

## Department of Veterans Affairs

### **Guidance for Submitting Career Development Letter of Intent (LOI) to BLR&D and CSR&D Services**

Updated February 2018 for May 1, 2018 deadline

*This guidance document supplements VHA Handbook 1200.4--Research Career Development Program and describes Biomedical Laboratory Research and Development (BLR&D) and the Clinical Science Research and Development (CSR&D) Services implementation of the program and does not apply to RRD and HSRD.*

#### **I. INTRODUCTION**

The application process for a Career Development Award (CDA) begins with a Letter of Intent (LOI). A full proposal may not be submitted without an approved LOI. Prior to the submission of an LOI to the BLR&D and CSR&D Services, applicants should review VHA Handbook 1200.4--Research Career Development Program, and work closely with their local VA Research and Development office to ensure compliance with eligibility, BLR&D and CSR&D requirements, and preparation of the LOI and application for submission. Consistent with the Office of Research & Development's (ORD) overall mission to discover knowledge, develop VA researchers and health care leaders, and create innovations that advance health care for our Veterans and the nation, applicants should review the purview of each research service outlined below and select the appropriate research service (i.e., BLR&D or CSR&D) for their LOI based upon the proposed research. Prior to LOI submission, applicants are encouraged to confirm the appropriate research service for the work with their respective local VA Research and Development office or the Program Manager for the Career Development Program, especially in cases where the questions may be of interest to both services.

#### **BLR&D Purview**

The BLR&D purview includes *in vitro* and *in vivo* laboratory studies on tissue cultures, animal models, and human biological samples. This purview includes research involving minimally invasive procedures to obtain biological specimens from human subjects (e.g., drawing blood, collecting urine, or performing buccal swabs), use of biopsy tissues (e.g., tissue bank or excess pathology material; the VA will not fund studies of human fetal tissue) and big data analyses (analyses using data science approaches and advanced analytic techniques) of datasets from within or outside of the VA including but not limited to the Million Veteran Program (MVP), VA Informatics and Computing Infrastructure (VINCI), or the National Cancer Institute Genomic Data Commons (GDC). The proposed studies should significantly advance discoveries related to genetic or molecular risk factors of the diseases and/or conditions and the disease-associated molecular pathways, as well as discovery of pharmacogenomic markers, utilizing the datasets for either discovery or important replication studies. Studies should be designed to (1) identify and confirm clinically relevant biomarkers as diagnostic, prognostic, and therapeutic indicators in diseases/disorders relevant to Veterans or (2) develop innovative analytical strategies/tools for defining genome-wide

association (GWA) of genotypes and phenotypes, gene-gene interactions, gene networks, gene-by-environment interactions, and/or complex molecular pathways.

### **CSR&D Purview**

The CSR&D purview includes interventional, experimental, and/or observational studies involving human subjects. Applications involving administration of survey instruments or questionnaires, new/prospective collection of medical histories from research subjects (i.e., not from existing medical records), and/or performing medical procedures (including imaging studies or surgical biopsies) or treatment regimens must be submitted to CSR&D even if some specific aims in the application meet the purview of BLR&D. CSR&D research priorities for big data analytics should focus on projects that will potentially lead to better effectiveness underlying therapeutic approaches (e.g., studies on validation of pharmacogenomics markers), and clinical epidemiology. Proposals to CSR&D must have a focus on potential application to advancing treatment based upon genetic and molecular understanding and must be differentiated from other ongoing studies.

## **II. BLR&D and CSR&D CAREER DEVELOPMENT PROGRAM GOALS**

The Research Career Development Program is an intramural funding mechanism designed to attract, develop, and retain talented VA-ORD researchers in areas of particular importance to VA and to Veteran health care. The CDA-2 award provides salary and/or project funds to support a mentored program of research and training that can range from three to five years (applicants pursuing big data projects are expected to fully justify the requested period of support). In this program awardees may gain mentored research time intended to develop independent research skills, experimental approaches, and advanced methods needed to become independent VA scientists. At the completion of the mentored CDA-2 award, it is anticipated that awardees will have competed for independent VA research funding. Implicit in all Career Development Award applications is the understanding that the applicant plans to continue their career within VA.

Applicants are highly encouraged to pursue research projects that are innovative, high-impact, translational, and clinically relevant with the potential to lead to significant advances in health care for Veterans. Proposed studies must be supported by sound rationale, thorough review of the literature, and a well-designed research strategy that is feasible. It is expected that the applicant, with sufficient input from the mentor(s), will carefully choose a research project that is both feasible and will lead to successful outcomes. Therefore, the results of studies conducted should provide the scientific rationale upon which an innovative hypothesis can be based for new investigations in a Merit Review application. Since the award emphasizes both the quality of the research and the training proposed, applicants should demonstrate a high degree of creativity and productivity in their scientific area of interest and exhibit strong VA commitment.

