Part I - Overview Information

Department of Veterans Affairs

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

Forms of Participating Organizations
Biomedical Laboratory Research and Development (BLRD) Service, VA-ORD

Title
BLRD Merit Review Award for Military Exposure Research Program (MERP) (I01)

Announcement Type
New

Summary of changes incorporated into this Announcement (2/21/2023)

- References to non-clinician eligibility memos were removed from Tables 1 and 2. Non-clinician eligibility is not required to apply to this RFA.

Catalog of Federal Domestic Assistance Number:
64.054

Note:
Hyperlinks direct the applicant to information and resources whenever possible.

- Blue hyperlinks redirect the applicant to other sites within this document and to outside information that is accessible to the public.
- Red hyperlinks are only accessible using the VA intranet environment.

Request for Applications (RFA) Number: BX-23-009

Key Dates
Release/Posted Date: January 25, 2023

Application Deadlines, Submission, Peer Review, and Start Dates: See Table 3.

Expiration Date: December 31, 2023

Application Instructions: Applications submitted in response to this RFA must be submitted electronically by the local VA R&D signing official to Grants.gov using the VA SF424 Research and Related (R&R) Forms (VA-SF424) as described in the SF424 (R&R) Application Guide for VA-ORD (VA-SF424 AG).

This RFA must be used in conjunction with the VA version of the Application Guide SF424 (R&R) available on the VA-ORD Intranet site. The instructions in this RFA may differ from, and supersede, the general instructions contained in the VA-SF424 AG.

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Part II - Full Text of Announcement

Section I. Funding Opportunity Description

1. Research Objectives

BLRD funds preclinical biomedical and behavioral studies of disorders and diseases of importance to the health of Veterans. The BLRD purview includes *in vitro* and *in vivo* studies using tissue cultures, animal models, or human biological samples collected using minimally invasive procedures (blood, urine, buccal swabs) or from tissues acquired without direct contact with subjects (e.g., from tissue banks or pathology material). The VA will not fund studies of human fetal tissue. Applications that seek to administer surveys or questionnaires (e.g. new clinical data collection), or perform medical procedures and treatments (including biopsies) or observational studies should be submitted to the Clinical Sciences R&D Service (CSR&D) RFAs.

Research studies under this Request of Applications (RFA) should focus on key priority areas as outlined in the PACT Act, public law 117-168 and the mission and goals of the Military Exposure Research Program (MERP), see below. Applications under this RFA involving human subject's biological materials must include Veterans who have experienced the impact of toxic military exposures (ME). See link for PACT Act description: https://www.congress.gov/117/plaws/publ168/PLAW-117publ168.pdf

> **MERP Mission Statement**: The VA-ORD Military Exposures Research Program seeks to advance military exposure assessments and to understand the effects of military exposures on Veterans' health outcomes to inform care and policy.
>
> **Military Exposures**: Military Exposures are defined as toxic agents, singly or in combination, incurred through military service (Deployment, Occupation, or Garrison)
>
> **Exposures Assessment**: Exposure assessment refers to identifying and quantifying of toxic agent(s) to which a Veteran was exposed during military service. Exposure assessment may include the development of new methods and/or assays that will directly or indirectly identify an exposure to a toxic agent using biological materials or surrogates.
>
> **Health Outcomes** include changes in health status such as any measurable disease, disability, injury, syndrome, symptom, biological or subclinical marker, organ system function or health state arising from military exposures.

Priority Areas of Military Exposures include:

- Particulate Matter 2.5 μm (PM2.5)
- Burn Pit Exposure
- Per- and polyfluoroalkyl substances (PFAS)
- Radiation (non-ionizing and ionizing, including cosmic radiation)
- Jet Fuels
- Pesticides and Herbicides
- Explosive Ordnance (chemicals)
- Other chemical agents: industrial solvents, polychlorinated biphenyl, depleted uranium, and hexavalent chromium.

** **Exclusion of Military exposures** for this RFA include the below examples. (Contact the MERP Program Manager with specific questions and for guidance.

- Noise
- Traumatic Brain Injury
- Non-Deployment infectious diseases

Particular areas of research interest for Military Exposures (ME) include: **1)** exposure assessment at the individual level and **2)** studies that contribute toward the understanding of ME-induced illnesses, including the etiology, pathobiology, and diagnostic/prognostic biomarker indicators.

