

Biomedical Laboratory Research & Development (BLRD)

Guidance for Submission of a Letter of Intent for a BLRD Merit Review Award for Lead Isolation and Optimization and Pre-IND studies of Drugs and Biologics

I. Introduction

The application process for a BLRD Lead Isolation and Optimization and Pre-IND studies of Drugs and Biologics Merit Review application begins with the preparation and submission of a Letter of Intent (LOI). **The primary purpose of the LOI is to provide BLRD with the opportunity to determine if proposed studies will jointly address a critically important area of concern that is prevalent in the Veteran population; and whether or not the proposed studies fit within the BLRD purview.**

In addition, submission of the LOI allows BLRD the opportunity to access and provide feedback on the clinical and/or scientific focus and design being considered for the merit review application, the proposed innovations, and the overall impact on the veteran population.

II. BLRD Drug Development Merit Definition

The goal of this RFA is to accelerate translation of research from demonstration of efficacy *in vivo* to submission of an investigational new drug application (IND) to the FDA, with an ultimate goal of expediting novel therapeutic products to improve the clinical care of Veterans. To accomplish this mission, BLRD will provide resources to support lead isolation and optimization, pharmacological and toxicological testing or manufacturing services for a lead agent.

In order to be eligible to submit this RFA, an investigator must have a validated target with a filled invention disclosure with VA-Technology Transfer Program for requesting support for lead isolation or at least one lead agent (or no more than 3 optimized lead agents for a target) with at least a pending patent application where VA has asserted rights to the invention, for conducting IND-enabling studies. The lead agent must have the potential for commercial licensing and to be developed further for clinical use.

Lead agents include novel biologics, chemical or molecular therapeutics, or imaging agents (i.e. chemotherapeutics, antibodies, contrast imaging agent, specialized nanoparticles etc.).

Applications to this RFA for isolation of a lead agent should provide data that convincingly demonstrates the target as a novel therapeutic candidate with potential to

address an unmet clinical need of Veterans. Additionally, PI should have established a high-throughput assay with appropriate controls, and have defined criteria for lead selection, optimization and validation.

Applications to this RFA for IND-enabling studies require strong preliminary data demonstrating mechanism of action, reproducibility, reliability, and sensitivity and specificity (effectiveness) of the lead agent for the target. Data should also demonstrate in relevant human tissue the target availability and distribution. Investigator should provide substantive data that supports the efficacy of the lead agent in humans from model systems. Further, applications should demonstrate an awareness of existing FDA guidelines and milestones supporting the conduct of preliminary studies and collection of data in support of an IND application.

Note: Clearly defined milestones and timelines with Go/No-Go criteria are required in a BLRD Lead Isolation and Optimization and Pre-IND studies of Drugs and Biologics Merit Review application.

Studies focused on target discovery, new combinations or formulations of agents already in practice or already being tested (unless being combined with a new agent), prevention, studies on mechanism of action are not appropriate for this RFA.

III. LOI Approval Considerations

The BLRD Drug Development Merit LOI must:

- a. Fall within the BLRD purview.
- b. Have translational potential for the improvement of the healthcare of Veterans, or an individually tailored treatment that will directly improve the healthcare of Veterans.
- c. Have the potential to add to for commercial licensing and to be developed further for clinical use.
- d. Have convincing rationale supporting the selection of target/lead agent.
- e. Have evaluated specificity, efficacy, and developability concerns.
- f. Have the potential to move the lead agent to the next stage of drug and clinical development.
- g. Address Department of Veterans Affairs (VA) investigator eligibility.
- h. Provide BLRD an opportunity to plan for appropriate resources that allow for an efficient and effective review process.

IV. 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 BLRD [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.

V. Submission of the LOI

BLRD 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 VHABLRD-CSR@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 VHABLRD-CSR@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 BLRD and/or research priority area;
- Are overly represented by ongoing ORD-funded studies.

VI. 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 clinical trial application must not deviate significantly in specific aims from the original approved clinical trial LOI. BLRD may administratively withdraw from review any application that substantially deviates from what was described and approved at the LOI stage.**

An approved drug development 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.