Do not use the Subaward Component to submit a separate budget for each site**.

3. Submission Dates and Times

3.A. Submission, Review, and Anticipated Start Dates

See Table 4 below.

Deadlines. Avoid delays and misunderstandings by reading and following the instructions carefully. Table 4 contains deadlines for Merit Review Award Program applications. Depending on the investigator's particular circumstance, requests for off-site waiver, eligibility determination, acceptance into the intramural program, or approval to exceed budget limits may be needed. The Office of the ACOS for R&D or RR&D Scientific Review Administrators can help determine which approvals may be required.

Table 4. Deadline*, Review, and Award Dates

SUBMISSION CYCLES:	CYCLE I (WINTER)	CYCLE II (SPRING)	CYCLE III (SUMMER)	CYCLE IV (FALL)
Deadline for submitting Letter of Intent and Waiver requests (eligibility, off-site research, or exceeding duration/budget caps). Applicants are strongly encouraged to submit waiver requests early to allow sufficient time for processing. Applications submitted without the necessary approvals will be returned without review.	**November 1**	**February 1**	**May 1**	**August 1**
First day to submit Merit Review Award applications (to Grants.gov)	**November 15**	**February 15**	**May 15**	**August 15**
Down to the Wire Deadline (to Grants.gov) – after this date the 2-day correction window cannot be used	**5 business days prior to the Verification Deadline**			
Last Possible Submission Date (Submission Deadline to Grants.gov) – assumes no errors (Grants.gov or eRA) will be identified or need to be corrected **WARNING:** If you submit an application on the Submission Deadline above and errors identified are by either Grants.gov or eRA Commons there may not be enough time to fix the errors, resubmit, and have the application received and verified by eRA. If your application is accepted by eRA with no errors, **do not withdraw** the application during the 2 business day examination window unless there is sufficient time to resubmit a changed/corrected application by this submission deadline. **Changed/Corrected application submitted after this deadline will not be accepted for review.**	**3 business days prior to the Verification Deadline**			
Verification‡ Deadline (in eRA) **Once verified, an application is considered final and no other version will be accepted for review.**	**December 15**	**March 15**	**June 15**	**September 15**
REVIEW AND AWARD CYCLES:	**CYCLE I (WINTER)**	**CYCLE II (SPRING)**	**CYCLE III (SUMMER)**	**CYCLE IV (FALL)**
Scientific Merit Review	March	June	August	November
Administrative Review	March - April	June - July	August - September	November - December
Earliest Project Start Date Note: VA-ORD R&D Services may not always be able to honor the requested start date of an application; therefore, applicants should make no commitments or obligations until confirmation of the start date by the awarding service.	June	September	November	February

*If the deadline falls on a weekend or Federal holiday, the due date is the next business day.

‡Verification occurs 2 business days after receipt of an application with no errors or only warnings.

3.A.1. Letter of Intent

A letter of intent is required for each review round, including resubmissions and revisions. See Table 4 above. Instructions for Submitting a Letter of Intent are available on the RR&D website at http://www.rehab.research.va.gov/.

3.B. Submitting an Application Electronically

To submit an application in response to this RFA, applicants should access this RFA via http://www.grants.gov/applicants/apply_for_grants.jsp and follow steps 1–4. Note: Applications must be submitted electronically.

3.C. Application Processing

All new or changed/corrected applications must meet 2 separate deadlines:

1. **Submission and acceptance in Grants.gov on or before 6 p.m. (local time) of the Last Possible Submission Date (submission deadline) in Table 4.**
   AND
2. **Verification by eRA Commons on or before the Verification Deadline in Table 4.**

Applications that miss either deadline will not be accepted for review.

NOTE: Applications accepted by eRA Commons with no errors (with or without warnings) are provided a two-business day examination window to check for errors. The application is automatically verified on the third business day if it is not explicitly rejected (withdrawn) by the signing official (SO) during the 2-day examination window.

Once verified, an application is considered final and no other version will be accepted for review. It is the responsibility of the PD/PI and AOR/SO to check for errors during the 2-day examination window.

It is strongly recommended that submissions to Grants.gov be completed by the Down to the Wire Deadline in Table 4 to ensure sufficient time to correct any errors that may be identified by either Grants.gov or eRA Commons.

New or Changed/Corrected applications submitted to Grants.gov and accepted after the "Last Possible Submission Date" in Table 4 will cause the verification deadline to be missed; late applications will not be accepted for review.