1) Exposure assessment at the individual level:

- Identify direct or indirect markers (chemical, metabolites, biosurveillance, biomarkers) indicative of past exposure(s) using biological materials or surrogates. This might include studies that utilize technologies capable of detecting toxic agents or secondary metabolites retained for many years following exposure, or studies that identify persistent or "downstream" changes in biochemical processes in relation to past ME.
- Utilize state-of-the-art technologies or develop new methods and/or assays that will directly or indirectly identify/measure an exposure using biological materials or surrogates.
- Validation studies to test strength of evidence in the condition of interest for effectiveness.
- Identify and characterize epigenetic signatures/markers of ME.
- Determine the usefulness of blood spots as a resource for exposure assessment or biomarker validation.
- Utilize the DOD serum repository as a resource for validation studies.
- Using the Million Veterans Program (MVP) identify biological epigenetic signatures linked to ME.
- Develop alternatives to animal testing using new alternative approaches (NAM) such as, computer modeling or artificial intelligence (AI) is encouraged.

2) Health Outcomes of ME-induced illnesses:

- Identify rates of diagnosed neurological diseases (including multiple sclerosis, Parkinson's disease, amyotrophic lateral sclerosis, and/or brain cancers) as well as central nervous system abnormalities in Veterans with risk of ME during service deployment, occupational, and/or in Garrison using retrospective epidemiological approaches.
- Assess cancer incidence, prevalence, and mortality rates in Veterans with ME. Such retrospective epidemiological studies should maximize the use of cancer registries and other relevant sources, data, and approaches, and should have sufficient sample sizes to account for relatively rare cancers.
- Identify, characterize, and validate specific pathophysiological mechanisms or diagnostic/prognostic indicators using state-of-the-art technologies, preclinical rodent/transgenic models, and biospecimens underlying ME-induced illness.
- Assess accelerated aging outcomes induced by ME.
- Elucidate mechanisms of ME-induced cancers (including rare cancers such as male breast cancer) and other diseases.
- Evaluate and elucidate the effects of ME on reproductive health.

- Evaluate parameters of immune system, central nervous system and autonomic function, hypothalamic-pituitary-adrenal axis, central proinflammatory and inflammatory processes in biological specimens of Veteran cohorts with presumed ME.
- Using the Million Veterans Program (MVP):
    - identify biological and genetic variability, potentially linked to differences in vulnerability to ME and/or treatments, including studies that evaluate associations between ME and genetic polymorphisms and activity levels of enzymes associated with uptake and metabolism.
    - identify ME-induced gene-environmental interactions and affected biological pathways of significance.
- Over sample underserved Veterans including but not limited to women Veterans, racial and ethnic minority Veterans, Veterans with disabilities, and LGBTQ+ Veterans to evaluate ME health disparities.
- Use of alternatives to animal testing using new alternative approaches (NAM) such as, computer modeling or artificial intelligence (AI) is encouraged.

Where applicable, standard sharing and repository banking are regulatory requirements: Applicants will be required to participate in cohort and data- and bio-repository building. Specific language to include cohort recontacting and agreement to share data and biospecimens are required. Projects must use common data elements (where applicable). Pre-submission consultation and future use language to include in the application and/or regulatory documents can be assisted by the ORD MERP Director or staff.

This enumeration should not be interpreted as exhaustive, or as a suggestion that funding preference will be given to studies in a particular category.

Section II. Award Information

1. Mechanism of Support

This RFA will use the VA Merit Review Award (I01) mechanism for investigator-initiated VA research. The Merit Review Award Program is an intramural funding mechanism to support investigator-initiated research conducted by eligible VA investigators at VA Medical Centers (VAMCs) or VA-approved sites. Merit Review Awards are BLRD's principal funding mechanism for preclinical biomedical and behavioral studies of disorders and diseases of importance to the health of Veterans.

Applications electronically submitted to BLRD through Grants.gov will be peer-reviewed by a Scientific Review Group (SRG) to provide the Director, BLRD with an evaluation of the scientific merit of the proposed research including recommendations on budgets, funding durations, and potential ethical concerns. All funding decisions are made by the Director, BLRD.

Before funds are released, all applicable regulatory and research compliance approvals must be obtained locally and submitted to the "Just In Time" (JIT) system. JIT requires the local assurance forms to ensure all VA regulations and policies are met. All JIT requirements must be completed within 180 days of selection to ensure availability of funding. Approval for funding may be withdrawn for applications that fail to clear JIT over 180 days. All Specific Aims of an application must be able to be cleared in JIT. If a portion of the application is not ready for JIT clearance, the funding decision may be rescinded.

2. Application Types Allowed

New: Proposals that have not been previously reviewed or funded by BLRD under this RFA will be accepted as "new" in response to this RFA.

Resubmissions: Submission of up to two revised applications (resubmissions) is allowed if the initial submission is not selected for funding. All resubmission applications must include a brief Introduction that addresses the concerns raised in the previous review. If an application is not funded after two resubmissions it is not eligible to receive funding and any new submission by the PD/PI must contain significantly revised Specific Aims. "New" applications submitted without significantly revised Specific Aims will be withdrawn from review.