### ***New: Big Data Applicants***

The BLR&D and CSR&D Career Development Award program will recruit and train early research scientists in data science and big data analytics to facilitate integration of genomic, epigenetic, and proteomic data with clinical and other health information to

understand diseases and conditions affecting Veterans. The outcome from this research effort will enable clinicians to identify therapeutic targets, biomarkers, risk factors, etc., to improve Veteran disease risk assessment, diagnosis, treatment, and care. This new effort is consistent with the ORD CDA program, which aims to attract, develop, and retain talented VA researchers pursuing Veteran-centric research that advances health care for Veterans and builds a diverse workforce prepared to meet future challenges. A CDA to pursue big data science will support a mentored training experience to prepare talented individuals for an independent research career in the VA. Applicants will utilize the current CDA mechanism with an emphasis on utilization of big data to address current issues affecting Veteran health and well-being that often involve a team science approach.

### III. SUBMISSION AND DEADLINES

Letters of Intent (LOIs) submitted to the BLR&D or CSR&D Services are due by **May 1** or **November 1**, and must be submitted to the BLR&D/CSR&D Career Development mailbox: [vhacadereview@va.gov](mailto:vhacadereview@va.gov).

**Important!** An approved CDA-2 LOI allows a maximum of three (3) submissions of a CDA-2 application (original and up to two (2) resubmissions) during the four (4) consecutive review cycles following the LOI approval. An applicant is **only allowed one (1) approved LOI** for their entire career. Therefore, once approved, the applicant may **not** renew, extend, or submit a new LOI.

#### A. APPLICANTS

##### Citizenship

**All applicants must be US citizens;** the CDA-2 LOI **must** include a completed and signed copy of the BLR&D and CSR&D CDA Citizenship Certification, certified by the Associate Chief of Staff for Research (ACOS) that the applicant is a US citizen (proof of citizenship should be provided to the ACOS for certification). **Only the Citizenship Certification** should be included in the LOI; please do not attach supporting documents.

For all applicants, a letter from the local VA Human Resource Management (HRM) office must be provided indicating that the applicant is eligible for the respective appointment and can be hired by the VA Medical Center (VAMC). Indicate in the letter if the nominee is currently employed by the VAMC.

#### B. Eligibility

The CDA-2 award is intended for individuals early in their research career who do not currently or who have not previously held independent peer-reviewed funding (i.e., as a PI or co-PI).

- A VA appointment is not required for submission of an LOI or CDA-2 application; however, a VA-paid appointment must be obtained before funds can be released.
- Non-clinicians must be no more than 5 years beyond receipt of their terminal degree (e.g., PhD) including MD or MD/PhD applicants who do not have a license to practice medicine in the US.

- Clinicians (licensed to practice in the US and eligible for a VA-paid clinical appointment) must be no more than 5 years past their last clinical training (e.g., residency, internship, clinical fellowship) and no more than 10 years past receipt of their MD degree (or PhD for clinical psychologist).

**C. Requirements for VA Research Appointment and Salary**

Salary on awards is shared between research and clinical care, so the local VAMC commitment must be clear in the LOI. ***If applying as a clinician, a letter from the Medical Center Director should be included in the LOI application. The letter must also include a commitment to provide a VA-paid clinical appointment at the end of the CDA-2 award.***

Licensed clinicians who are not physicians (e.g., clinical psychologist, audiologist, etc.) may apply as either a clinician or non-clinician using one of the following approaches:

- For clinicians, the table below outlines the expected VA appointment and salary support devoted to the CDA-2 award;

VA Appointment	Salary Support	
	CDA-2 – Calendar Months	Local VAMC
8/8ths	9	3
7/8ths	7.5	3
6/8ths	6	3

- Non-clinician applicants may request an 8/8ths VA appointment for 12 months of salary support paid by the CDA-2 award. If the applicant is requesting less than 8/8ths VA appointment, any additional non-VA salary support requires submission of a memorandum of understanding (MOU) to ensure that there will be no potential for dual compensation for time and/or effort. (See [https://www.research.va.gov/resources/ORD\\_Admin/Time-Effort-MOU.pdf](https://www.research.va.gov/resources/ORD_Admin/Time-Effort-MOU.pdf).)  
Non-clinicians may not have any 8ths of VA-paid clinical appointment.

