

## Clinical Science Research & Development (CSR&D) Service

### Guidance for Merit Review Epidemiology: Letter of Intent (LOI)

#### I. Introduction

The application process for a CSR&D Merit Review Epidemiology application begins with the preparation and submission of a Letter of Intent (LOI). The primary purpose of the LOI is to provide CSR&D with the opportunity **to determine if a proposed study will address a critically important disease that is prevalent in the Veteran population, and whether or not the proposed study fits within the CSR&D purview.**

Epidemiology applications typically fall within the purview of the Epidemiology Merit Review Panel (EPID). EPID includes traditional population-based epidemiology projects as well as projects in the clinical epidemiology discipline that focus on questions that arise in the clinic or at the hospital “bedside.” The proposed clinical topic would not be restricted by the specialty or subspecialty designation of a disease, but **must** address a health-related problem that is prevalent in the Veteran population.

In CSR&D, an epidemiology application typically satisfies the following criteria:

- The unit of observation for the primary analysis of results is an intact human being (e.g., a Veteran in a health care facility or in the community);
- The research question being addressed involves the etiology, prevention, diagnosis, prognosis, therapy, or related aspects of health and disease;
- The type of epidemiological study is either:
  - observational (e.g., cohort, cross-sectional, or case-control studies) designed to test a specific hypothesis;
  - descriptive (e.g., examines the distribution of disease and possible determinants of disease in the Veteran population, and aims to suggest important risk or protective factors).

In CSR&D, an epidemiology application would not include the following:

- Laboratory-based projects that focus on molecular or genetic testing (e.g., molecular epidemiology, with genotypes serving as the unit of analysis);
- Projects that focus on anatomic pathophysiological mechanisms of disease (e.g., at the tissue or organ level);
- Projects that focus on individual patients and not the Veteran population (e.g., clinical medicine);
- Projects that assess the delivery and outcomes of health care (e.g., issues related to quality of care, access, or cost);
- Randomized controlled trials.

If questions arise regarding whether a study meets the EPID criteria, investigators are encouraged to contact the EPID portfolio manager to discuss the proposal and to determine the most appropriate service.

## II. LOI Approval Considerations

### A. Focus:

A CSRD epidemiology LOI must:

- a. Address a critically important exposure/disease that is prevalent in the Veteran population and that has translational potential for the improvement of the healthcare of Veterans;
- b. Clearly define the type of epidemiological study being proposed (e.g., observational or descriptive).

### B. Design:

An Epidemiology LOI must:

- a. Include an appropriate study design with a sufficient sample size (n) and statistical power;
- b. Define the target Veteran population exposed to the factor/disease of interest, as well as a control population (except in a prospective cohort study where a single cohort is studied and analysis is on exposure status);
- c. Describe in sufficient detail the significance tests to be used;
- d. Demonstrate with sufficient evidence the feasibility of enrolling the target Veteran population (if a prospective observational study).

## III. Components of the LOI Submission

LOIs must be prepared using only letter-quality print, and all text must be prepared with at least 11-point font, with no more than 15 characters per inch and no more than 6 lines per inch. Page margins must be a minimum of 1 inch at each edge. Each LOI must contain the following materials:

**A. VHA Research & Development Letter of Intent Cover Page** (VA Form 10-1313-13) (<http://www.research.va.gov/funding/process/forms.cfm> )

**B. LOI Text** – Limited to three (3) pages. Please clearly and succinctly address the following in the specified order:

### **I. Study Outline and Statistical Methods (*Observational and Descriptive Studies*):**

1. Brief description of the objectives of the proposed study and the hypothesis to be tested.
2. Scientific Rationale and Significance to the Veteran population.

3. Background Data/Preliminary Studies conducted to support application.
4. Study Design/Statistical Methods.
5. Data Analysis Plan.

## **II. Subjects, Sample Size, and Feasibility (*Observational Studies only*):**

1. Proposed number of subjects = \_\_\_\_\_
2. Duration = \_\_\_\_\_ years. *Note:* Descriptive (retrospective) studies are limited to a maximum of 2 years. Combined retrospective and prospective studies may be funded for a total of 4 years.
3. Sample size determination including a power analysis to justify the number of subjects. Describe the assumptions for sample size including effect size, event rates, or mean differences with standard deviations and expected drop-out rates. Specify the statistical methods used to calculate sample size.
4. Brief description of subject screening/recruitment methods and inclusion/exclusion criteria.
5. Projected recruitment rate.
6. As evidence of feasibility, data describing the size of the subject population available at the recruiting site(s) and verification of access to the appropriate Veteran population must be provided.

## **C.: PI's Biographical Sketch**

1. Attach completed form listed under "Additional Format Pages", Biographical Sketch Format Page: <http://vaww.research.va.gov/funding/electronic-submission.cfm>

## **IV. Submission of an LOI**

LOIs must be submitted no later than **November 1<sup>st</sup>** for proposals intended for submission to the Spring Merit review cycle, and **May 1<sup>st</sup>** for proposals intended for submission to the Fall Merit review cycle. LOIs may 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.** A Principal Investigator may only submit one LOI per review cycle. Multiple submissions on behalf of the same PI will be administratively withdrawn. As well, an LOI lacking any of the requisite information will likewise be administratively withdrawn.

*Note: LOIs meeting all of the administrative requirements but a) lacking innovation/impact or that do not address a clinically relevant disease prevalent in the*

*Veteran population; b) that do not fall within CSR&D purview and/or a research priority area; c) are overly represented by on-going ORD funded studies; or d) LOIs submitted by investigators that are not eligible to receive VA funding are likewise subject to disapproval.*

## **V. Approval**

If an LOI for an epidemiology study is approved, the approval letter must be included in the proposal application submission (Letters attachment). **A submitted epidemiology proposal must not deviate in specific aims from the original approved LOI. CSR&D may administratively withdraw from review any proposal that substantially deviates from what was described and approved at the LOI stage.**

An approved Epidemiology 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.

E-mail questions to: [VHABLRD-CSR&D@va.gov](mailto:VHABLRD-CSR&D@va.gov).

Effective: August 5, 2016