Renewals: Funded Merit Review Awards can be renewed by competitive application for an additional project period of up to 4 years. If three attempts to renew an application do not result in a decision to fund, a "New" application must then be submitted.

Refer to the VA -SF424 AG for guidance on how to fill out the VA-SF424 Cover Form for each application type. *Note: Renewal applications that are being resubmitted should be marked as "Resubmission" in Box 8 of the SF424 (R&R) Form.*

3. Multiple Awards and Submissions

An investigator may submit concurrent applications to more than one BLRD RFA. An investigator may not be a PD/PI (either Contact PD/PI or one of multiple PD/PIs) for more than one application to the same RFA per review cycle. An investigator may only have one funded project for each RFA. An investigator may submit applications to a maximum of three RFAs in any given review cycle (combined submissions to BLRD and/or CSR&D). Concurrent awards for supporting multiple projects under different RFAs will only be considered in unusual cases such as exceptionally meritorious research that addresses high priority research areas and current programmatic needs.

Submission of multiple applications with similar subject matter to different BLRD and CSR&D RFAs may result in the applications being assigned to the same SRG; if this occurs BLRD will not entertain requests to move one of the applications to a different SRG.

4. Funds Available

Duration of MERP Awards: MERP Merit Review Awards have durations of three to five years.

MERP Award Budget Cap: The recurring (annual) budget may not exceed $250,000 per year. The first-year budget may include up to an additional $50,000 for equipment and other startup costs (for a total year 1 budget cap of $300,000). The salary for a non-clinician contact PD/PI identified in Box 14 of the SF424 (R&R) Cover Form is excluded from this cap. In an application with multiple PD/PIs, only the Contact PD/PI may have their salary excluded from this cap. A Merit Review Award budget must request at least $50,000 per year.

Applications may only exceed the budget and duration requirements if a copy of the letter of approval for a waiver is included in the Letters of Support section. Rare exceptions to the budget cap and/or maximum duration may be granted prior to application submission for fully justified

and compelling circumstances. Waiver requests must be submitted by the local R&D Office to vhacoblcsrdrev@va.gov. Deadlines for submission are in Table 3.

5. Cost Sharing or Matching Funds

Not Applicable

6. Location of Research Space

All performance sites (VA and non-VA) must be included in the Project/Performance Site Locations Form of the SF424 (R&R) Application package. Provide a detailed description of the institutional facilities and resources available to the project. Specify the campus location (VAMC or affiliate) for each facility and resource cited.

It is expected that PD/PIs will perform VA-funded research within a VA facility or VA-leased space controlled by them. If any of the proposed work will be carried out in non-VA space controlled by a PD/PI or other VA investigator, a waiver to perform the research off-site must be obtained prior to the start of work done in an off-site research space. Work performed in a non-VA collaborator's off-site laboratory or off-site Core Facility does not require an off-site research waiver, except when a VA investigator is the Core Facility Director. If available, a copy of the approval letter for the off-site waiver should be included in the Letters of Support attachment (refer to VHA Program Guide 1200.16).

7. Duplicate Submissions

No portion of the proposed research may be simultaneously submitted to more than one RFA in the same review cycle. Applications submitted to BLRD should not be submitted to any other VA-ORD Service. In cases where it is not clear which Service's purview is the best fit for a particular application, the VAMC research office should seek advice from ORD program staff about where to submit.

Section III. Eligibility Information

1. Eligible Institutions

Applications may be submitted from any VAMC with an active Federal Wide Assurance (FWA) of compliance with the US federal regulations for the protection of human subjects in research.

2. Eligible Individuals

The Merit Review Award Program is an intramural program to fund research conducted by VA-salaried investigators at VAMCs or VA-approved sites. A PD/PI shall hold an MD, PhD, or equivalent doctoral degree in a medical, biological, or behavioral science field. All PD/PIs must have a VA paid appointment of at least 25 hours per week (5/8ths) to receive ORD research funding (VHA Program Guide 1200.15). Contract clinicians are not VA employees.

The VA employment status, including 8^{ths} appointment of each PD/PI must be indicated in the Letter of Support of the Medical Center Director in the application. If a clinician/non-clinician PD/PI does not have a current, 5/8ths VA paid appointment then the Letter of Support from the

Medical Center Director must include a commitment to offer the PD/PI a 5/8ths (or greater) appointment at the VAMC if the application is approved for funding.

The PD/PI must be current with all requirements related to intellectual property (VA invention documents and certifications), submission of annual progress reports (Research Performance Progress Reports (RPPRs)) and Final RPPRs, clinical trials registration, and clinical trials results reporting for existing and previous awards.