**D. Publication Record**

Although the Career Development Handbook indicates that applicants need to have at least one (1) senior-authored publication (e.g., first or last author depending on the scientific field), the more successful applicants in the BLR&D/CSR&D peer review process have two to three (2-3) senior-authored manuscripts, as well as postdoctoral or research fellowship experience.

## IV. MENTOR(S) AND TRAINING PLAN

### A. Mentoring and Training

Strong applications to the BLR&D and CSR&D contain the following details concerning the training plan and mentor(s) involvement. When planning the LOI considerations should be given to these details:

The applicant and mentor should work together to develop a robust individualized training and mentoring plan, which may include lab work, course work, seminars, conferences, grant writing, and/or other activities appropriate to the proposed research and area of interest, as well as the applicant's own experience to date. Big data science is interdisciplinary by nature and a multidisciplinary skill set is critical for an independent career; therefore, applicants seeking a big data CDA are expected to acquire foundational training that creates competency in both biomedical science and data science/big data approaches. For those individuals with a data science background, for instance, the training plan should include activities to increase competency in biomedical science. The mentor(s) should demonstrate a strong commitment to the applicant's training and research project and develop a communications plan that fosters consistent and intensive one-on-one interactions to ensure completion of the project and all relevant training. Sufficient details should be provided describing the nature and frequency of the interaction between the mentor(s) and applicant for the duration of the award. The training plan should be integrated with and designed to support the proposed research. It should also demonstrate that it is supported by the training environment and ongoing research at the local VAMC. The applicant's research and training plan should be written by the applicant and its quality should demonstrate that the mentor has provided sufficient guidance in its preparation. In order to provide the applicant with critical experiences in their area of interest and foster the applicant's development towards an independent research career as a VA researcher, the applicant is encouraged to collaborate with other investigators to enhance/augment his/her expertise to address the proposed research question and maximize their training. To that end, studies involving clinical epidemiology or clinical trials should include a biostatistician as a collaborator. Studies involving genetic epidemiology should include a statistical geneticist; any applicant planning to perform this role must demonstrate possession of such skills. Big data science studies involving the VA Corporate Data Warehouse (CDW) should include appropriate experience with cleaning and curating CDW data or demonstrate that they have similar experience.

### B. Mentor(s)

The CDA requires the involvement of ***at least one mentor who is a funded VA investigator*** with an established research program evidenced by publications, funding, and previous successful mentorship. ***The VA mentor must have a defined role in both the research and training proposed***, and be committed to supporting the development of the applicant towards independence. In such instances where the VA mentor does not have prior mentoring experience, a co-mentor with a successful history of mentoring should be included. The co-mentor should have experience in training and a demonstrated record of research, funding, and publications relevant to the applicant's proposed research project. Successful

applications often have a mentoring team that includes a VA-funded investigator with expertise and involvement in the proposed research project.

### ***New: Mentorship for Big Data Science***

In the absence of a VA mentor with an established research program and demonstrated experience and/or expertise in big data science/genomic data (or bioinformatics), co-mentor(s) with experience and expertise in computation and big data analytics may be included. Ideally, if a co-mentor from the affiliate is proposed, the co-mentor's appointment would be "without compensation" (WOC) at the local VAMC and the co-mentor would work together with the VA mentor to assist the applicant throughout the training period in their development towards independence. Additionally, mentors with expertise in disease mechanism(s) should be included as needed. If use of the CDW data is planned, it is highly encouraged that applicants build a mentoring team that has experience with VA CDW.

In light of limited travel support and the BLR&D and CSR&D requirement for ongoing and regular, sustained interaction between the mentor and trainee, the mentoring plan should be developed with significant consideration given to the impact of the mentor's geographic location. Applicants are strongly advised to seek mentor(s) located within their local VAMC and/or local affiliate (i.e., same facility as the VA mentor). If a mentor outside the local VAMC is proposed (e.g., outside the Federal definition of local travel) then a full justification (including subject matter, nature and frequency of interactions, and duration) must be provided in the form of a letter to the appropriate Service Director and attached to the LOI. The justification should also include a detailed explanation of why the mentor (including non-VA mentor) is critical to the trainee's development and research project, and how his/her contributions will significantly enhance the applicant's training that is not available at the local VAMC and/or affiliate.