Once an application has been successfully submitted through Grants.gov, any errors have been addressed, and the assembled application has been created in the eRA Commons, the PD/PI and the Authorized Organization Representative/Signing Official (AOR/SO) have 2 business days to view the application image.

- During the 2-day examination window the PD/PI and AOR/SO should determine whether any warnings should be addressed or any other corrections need to be made. Please remember that some warnings may not be applicable or may only need to be

addressed after application submission (i.e., JIT). Warnings do not stop further application processing. If eRA Commons identifies errors in an application submitted to Grants.gov, it will be rejected.

- If warnings or other problems identified during the 2-day examination window need to be addressed, **the SO must reject (withdraw) the application before a Changed/Corrected application can be submitted to Grants.gov**. **All Changed/Corrected applications must be submitted to Grants.gov by the stated submission deadline**.
- If everything is acceptable, no further action is necessary. The application will automatically become verified on the 3rd business day. **Once an application becomes verified it is considered final and no changed/corrected applications will be accepted for review.**
- VA-ORD will not penalize the applicant for an eRA Commons or Grants.gov system issue. However, unless there is documentation of a processing error at either Grants.gov or eRA Commons, applications that fail to meet either the submission or verification deadline will not be accepted for review. **In such cases, prior approval will be required for late submission. The Program Analysis and Review Manager, Tiffany Asqueri (tiffany.asqueri@va.gov), must be notified of any system errors prior to the submission deadline (for Grants.gov issues) or the verification deadline (for eRA issues).**
- There will be an acknowledgement of receipt/acceptance of applications from Grants.gov and eRA Commons. The submitting AOR receives the Grants.gov acknowledgment. The AOR/SO and the PD/PI receive Commons acknowledgments. Information related to the assignment of an application to a Merit Review Panel is also in the Commons. **Note: Since email can be unreliable, it is the responsibility of the applicant and Signing Official(s) to check periodically on the application status in Grants.gov and eRA Commons to confirm receipt and/or acceptance of the application.**

Upon receipt, applications will be evaluated for completeness by the RR&D Program Review staff. **Incomplete applications will not be reviewed.**

No additional or replacement information will be accepted after submission of the application, unless requested by the Program Review staff. The only exceptions are official letters of acceptance for publication of manuscripts submitted by the PD/PI. These may be sent by e-mail to the Program Analysis and Review Manager (Tiffany Asqueri; tiffany.asqueri@va.gov) at any time.

VA-ORD will not accept any application in response to this RFA that is essentially the same as one currently pending initial merit review unless the applicant withdraws the pending application. VA-ORD will not accept any application that is essentially the same as one already reviewed. This does not preclude the submission of an application already reviewed with substantial changes, but such application must include an "Introduction" (3 pages

maximum) addressing the previous critique. Note such an application is considered a "resubmission" for the SF424 (R&R).

4. Intergovernmental Review

Not Applicable

5. Funding Restrictions

Not Applicable

6. Other Submission Requirements

PD/PI Credential (e.g., Agency Login)

VA-ORD requires the PD/PI(s) to fill in his/her Commons User ID in the “PROFILE – Project Director/Principal Investigator” section, “Credential” log-in field of the “Research & Related Senior/Key Person Profile” component.

In addition, the investigator profile (Page 18) in ePromise must be completed (including the Commons ID) for all PD/PIs.

Organizational DUNS
The applicant organization must include its DUNS number in its Organization Profile in the eRA Commons. This DUNS number must match the DUNS number provided at CCR registration with Grants.gov.

Appendix Materials
Applicants **must** follow the specific instructions on Appendix materials as described in the VA-ORD Application Guide SF424 (R&R).

Plan for Sharing Research Data

Not Applicable

Sharing Research Resources

Not Applicable

Section V. Application Review Information

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1. Criteria

Only the review criteria described below will be considered in the review process.

2. Review and Selection Process

Overview

Applications submitted in response to this RFA will be reviewed through a two-tier system. The first level of review will be performed by a Scientific Review Group (SRG) composed of scientists who have expertise in relevant scientific disciplines and current research areas. The purpose of the SRG is to evaluate the scientific and technical merit of applications. The SRG does not make funding decisions.

The second level of review will be performed by RR&D, based not only on considerations of scientific merit (as judged by the SRGs), but also on the relevance of the proposed study to the mission, programs, and priorities of VA-ORD and RR&D. Final funding decisions are made at the discretion, and approval, of the Director RR&D.