VA Career Development Awardees: Investigators with a VA Career Development Award (CDA) may submit an initial Merit Review Award application during the last two years of their CDA award. If needed, up to 2 additional applications (revised or new) may be submitted during the following 3 consecutive review cycles. After the 3rd submission or 3rd consecutive review cycle after the initial submission, whichever comes first, applicants need to follow the normal eligibility rules for submitting applications for Merit Review award funding.

Multiple PD/PIs: The "Contact" PD/PI identified in the VA-SF424 Cover Form will be responsible for all communication between the PD/PIs and VA-ORD. Only individuals assigned the PD/PI role in the Budget Form and the Key Personnel Form are considered as PD/PIs. All PD/PIs must meet the eligibility requirements described above. The inclusion of a non-eligible Co-PI/MPI may lead to the administrative withdrawal of the application. The justification for inclusion of more than one PD/PI must be included in a Multiple PD/PI Leadership Plan and each of the multiple PD/PIs must be assigned the PD/PI role. The terms Co-PD/PI are no longer recognized by eRA or VA-ORD.

Section IV. Application and Submission Information

Several registration processes must be completed by the local R&D Service before submission of an electronic application (see Section 2.2 of the VA-SF424 AG). Applications must be submitted to Grants.gov by the local research signing official (SO). Applicants are highly encouraged to start the submission process well in advance of the submission deadline to ensure it passes the validations performed at Grants.gov and the eRA.

1. Request Application Information

See the VA-ORD Application Guide SF424 (R&R) for step-by-step guidance.

2. Content and Form of Application Submission

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

A summary of the main components required for this application is shown below in Table 1. Table 2 below contains instructions for SF424 Research and Related Forms specific to this RFA. Instructions in Table 2 are in addition to, or supersede, instructions in the VA-SF424 AG as appropriate.

Guidance specific for this RFA:
Unless otherwise noted in this RFA, all instructions contained in the VA-ORD Application Guide SF424 (R&R) must be followed. Failure to follow instructions may cause delays in submission or withdrawal of applications from review.

Research and Related Other Project Information Form
Table 2 below contains descriptions of the required content of the separate files that must be attached to Item 12 "Other Attachments" of the Research and Related Other Project Information Form. For guidance on the creation of attachments and format specifications see the VA-ORD Application Guide SF424 (R&R) on the VA-ORD Intranet at http://vaww.research.va.gov/funding/electronic-submission.cfm.

*Note: The file names for Attachments #1-10 are **mandatory** and may not be changed. Altered file names will cause an error to be generated. Only the descriptor in the file names for Appendices #11, 12, 13… etc., may be changed. Altering any other part of the file name may result in parts of your application being excluded from the final electronic image that the reviewers receive or for the attachments to appear in the wrong order.*

All applications must be self-contained (i.e., without use of URLs or video clips) within specified page limits. Internet website addresses (URLs) and video clips may not be used to provide information necessary to the review. URLs may only be placed in the Biographical Sketch and Bibliography and References Cited attachments.

Table 1. Summary of Required Forms and Attachments

Forms, Attachments, and Templates with Size Limits as Applicable	Required When?	VA-SF424 Instructions
SF424 (R&R) Form	Always	Section 3.2
Project/Performance Site Locations Form	Always	Section 3.3
Research and Related Other Project Information Form:		Section 3.4
Project Summary/Abstract (40 lines of text)	Always	
Project Narrative (10 lines of text)	Always	
Bibliography & References Cited (4 page limit)	Always	
Facilities & Other Resources	Always	
Equipment	Always	
Other Attachments:		
1. Introduction to Revised Application (3 page limit)	Resubmission	
2. Specific Aims (1 page limit)	Always	
2a. Research Plan (14 page limit)*	Always	
3. Progress Report (5 page limit)*	Renewal†	
4. Human Subjects	If Applicable	
5. Vertebrate Animals	If Applicable	
6. Multiple PD/PI Leadership Plan	If Applicable	
7. Consortium/Contractual Arrangements	If Applicable	
8. Signed Director's Letter*	Always	
8b. Letters of Support	If Applicable	
9. Data Management and Access Plan	Always	
10. Financial Disclosure	Always	
Appendices:*		
11. List of Appendix Items*	Always	
12. List of Abbreviations*	Always	
13. SRG Request*	Always	
SF424 (R&R) Senior / Key Person Profile(s)	Always	Section 3.5
SF424 (R&R) Budget	Always	Section 3.7
SF424 Summary Budget Worksheet	Always	Section 3.7

* These sections have special instructions for this RFA that are in addition to or supersede instructions in the VA SF424. See Table 2 below.

† New applications from previous awardees require a progress report. See Table 2 below.