## **VI. RESEARCH PLAN**

BLR&D and CSR&D seek applications from preclinical biomedical, behavioral, epidemiological, and clinical research studies on disorders and diseases of importance to the health of Veterans. Applicants should carefully choose a research project with appropriate guidance from the mentor(s) that addresses a VA priority research area and/or critical problem of importance to Veterans' health. Importantly, the research proposed may be complementary **but distinct from ongoing work by the mentor(s)** (i.e., specific aims do not overlap or duplicate the mentor's ongoing research). Stronger applications will be those evaluated as opening new directions in the research area as this will more likely lead to a research program independent from the mentor(s). Since the training and research supported by the CDA-2 award is intended to advance awardees towards independence, it is expected that the results from studies conducted through this award will provide the scientific rationale for an innovative hypothesis for new investigations in a future Merit Review application. Applicants should outline their research plan as described in the ORD's LOI instructions and attach it to VHA Research and Development Letter of Intent Cover Page - VA Form 10-1313-13. The applicant should ensure that the hypothesis/objective, aims, and significance of the

research to Veterans are clearly stated. The project design and method narrative should be well described including any intervention(s)/treatment(s), if applicable.

### ***New: Big Data Projects***

Applicants are highly encouraged to propose a research project addressing an area of interest to Veterans and Veteran health care that uses data from the VA CDW and MVP. In order to gain access and use data from the VA CDW and MVP, applicants must be able to work behind the VA firewall. Applicants will have access to aggregate data from MVP in order to determine preliminary numbers to justify the study (i.e., establish sample size calculation to obtain statistical significance, etc.). If other non-VA data sets (i.e., other than VA CDW or MVP) will be utilized for the proposed project, the applicant will be expected to demonstrate access to the data and its relevance to Veterans. Applicants are expected to engage existing genomics expertise either at a VAMC or affiliate to enhance their training. In addition to salary and research support provided for by the CDA-2, applicants may also include in their application budget cost to travel to an established data science program/center for training (i.e., for a defined period of time) if necessary and appropriately justified.

**Key aspect for big data projects:** All big data science applications will be expected to demonstrate how they will have access to the required dataset(s).

### **Veteran-Centric Research**

The Veteran-centric nature of VA-funded research from the BLR&D and CSR&D Services require that enrolled participants be Veterans or that the samples/tissues or data used in the research be derived/obtained from Veterans or Veteran-derived cohorts such as MVP. It is the responsibility of the applicant to describe the Veteran-centric nature of their proposed research and how the proposed research will contribute to advancing health care for Veterans while augmenting their expertise for an independent research career in the VA. This description should explain how the applicant plans to leverage existing unique resources available at the local VAMC to address research ideas in the proposed project. Examples of unique resources may include Veteran-derived patient cohorts, biorepositories including tissue samples (fresh or archived), clinical databases, transcriptome or proteome datasets, epidemiological resources, etc.

### **Clinical Trials**

If the research proposed is a clinical trial, the applicant must follow the **CSR&D CDA Clinical Trial LOI Instructions** in addition to consulting this guidance for additional requirements. Applications to the CSR&D Service require the enrollment of Veteran subjects and use of Veteran samples/tissues.

CSR&D supports submission of only Phase II or III clinical trials as part of the Career Development Program when the proposed trial is the only focus of the application. The trial should encompass the entire application; any additional specific aims that are included should be directly related to the trial. Applications that include specific aims not directly related to the trial will not be accepted for review. Given the fact that clinical trials take time to complete and frequently lead to fewer publications, the applicant should develop a plan to ensure a record of productivity (with respect to publications) at the conclusion of the CDA-2 award as

well as the development of a new hypothesis for a subsequent application for independent funding.

A clinical trial application would typically involve human subject randomization and appropriate controls designed to assess the potential safety and/or effectiveness of an intervention, measured via a clinical outcome directly or indirectly or with a surrogate endpoint such as a biomarker assessment. The intervention may involve the use of pharmaceutical compounds or agents, treatments, or devices. *Note:* Assessment of diagnostics by experiments designed to show equivalence of test results with those of existing diagnostic devices or methods are usually not considered clinical trials. Studies focused on mechanisms underlying an intervention, without a primary clinical outcome measure of interest are typically not considered clinical trials unless there is a major concern about safety. Questions about CDA-2 clinical trials may be directed to [CLIN-Review@va.gov](mailto:CLIN-Review@va.gov).

*Note:* The definitions for a trial may be less broad than that describing the requirements of a trial to be registered on [clinicaltrials.gov](http://www.clinicaltrials.gov):  
[http://www.research.va.gov/resources/ORD\\_Admin/clinical\\_trials/](http://www.research.va.gov/resources/ORD_Admin/clinical_trials/)

## VII. BIOGRAPHICAL SKETCH FOR APPLICANT AND EACH MENTOR

In addition to highlighting only the most recent publications, presentations, and activities relevant to the application, all current, previous (awards ending within the past 4 years), and pending research support should be included. Also, include the role, title, supporting agency, performance period, and level of funding for each award.

