I. Introduction

The application process for a BLR&D Validation Merit Review application begins with the preparation and submission of a Letter of Intent (LOI). The primary purpose of the LOI is to provide BLR&D with the opportunity to determine whether the proposed studies fit within the purview of the validation RFA and if the proposed studies will address a critically important area of concern that is prevalent in the Veteran population.

II. Purpose

The purpose of this RFA is to allow BLRD to fund studies which validate published results which are of high importance to Veteran health. Applications submitted to this RFA should be for validation of published studies involving animal models, human biological samples collected using minimally invasive procedures, previously acquired tissue specimens or previously acquired phenotypic and -omic data. Further, the studies to be validated must have important implications in terms of the etiology, pathogenesis, and/or genetics of service related illness and injury in or illnesses which are more common in US military Veterans. Validation studies on the identification of therapeutic targets leading to the development of new treatments for service related illness and injury is encouraged.

Veteran related health topics responsive to this announcement include, but are not limited to:

- Long- and short-term consequences of military environmental exposures (e.g., burn pits) relevant to deployment in Iraq and Afghanistan
- Spinal cord injury (SCI)
- Traumatic brain injury (TBI)
- Polytrauma
- Post-traumatic epilepsy
- Vision and/or hearing deficits related to blast injury
- Burns
- Fracture Repair
- Chronic pain related to neurotrauma
- Wound Healing
- Mood and anxiety disorders (including depression, PTSD, acute stress disorder, etc.)

III. Types of studies supported:
• Rigorously duplicate a published result of an animal study which has important implications for Veteran health. Note that this RFA is not for validation of small unpublished studies or for mechanistic studies of unpublished or published findings.
• Validation of a new animal model for a Veteran health condition (see the list of included conditions above) including validation of an animal model to replace an existing model in primates, canines or felines.
• Take published results which are important for Veteran health (see the list of included conditions above) obtained in a rodent model and duplicate them in an alternate model in a larger animal species as a step forward toward developing a product for studies in Veteran subjects.
• Replicate -omic findings which are important to Veteran health from one large population (such as MVP) in a second large sample. Note that this RFA does not fund the collection of -omic data but only funds studies involving existing data sets.
• Validation of tissue culture models of diseases important in the Veterans population to replace currently used animal models.

IV. Studies that are not appropriate for this RFA:

• Studies for hypothesis driven validation of preliminary results that have been obtained prior to submission are not appropriate for this RFA and can be submitted under other RFAs.
• Merit award applications from investigators who already have BLRD funding under another RFA but want to obtain a second merit award.
• Merit award applications that could be submitted under other RFAs from investigators lacking BLRD eligibility.
• Merit award applications that could be submitted under other RFAs from investigators who wish to access the higher budget cap of this RFA.

V. LOI Approval Considerations

• The proposed project must fall within the BLR&D purview.
• The proposed project must have translational potential for the improvement of the healthcare of Veterans, or an individually tailored treatment that will directly improve the healthcare of Veterans.
• The proposed project must have the potential to add to for commercial licensing and to be developed further for clinical use.
• The proposed project must address Department of Veterans Affairs (VA) investigator eligibility.
• The proposed project provides BLR&D an opportunity to plan for appropriate resources that allow for an efficient and effective review process.

VI. Components of the LOI Submission
LOIs must be submitted using the following template. Each LOI must contain the following three required components (A-C):

A. VHA Research & Development Letter of Intent Cover Page (VA Form 10-1313-13)

This form is available on the forms page of the VA Research website.

B. Completed LOI Template

The template is available on the BLR&D webpage. Please clearly and succinctly address all of the requirements.

C. PI’s Biographical Sketch

The biographical sketch template is available on the VA Research Intranet. If you cannot access the intranet, please contact your local research office.

VII. Submission of the LOI

BLR&D will review and respond to submitted LOIs at any time; however, an LOI must be submitted no later than the date specified in the RFA. LOIs must be e-mailed to VHABL RD-CSRD@va.gov by the local VA facility research office. Applicants may not upload LOIs directly to the mailbox. Questions relating to the LOI preparation and submission process may also be directed to VHABL RD-CSRD@va.gov. Applicants are strongly encouraged to submit LOIs as early as possible.

LOIs with the following issues will be administratively withdrawn:

- Multiple submissions on behalf of the same PI;
- LOIs lacking the requisite information;
- LOIs submitted by investigators who are not eligible to receive VA funding.

LOIs meeting all of the administrative requirements are subject to disapproval if:

- Lacking in innovation/impact;
- Do not fall within the purview of BLR&D and/or research priority area;
- Are overly represented by ongoing ORD-funded studies;

VIII. Approval

The LOI approval letter must be submitted with the full application package (in the Letters of Support attachment, o8b_VA_Letters.pdf). A submitted validation application must not deviate significantly in specific aims from the original approved validation trial LOI. BLR&D may administratively withdraw from review any application that substantially deviates from what was described and approved at the LOI stage.
An approved validation application LOI is valid for a maximum of three (3) submissions of an application (initial submission and up to two resubmissions) during a period that encompasses four (4) consecutive review cycles following the initial approval of the LOI.
Decision Tree for BLRD Drug Development LOI

Identified lead compound?
  Yes
  Is the lead compound proven in animal models?
    Yes
    Is the lead compound FDA approved?
      Yes
      FDA requires additional testing before clinical trial for indication?
        No
        NOT RESPONSIVE
        Yes
        Investigators have met with FDA and have required studies
          No
          NOT RESPONSIVE
          Yes
          Required studies fall within Pharmacology & Toxicology
            No
            NOT RESPONSIVE
            Yes
            Is the lead compound patented?
              Yes
              Is the VA on the patent?
                No
                NOT RESPONSIVE
                Yes
                Is the indication a VA priority area?
                  No
                  NOT RESPONSIVE
                  Yes
                  Approve LOI

Effective: October 2018