Table 2. RFA Specific Instructions for VA SF424 Forms and Attachments

Form/Attachment Name **Page Limit** ***Required File Name***	**Instructions**
2a. Research Plan **14 Page Limit** *02a_VA_Research_Plan.pdf*	The Research Plan must include sufficient information 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 (e.g., published literature, etc.), and specify the gaps that the project is intended to fill. State concisely the importance and Veteran health relevance of the research described in this application. Relate the specific aims to the broad, long-term objective of improving Veteran health. If the aims of the application are achieved, state how scientific knowledge or clinical practice will be advanced. Additionally, describe the effect of these studies on the concepts, methods, technologies, treatments, services, or preventative interventions that drive the field. **Preliminary Studies** Use this section to provide an account of the PD/PI's preliminary studies pertinent to this application. This information will also help to establish the experience and competence of the investigator to pursue the proposed project. For clinical and epidemiology research applications, pilot data demonstrating the feasibility of obtaining samples, recruiting subjects, and/or data needed for the project must be included, if applicable. **Research Design and Methods** Describe the research design 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. Describe steps that will be carried out to minimize subjective bias (e.g. randomization, experimental and control group matching, blinded assessment of outcomes, etc.). Discuss the potential difficulties and limitations of the proposed procedures and alternative approaches to achieve the aims. As part of this section, provide a timetable for the project. Point out any procedures, situations, or materials

Form/Attachment Name **Page Limit** ***Required File Name***	**Instructions**
	that may be hazardous to personnel and the precautions to be exercised. For animal studies, include estimates of samples sizes, study power, and the statistical methods used to obtain them. Explain how relevant biological variable such as species, strain, sex, developmental stage (age), and weight are factored into the research design and analysis. All animal models, cell lines and/or sources of tissue to be used must be clearly identified and described in this section. <u>Do not</u> repeat the Specific Aims in the Research Plan. <u>Do not</u> include the Progress Report for renewal applications in the Research Plan.
3. Progress Report **5 Page Limit** *03_VA_Prog_Report_Pubs.pdf*	Progress Reports are required for all applications from a PI who has had any VA funding including on-going or completed Merit or Career Development from any VA-ORD Service. Progress Reports are required for all renewal applications.
5. Vertebrate Animals *05_VA_Animals.pdf*	See the VA-ORD Application Guide SF424 (R&R), Attachments for Item 12, for guidance on this document.

Form/Attachment Name **Page Limit** ***Required File Name***	**Instructions**
8. Signed Director's Letter *08_VA_Director_Letter.pdf*	A signed (e-signature accepted) and dated (within the last year) copy of a letter of support from the VAMC Director is required 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. • An explicit statement of where research will be conducted, whether it is in VA space, VA-leased space, or space at the affiliate; that appropriate offsite waivers have been requested, and that the VA space described in the application and necessary support of the VA facility will be available. • If human samples are used, an explicit statement of source of samples. • Current VA employment status of the PI, including 8ths. • If a PD/PI's appointment is to start at the time of funding, the Director's memorandum must contain a statement indicating that the PD/PI will be given a VA-paid appointment of at least 5/8ths time. NOTE: For multiple PD/PI applications where the PIs are at different VAMCs, a letter from each VAMC Director is required. **Applications submitted without this signed letter attachment will not be accepted for review.**
10. Financial Disclosure *10_VA_Financial_Disclosure.pdf*	Provide a clear statement disclosing any financial conflict of interest that each PD/PI may have with the proposed research (e.g., purchase of a device or specialized compound from a company in which the PD/PI has a financial interest). VA researchers with outside consulting, employment, or royalty payment opportunities should disclose those potential opportunities to their local VA facility to ensure compliance with the facility policy on financial conflict of interest. A single page containing "N/A" or "No Disclosures" should be used if there is nothing to disclose.
11, 12, 13… Appendices *11_VA_Appendix_1.pdf* *12_VA_Appendix_2.pdf* *13_VA_Appendix_3.pdf* (additional attachments as needed: same file name format)	**Page Limit: None** See the VA-ORD Application Guide SF424 (R&R), Attachments for Item 12, for guidance on content and naming of files of appendices.

Form/Attachment Name Page Limit *Required File Name*	Instructions
	Appendices must be uploaded in the order in which you wish them to appear in the e-application. To check for the correct ordering of attachments, review the Bookmarks and Table of Contents (ToC) within the final e-application. The first appendix should be a summary sheet listing all of the items included in the appendices; it should be named: **"11_VA_Appendix_1_List of Appendix Items.pdf."** The second appendix should be the alphabetized list of abbreviations used in the application; it should be named: **"12_VA_Appendix_2_Abbreviations.pdf."** The third appendix should be a brief letter stating what panel the PD/PI would like the application assigned to; it should be named: **"13_VA_Appendix_3_SRG Request.pdf"** See the BL/CSR&D Merit Review Panel Purview document for a description of the purview of each of the review panels. Additional appendices can be added using the file name conventions described above. Please refer to the SF424 AG for guidance on allowable appendix attachments.