Discussed and Non-discussed Applications

The initial scientific peer review of research applications may include a process in which only those applications deemed by the reviewers to have the highest scientific merit, potentially the better half of the applications under review, will be discussed and assigned an impact score at the SRG meeting. Applications in the lower half are reviewed by SRG members but they are not discussed or scored at the SRG meeting. This process allows the reviewers to focus their discussion on the most meritorious applications.

Before the SRG meeting, each review assigned to an application will provide a preliminary score for that application based on the review criteria described below. The preliminary scores will be used to determine which applications will be discussed.

Scoring

SRG members are instructed to evaluate research applications by addressing the review criteria described below. For each application that is discussed, a final global impact score will be given by each eligible committee member (without conflicts of interest) following the panel discussion. Each member's global score will reflect his/her evaluation of the overall impact of the project in its entirety, rather than an arithmetic formula applied to the reviewer's evaluation of each criterion. VA-ORD uses a scoring scale of 1.o to 5.0; the final impact score for each discussed application will be determined by calculating the arithmetic average of all the eligible members' scores, and multiplying the average by 100. RFAs for different types of funding opportunities may have different and/or additional review criteria.

All applicants will receive a written "**Summary Statement,**" which contains the Program Description/Abstract and Project Narrative (Relevance) sections from the submitted application, all of the reviewers' pre-meeting written comments, and a roster of the review meeting participants.

For applications discussed by the review panel, the Summary Statement will also include a summary of the members' discussion during the review meeting, the final impact score, recommendations of the review panel, and administrative notes of special considerations.

Research Project Evaluation Criteria

Significance: Does this study address an important Veterans' health problem? If the aims of the application are achieved, how will scientific knowledge or clinical practice be advanced? What will be the effect of these studies on the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field?

Approach: Are the conceptual or clinical framework, design, methods, and analyses adequately developed, well integrated, well reasoned, and appropriate to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternative tactics?

Innovation: Is the project original and innovative? Does the project challenge existing paradigms or clinical practice; address an innovative hypothesis or critical barrier to progress in the field? Does the project develop or employ novel concepts, approaches or methodologies, tools, or technologies for this area?

Investigators: Are the investigators appropriately trained and well suited to carry out this work? Is the work proposed appropriate to the experience level of the PD/PI and other researchers? Does the investigative team bring complementary and integrated expertise to the project (if applicable)?

Environment: Does the scientific environment in which the work will be done contribute to the probability of success? Do the proposed studies benefit from unique features of the scientific environment or subject populations, or employ useful collaborative arrangements? Is there evidence of institutional support?

Feasibility: Is there sufficient evidence to determine that the proposed studies can be successfully completed? Is there sufficient evidence for successful recruitment and enrollment of subjects, if applicable, availability of animal models, attainment of samples and/or data, etc.?

2.A. Additional Review Criteria

In addition to the above criteria, the following items will continue to be considered in the determination of scientific merit and the impact score:

***Resubmission Applications*:** Are the responses to comments from the previous scientific review group adequate? Are the improvements in the resubmission application appropriate?

***Protection of Human Subjects*:** SRGs will also evaluate the proposed use of human subjects and protections from research risk relating to their participation according to the following criteria: (1) Risk to subjects; (2) Adequacy of protection against risks; (3) Potential benefits of the proposed research to the subjects and others; (4) Importance of the knowledge to be gained; and (5) Data and safety monitoring for clinical trials.

***Inclusion of Women, Minorities, and Children*:** When human subjects are involved in the proposed clinical research, the SRG will also evaluate the proposed plans for inclusion of minorities and members of both sexes/genders, as well as the inclusion of children in clinical research. **Research involving children is restricted and must not be conducted by VA investigators while on official duty or at VA or approved off-site facilities unless a waiver has been granted by the Chief, Research and Development Officer.**

If such a waiver is approved, the involvement of children as subjects in research must be in compliance with all applicable Federal regulations pertaining to children as research subjects (see VHA Handbook 1200.5, Appendix D).
NOTE: Congressionally-mandated research programs that involve children are exempt from this policy

***Vertebrate Animals*:** The SRG will evaluate any proposed involvement and protection of vertebrate animals for the following: (1) detailed description of the proposed use of the animals; (2) justification for the use of animals and for the appropriateness of the species and numbers proposed; (3) adequacy of proposed veterinary care; (4) appropriate procedures for limiting pain and distress to that which is unavoidable; and (5) appropriate of methods of euthanasia.

***Biohazards*:** If materials or procedures are proposed that are potentially hazardous to research personnel and/or the environment, determine if the proposed protection is adequate.