***Mentors only:*** Using a table format, **list all VA Career Development Award awardees**, if any, for which the mentor previously served or currently serves as mentor, co-mentor, or collaborator (include dates and role, i.e., Primary Mentor, Co-Mentor). Indicate whether the awardee transitioned to independence, e.g., obtaining independent research grants and/or advancement in their academic position, and highlight any VA Career Development Awardees.

## VIII. RESEARCH PERFORMANCE SITE

CDA-2 awardees may not establish an independent off-site laboratory. At a minimum, some of the proposed work must be performed in the VA mentor's research space at the VAMC. If the VA mentor's laboratory is not located at the VA, the mentor must have an approved Off-Site Waiver. Off-Site Waivers are not required for work performed on a CDA-2 award in an off-site mentor's laboratory.

***Note: In order to gain access and use data from the VA CDW and MVP, applicants pursuing big data projects must be able to work behind the VA firewall.***

## IX. LOI REVISIONS, TITLE CHANGES, AND PERMISSIONS

Title changes for resubmitted applications do not need prior approval or submission of a revised LOI, provided that the application remains within the scope of work proposed in the approved LOI.



After an LOI is approved and prior to any submission, if a change in mentor(s) becomes necessary, the applicant must obtain approval for the new mentor(s) from the BLR&D or CSR&D Director.

If a change in scope of work (i.e., moving outside the scope of the approved LOI) will be proposed, a revised LOI must be submitted via the regular LOI submission process describing the new scope of work; approval of the revised LOI will not change the original expiration date of approval or number of submissions remaining on the original LOI. A copy of the revised LOI approval letter must be included in the revised application.

## **X. REQUESTS FOR ADDITIONAL GUIDANCE**

If an applicant requires additional guidance in the preparation of an LOI, the applicant should communicate with their ACOS or VA mentor, who will contact the BLR&D and CSR&D Program Manager for the Career Development Program for additional guidance. While applicants may contact the Program Manager directly to discuss their work, it is preferred they –especially non-VA applicants – include their ACOS/R and/or VA mentor in such discussions.

**Upon receipt, LOIs will be checked for completeness. LOIs that are incomplete or late will not be reviewed.** Please utilize the [checklist](#) to ensure all components of the LOI are included prior to submission.

## **BLR&D and CSR&D Services Career Development LOI Checklist**

\_\_\_ Is the applicant a US citizen? Only US citizens or permanent residents who have applied for US citizenship and have been notified by the Immigration and Naturalization Service of a date for a swearing-in ceremony may apply.

\_\_\_ Determine applicant's eligibility

\_\_\_ Identify research area of interest

\_\_\_ Identify appropriate Service (BLR&D or CSR&D)

\_\_\_ Identify VA mentor(s)/co-mentors

\_\_\_ Identify collaborators, if applicable

\_\_\_ Complete ORD LOI cover page Form 10-1313-13

**The following items should be limited to one (1) page:**

\_\_\_ Statement on Budget & Study Duration

\_\_\_ Brief description of the applicant's prior training and research experience(s) (include number of years since clinical training and number of years of research experience)

\_\_\_ Brief description of the applicant and mentor(s)' qualification

**The following items should be limited to two (2) pages:**

\_\_\_ Description of the proposed study or research plan (rationale, significance of research, program objective, project design and methods, description of intervention(s)/treatment, statement of disclosure, acknowledgement of VA policy to include women and minorities in research (if applicable)) [**Note: three (3) pages for clinical trials only**]

**Attach the following items:**

\_\_\_ Attach documentation of approved IND or IDE, if applicable (for clinical trials)

\_\_\_ If applicable, attach documentation of supplemental funds from other sources to support clinical trials

\_\_\_ Attach up to **five** reference citations relevant to the proposed project

\_\_\_ Attach completed and signed CDA Citizenship Certification, available on ORD Career Development website (do not include any extra documents)

\_\_\_ Attach appointment Eligibility Documentation (Letter from VA Human Resource Management office indicating that the applicant is eligible for appointment and can be hired by the VAMC)

\_\_\_ Attach a letter from the Medical Center Director outlining their commitment to provide a VA-paid clinical appointment at the end of the CDA-2 award **if applying as a clinician**

\_\_\_ Attach biographical sketch for applicant and all mentor(s)