Summary Budget Worksheet and R&R Budget Form

Budget Guidance
See the VA Application Guide SF424 (R&R), Section 3.7 Summary Budget Worksheet and R&R Budget Form for guidance on budget content for Sections A-L. Both of these forms are mandatory for each application.

Personnel (Section A): For a non-clinician PD/PI enter the calendar months that indicate the actual effort that the investigator will expend for the research described in this application only; salary consistent with their total VA effort may be requested. Describe the PD/PI's contribution to the proposed research, as well as the other activities comprising their total VA effort, in the Budget Justification section.

If the PD/PI is a Research Career Scientist, enter the calendar months that indicate the actual effort that the investigator will expend for the proposed research, but do not include salary in the budget. In the Budget Justification section discuss the investigator's contribution to the proposed research only.

Salary support may be requested only for activities that are uncompensated from other sources, such as the academic affiliate or other funding agencies. Any differences in the calendar months

effort for the work proposed and total VA effort (salary support) must be fully described in the budget justification.

Personnel (Section B): The last row of Section B should include all VA personnel involved in the project, except the PD/PI named in Section A.

Applications with Multiple PD/PIs: When multiple PD/PIs are proposed, only the Contact PD/PI (identified in Box 14 of the SF424 (R&R) Cover Form) is eligible to receive salary above the budget cap. Identification of multiple PD/PIs may not be used to exceed budget caps. Cost of living adjustments for personnel other than contact PD/PI may not cause the budget to exceed the stated cap.

Other Direct Costs (Section F): All Other Direct Costs described below should be totaled and entered in Section F, Line 8 of the R&R Budget Form. Leave all other fields blank in Section F (1-7, 9, and 10).

Equipment Description: Start-up Costs (maximum of $50,000, excluded from the $250,000 budget cap in Year 1) are intended to support the one-time purchase of non-recurring items. Start-up costs are limited to items of major equipment (> $5,000 per item), small equipment (< $5,000 per item), or one-time purchase of transgenic mice for breeding. Start-up costs should be included on the equipment line of the Summary Budget Worksheet and in Section F, Line 8 of the R&R Budget Form.

Start-up costs may not be used for salaries, consumables unique to the first budget period, or advance purchase of recurring items (e.g., experimental animals, glassware, electrodes, antibodies, or tissue culture supplies) to be used beyond the first budget period.
Only start-up costs may be used to purchase items of major equipment (> $5,000 per item). Start-up funds and recurring budget may not be combined to purchase additional or more expensive equipment.

In addition to the required budget justification for equipment, include a separate section for start-up funds requested. Include an itemized list of all items to be purchased with start-up funds, a justification for each item in the list, and the total amount of start-up funds.

Budgets requesting start-up costs that do not meet the above definition will be considered to be in excess of the $250,000 recurring budget cap and the application may not be accepted for review.

Travel: Travel costs for presenting research findings at scientific meetings may not exceed $2000 per year (total, not per individual). Travel costs required to perform the proposed specific aims are permitted if clearly justified in the budget justification section.

Materials and Supplies (item 1): Small equipment items (<$5,000 per item) may be requested as either Materials and Supplies or start-up costs. If requested as start-up costs, include on the equipment line of the Summary Budget Worksheet and Section F, Line 8 of the R&R Budget Form.

3. Submission Dates and Times

Deadlines: Table 3 below contains deadlines for Merit Review Award Program applications.

Renewal of Awards: In order to avoid a funding gap, submission of renewal applications for review one year prior to the award's end date is encouraged. If the submission is approved for funding prior to the end of the current award, the PD/PI may opt for one of the following scenarios: delay the new project start date until the conclusion of the currently funded project; or start the new project at the earliest possible start date, terminating the currently funded project before its conclusion.

Submitting renewal applications more than 1 year prior to the end date is discouraged. If the early submission is approved for funding the PD/PI will have two options: (1) replace the ongoing project with the new Award, losing the remaining time on the currently funded project; or (2) reject the new award and continue the ongoing project. Delaying the start of the new award until the conclusion of the currently funded project is not an option.

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

All new or changed/corrected applications must be submitted and accepted (error-free) in Grants.gov on or before 6 p.m. (local time) of the Last Possible Submission Date (submission deadline) in Table 3.

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 withdrawn by the SO during the examination window.

Errors will stop an application from proceeding in the system and must be addressed. Warnings will not stop your application from moving forward and are addressed at your discretion based on your situation.

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 examination window.