2.B. Additional Review Considerations

Budget and Period of Support: The appropriateness of the proposed budget and the requested period of support in relation to the proposed research may be assessed by the reviewers. The impact score should not be affected by the evaluation of the budget.

2.C. Sharing Research Data

Not Applicable

2.D. Sharing Research Resources

Not Applicable

2.E. Disapproved Applications

An application may be disapproved if the SRG determines that the proposed studies are unethical or are unlikely to yield useful information.

- Applications that are disapproved are not given a numerical score and may not be resubmitted.
- Studies disapproved for ethical considerations may not be carried out in VA space, with VA resources, even if the project is funded by another agency

2.F. Appeals

The appeals process is intended to ensure that the scientific review of all applications is fair and equitable. It is not intended as a means to resolve differences in scientific opinion between the

applicant and the reviewers, to adjust funding decisions, or to circumvent the peer review process.

The basis for an appeal and the procedure for submitting an appeal are detailed in the guidance document, Merit Review Appeal Process, found at http://vaww.research.va.gov/funding/docs/Merit-Review-Appeal-Process.doc.

If a PD/PI submits a revised application and an appeal of the previous application is subsequently sustained and funded before the revised application is reviewed, the revised application will be administratively withdrawn. If the revised application receives a fundable score and the appeal is sustained and fundable, the single project rule applies, and only one of the two projects will be funded.

Note: Applicants are encouraged to resubmit their Merit Review while an appeal is under review.

3. Anticipated Announcement and Award Dates

Standard dates apply; please see Table 4 in Part II, Section IV.

Section VI. Award Administration Information

1. Award Notices

After the peer review of the application is completed, the PD/PI will be able to access his or her Summary Statement (summary of discussion and written critiques) via the NIH eRA Commons.

If the application is under consideration for funding, RR&D will issue a notice of intent to award to the PD/PI and the research office. All required "Just-in-Time" (JIT) information will be listed in the VA JIT Document Manager. It is RR&D's expectation, and the PD/PI's and research office's responsibility to move forward with the completion of JIT documents to bring the study into compliance. For a project to remain under consideration for funding, RR&D must receive all JIT items via the VA JIT Document Manager within 180 days of the notice of intent to award.

2. Administrative and National Policy Requirements

Research Integrity. RR&D is committed to the highest standards for the ethical conduct of research. Maintenance of high ethical standards requires that VA medical centers and investigators applying for, and receiving, Merit Review Awards have appropriate procedures to preclude the occurrence of unethical research practices. All research data must be retained for 5 years after completion of a research project.

The PD/PI and others associated with the research must subscribe to accepted standards of rational experimental research design, accurate data recording, unbiased reporting of data, respect for the intellectual property of other investigators, adherence to established ethical codes, legal standards for the protection of human and animal subjects, and proper management of research funds.

Deliberate falsification or misrepresentation of research data will result in withdrawal of an application, possible suspension or termination of an award, and potentially, suspension of the investigator's eligibility to submit applications to RR&D.

Acknowledging VA Research Support. By accepting a Merit Review Award, the PD/PI agrees to properly acknowledge VA affiliation and support in all public reports and presentations (see VHA Handbook 1200.19). **Failure to acknowledge VA affiliation and support may result in termination of the award.**

Intellectual Property Rights. By accepting a Merit Review Award, the PD/PI agrees to comply with VA policies regarding intellectual property disclosure obligations and Federal Government ownership rights resulting from the proposed work (see VHA Handbook 1200.18).

Section VII. Agency Contacts

We encourage scientific/programmatic inquiries concerning this funding opportunity and welcome the opportunity to answer questions from potential applicants.

1. Scientific/Research Contacts:

Inquiries related to Merit Review submission or review should be directed to the Program Analysis and Review Manager. The PD/PI may contact the RR&D Scientific Program Manager, Dr. Audrey Kusiak at 202-443-5765 or audrey.kusiak@va.gov with questions specifically related to scientific issues raised in the summary statement for a reviewed proposal or the scientific content of a proposal to be submitted. The Associate Chief of Staff for Research and Development (ACOS/R&D) should make all other contacts with RR&D staff at VA central office (VACO), including questions relating to budget modifications noted in the summary statement. Contact information for RR&D may be found at http://www.rehab.research.va.gov/staff/index2.html#start .

2. Financial Management Contact(s):

Joann Johnson at jo.johnson@va.gov

Reminder: To ensure a timely response, all questions concerning electronic submission should be directed to the eRA mailbox in Outlook at: rd-era@va.gov. Telephone calls and/or emails sent to individuals may go unanswered if he/she is out of the office.