Table 3. Standard Dates for Application Deadlines for 2023

SUBMISSION CYCLES:	Spring 2023	Fall 2023
Deadline for budget cap waiver requests	November 1	May 1
Deadline for requests for Eligibility and/or Acceptance into the Non-Clinician Intramural Research Program	December 1	June 1
First day to submit applications to Grants.gov	February 1	August 1
Deadline to submit to Grants.gov (After this date the full two-day correction window cannot be used.)	March 8	September 7
Last Possible Submission Date (to Grants.gov) **WARNING:** If you submit an application on the Last Possible Submission Date and errors are identified 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 two-business day examination window unless there is sufficient time to resubmit a changed/corrected application by the submission deadline. Changed/Corrected applications submitted after the Last Possible Submission Date will not be accepted for review.	March 10 6:00 pm local time	September 11 6:00 pm local time
Review and Award Cycles:	**CYCLE I (Spring)**	**CYCLE II (Fall)**
Scientific Merit Review	May - June	Nov- Dec
Administrative Review	July - Aug	Jan - Feb
Earliest Project Start Date§	Oct 1	April 1

§BLRD 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.

3.A.1. Letter of Intent

A letter of intent is not required for this funding opportunity.

3.B. Application Processing

The local Research and Development Office (ACOS and/or AO) is responsible for submitting

a notification of any system errors to the eRA mailbox (rd-era@va.gov) prior to the submission deadline (for Grants.gov issues) or validation deadline (for eRA issues).

Upon receipt, applications will be evaluated for completeness. 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 must be sent by e-mail to the Review Mailbox (vhacoblcsrdrev@va.gov).

Applications will be withdrawn from review for administrative non-compliance if they do not adhere to the following:

- All applications must be self-contained (i.e., without use of URLs/hyperlinks) within specified page limits. URLs may only be placed in the Biographical Sketches and Bibliography and References Cited attachments. An eRA system validation provides detailed warning notifications about URLs found within an application. However, you should not rely solely on system validations to ensure a successful submission**. NOTE:** URLs within official documents that cannot be altered, such as letterhead (i.e., Letters of Support attachment) or published articles/manuscripts (i.e., Appendix attachments), will be accepted.
- All applications must contain a Summary Budget Worksheet. If the worksheet is missing, then the application cannot be adequately evaluated. Instructions for the budget section can be found in the VA-ORD Application Guide SF424 (R&R) and in this RFA. The worksheet template is available at http://vaww.research.va.gov/funding/electronic-submission.cfm. Verify that the total in the Summary Budget Worksheet and Research and Related Budget match and that the budget request does not exceed the allowable amount (per year and project total) found in the RFA, unless a waiver has been obtained.
- Applications not falling within BLRD purview may be returned without scientific peer review.

Section V. Application Review Information

An overview of the Peer Review process is described in Part 1, Section 4 of the VA-SF424 AG. The following review criteria described below will be considered in the review process for applications submitted to this RFA.

1. Review Criteria

Research Project Evaluation Criteria

Significance: Is there a strong scientific premise for the project? Does the proposed study address an important problem or critical knowledge gap in the field and specifically to the Veteran population? How do the research concepts, methods, technologies, treatments, services, or interventions advance the field? If successful, what is the likely impact of the proposed study on the scientific field and on Veterans' healthcare? Is there a stated translational pathway?

Innovation: Does the application challenge existing paradigms, explore new concepts, methodologies, or technologies, or otherwise exhibit significant creativity? To what degree does the proposed study represent more than an incremental advance on the published literature?

Approach: How well do the logical reasoning, critical review of the literature, and preliminary data support the rationale and the feasibility of the project? Are the hypotheses, aims, experimental design, methods, and analyses (including statistics) well developed? Are appropriate strategies to ensure a robust and unbiased approach presented? Are sample sizes and the statistical methods to obtain them described? Are relevant biological variables, such as species, strain, sex, developmental state (age), and weight considered? Are potential problems, alternative strategies, and benchmarks for success presented?

Feasibility: Is there sufficient evidence to determine that the proposed studies can be successfully completed? If applicable, is there sufficient evidence for successful recruitment and enrollment of subjects? Can the required animal models or samples be attained? Can the proposed study be completed within the duration of the award? Are proposed studies, including animal studies, adequately powered to answer the research questions?

Investigators: Do the PD/PI(s) and other key personnel have the expertise, experience, and record of accomplishments to enable successful completion of the proposed research? If applicable (Multiple PI/PD), how well are the efforts of the investigators and/or research teams integrated and is the collaboration synergistic or complementary? For Renewal applications, has the applicant been productive and shown research progress in the last funding period?

Multiple PD/PI Leadership Plan (if applicable): To what degree are the organizational plan, leadership approach, and roles and responsibilities of the PIs/PD appropriate with regard to expertise, resources, and commitment to ensure the completion of the project?

Environment: Do the scientific environment, facilities, and resources support the research requirements so as to enable the success of the project? Is there evidence of institutional support reflecting space, equipment, and other unique resources including availability of and access to populations adequate for the project proposed and/or to facilitate collaborative arrangements?

Ethical/Safety Issues: Are there any ethical, human subject, animal use, or biohazard concerns?

2. Other Considerations

In addition to the above criteria, the following additional instructions are provided to reviewers. These items will be considered; however, reviewers are instructed that these items should not influence their overall priority score.

Budget: Are there concerns with the requested budget (amount and duration)? Are there concerns with overlap with other funded projects listed as "Other support" for any of the key personnel? Is there appropriate justification for all categories of the budget?

Sharing Research Data: Is the Data Management and Access Plan or the rationale for not sharing data reasonable?

Resubmission (if applicable): Has the applicant responded to all or only some of the concerns raised in the previous Summary Statement? Are the responses appropriate? Has the application has been improved as a result of the revisions?

Biohazards: Are the proposed materials or procedures hazardous to research personnel and/or the environment? Is the proposed protection adequate?

Foreign/international studies: Does the project have any collaborations or involvement of foreign entities?

Select Agents: Is the use of select agents appropriate? Have the appropriate registrations for Select Agent(s) use been obtained? Are the procedures used to monitor possession use and transfer of Select Agent(s) appropriate? Are the plans for biosafety, biocontainment, and security of the Select Agent(s) appropriate?

Protection of Human Subjects: Are the human participant protections from research risk appropriate? Is the adequacy of protection against risks sufficient? Are there potential benefits of the proposed research to the participants and others? Importance of the knowledge to be gained; is there appropriate Data and safety monitoring for clinical trials?

Inclusion of Women, Minorities, and Children: Are the proposed plans for inclusion of minorities and members of both sexes/genders appropriate and adequate? The VAMC Director must approve participation in proposed research that includes children. (see VHA Handbook 1200.05 Requirements for the Protection of Human Subjects Research).

Vertebrate Animals: Is the proposed involvement and protection of vertebrate animals appropriate and adequate? Is there an appropriate and adequate justification for the use of animal species and numbers proposed? Is the proposed veterinary care adequate? Are the procedures for limiting pain and distress to that which is unavoidable appropriate? Are the methods of euthanasia appropriate?

For protocols which include canines, felines, or non-human primates, reviewers are asked to confirm that the research cannot be conducted with a) an alternative model involving less sentient species and b) that computer simulations and in vitro approaches such as tissue culture or organ-on- a chip technology cannot substitute for the proposed animal model, c) that procedures proposed are essential to meet the scientific goals of the project, and d) that the scientific value of the work proposed is sufficiently important to justify the use of canines, felines, or non-human primates.

For protocols which include canines, felines, or non-human primates, reviewers are asked to confirm that scientific objectives directly relate to an illness or injury that is combat-related, and the regulatory pathway to IND is comprehensive, logical and indicates where the current proposal fits into the pipeline.

For protocols with non-human primates, toxicology studies must have been completed on smaller animal models (e.g., rats, mice).

3. Disapproved Applications

An application may be disapproved if the SRG determines that the proposed studies are unethical.

- 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.

4. Appeals

BLRD accepts letters of appeal for applications submitted to this RFA. The basis for an appeal and the procedure for submitting an appeal are detailed in the guidance document located: https://www.research.va.gov/services/shared_docs/merit_review_guidance_docs/BLRD-CSRD-Merit-Review-Appeals-Process.pdf

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 the Summary Statement via the NIH eRA Commons. If the application is under consideration for funding, VA-ORD will request "Just-in-Time" information from the applicant

2. Administrative and National Policy Requirements

Research Integrity: VA-ORD is committed to the highest standards for the ethical conduct of research. Maintenance of high ethical standards requires that VAMCs and investigators applying for, and receiving, Merit Review Awards have appropriate procedures to preclude the occurrence of unethical research practices.

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 as a condition of acceptance of the award.

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 VA-ORD.

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 Directive 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 Directive 1200.18).

Annual Reports: By accepting a Merit Review Award, the PD/PI agrees to complete an annual Federal-wide research performance progress report (RPPR) for the project. Information and instructions for RPPR can be found here: http://www.research.va.gov/resources/RPPR.cfm.

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:

To ensure a timely response prior to submission, all questions concerning electronic submission should be submitted by appropriate Research and Development Office staff to the eRA mailbox: rd-era@va.gov.

If the initial assignment to an R&D Service or SRG seems inappropriate, the local Research & Development Office may request reassignment on behalf of the PD/PI, only after initial review assignments have been completed.

Inquiries from the local Research & Development Office related to the review process should be directed to vhacoblcsrdrev@va.gov.

Applicants may contact the appropriate Scientific Review Officer (SRO) directly after funding decisions have been made with questions specifically related to issues raised in the summary statement. SRO contact information for individual SRGs may be found at BL and CSRD Contact Information.