

**Department of Veterans Affairs
Office of Research and Development**

**Biomedical Laboratory Research & Development (BLR&D)
Clinical Science Research & Development (CSR&D)**

**Instructions for Submitting a Career Development
(CDA-1 or CDA-2) Letter of Intent**

This guidance document supplements VHA Program Guide 1200.4 (Career Development Program) and applies to Letters of Intent submitted to Biomedical Laboratory Research and Development (BLR&D) and Clinical Science Research and Development (CSR&D) only.

Revised March 2023

Summary of changes:

- *Removed requirement for HR letter.*
 - *Clarified policy regarding non-Veteran enrollment in CSR&D-funded studies.*
 - *Added information about requesting policy waivers.*
 - *Re-organized material for clarity (no additional policy changes).*
 - *Moved supplemental instructions for CDA-2 clinical trial LOIs from a separate document into this one (see Attachment 1)*
 - *Re-formatted LOI submission checklist.*
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I. INTRODUCTION AND SERVICE PURVIEW

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, applicants should:

- Review VHA Program Guide 1200.4 and the applicable Request for Applications (RFA) document (see <https://www.research.va.gov/funding/rfa.cfm> for more details).
- Work closely with the research office at their local VA Medical Center to ensure their submission complies with all applicable policies.
- Review the BLR&D and CSR&D purview statements below and select the appropriate service for their LOI based upon the work being proposed. In cases where the scientific question(s) may be of interest to both services, applicants are encouraged to contact the Career Development program mailbox at yhacadereview@va.gov for guidance.

A. 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.

B. 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. AWARD MECHANISMS AND PROGRAM GOALS

The 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.

A. Career Development Award 1 (CDA-1)

The CDA-1 provides salary only for an early mentored research experience, consisting of up to two years of salary support to investigators. The training experience should be closely integrated with the mentor's ongoing funded research. Submission of a CDA-2 application is strongly encouraged after one year into the CDA-1 award (and may be submitted without a Letter of Intent).

Note: Applications for this mechanism are limited to investigators and/or research topics in designated high-priority areas (see the list of active CDA-1 RFAs).

Although the work proposed by CDA-1 applicants is closely integrated with the mentor's ongoing funded research, it is expected that the project will develop into a distinct line of investigation (i.e., specific aims do not overlap or duplicate the mentor's ongoing research) by the conclusion of the CDA-1.

B. Career Development Award 2 (CDA-2)

The CDA-2 provides salary and 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.

Research proposed by **CDA-2** applicants may be complementary **but must be distinct from ongoing work by the mentor(s)** (i.e., specific aims do not overlap or duplicate the mentor's ongoing research).

Implicit in all Career Development Award applications is the understanding that the applicant plans to continue their career within VA.

Applicants are 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, feasible research strategy.

Career Development Awards emphasize both the quality of the research and investigator development. Working closely with their mentor(s), applicants should choose projects that will lead to successful proposals at the next level (i.e., a CDA-1 should lead to a successful CDA-2 funding application, a CDA-2 should lead to scientific independence and a successful VA Merit Review funding application).

III. MENTORING, TRAINING, AND RESEARCH PLAN

A. Mentor Requirements

CDA-1 and CDA-2 proposals require at least one member of the mentoring team have **current VA Merit Review (IO1) funding as PI**, and an established VA research program evidenced by publications and research support.

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 a successful, independent VA research career.

In instances where the VA mentor does not have prior mentoring experience, a co-mentor (may include non-VA scientists) with a successful history of mentoring should be included.

B. Mentoring and Training Plan

Applicants and mentors 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. For CDA-1, this is particularly important since support is only provided for the applicant's salary. Therefore, the mentoring and training experience should be closely integrated with the mentor's ongoing funded research.

The mentor(s) should demonstrate a strong commitment to the applicant's training and research and develop a communications plan that fosters consistent and intensive interactions to ensure completion of the project and all relevant training.

Studies involving clinical epidemiology or clinical trials (CDA-2 only) should include a biostatistician as mentor or collaborator. Studies involving genetic epidemiology should include a statistical geneticist.

Given limited travel resources available, and the requirement for ongoing, regular, sustained interaction between the mentor and trainee, the mentoring plan should be developed with consideration given to geographic locations. Applicants are strongly advised to seek mentors

within their local VAMC and/or academic affiliate. If a mentor outside the local area is proposed, applicants are encouraged to include with their LOI a letter of support in which the proposed mentor describes their contributions, and how they will enhance the applicant's training in ways that are not available locally.

C. Research Plan

BLR&D and CSR&D seek applications for 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.

Applicants should ensure that the hypothesis, objective, aims, and significance of the research to Veterans are evident in the LOI. The project design and method narrative should be well described including any intervention(s)/treatment(s), as applicable.

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 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 CDA-2 or Merit Review application (depending on the level at the time of entry by the applicant).

D. Additional Considerations for Big Data Projects:

Proposals that are dependent on large data sets, to include the Million Veteran Program (MVP), the Corporate Data Warehouse (CDP), etc. should demonstrate in their LOI (either via the narrative text or in a supplemental letter of support) that they have confirmed access to the required sources and that those sources contain the information required. Applicants are highly encouraged to build a mentoring team that has experience accessing, cleaning, and curating data from the sources to be used.

IV. CLINICAL TRIALS

CSR&D will accept LOIs that include a clinical trial under the **CDA-2** mechanism.

The definition of a clinical trial may be found in VHA Directive 1200.05(2), Section 3, (available at <https://www.va.gov/vhapublications/>). A decision tool to help determine whether a proposal is a trial is available at https://www.research.va.gov/services/shared_docs/resources.cfm (see Section IV, under "Career Development Clinical Trial").

CDA-2 LOIs that include a clinical trial must follow the **Supplemental Instructions for Submitting a Career Development Clinical Trial Letter of Intent**, in **Attachment 1** of this document.

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.

Questions specific to VA clinical trials may be directed to CLIN-Review@va.gov.

V. VETERAN-CENTRIC RESEARCH / NON-VETERAN ENROLLMENT

The Veteran-centric nature of VA-funded research 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 preparing them for an independent VA research career. 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.

Any enrollment of non-Veterans in VA research requires prior approval by the IRB, by the local R&D Committee, and by the VA office or program funding the research (as applicable). CSR&D's policy regarding non-Veteran enrollment may be found here: <https://www.research.va.gov/services/csrd/nonveterans.cfm>. Please note that CSR&D will not approve enrollment of non-Veterans in studies where the IRB has determined a greater than minimal risk to participants.

VI. RESEARCH PERFORMANCE SITE

CDA awardees may not establish an independent off-site laboratory. At a minimum, some of the proposed work must be performed in the VA-funded mentor's research space on VA-owned or leased premises. If the VA mentor's laboratory is not located in VA space, and the mentor has an approved Off-Site Waiver, a separate Off-Site Waiver is not required for work performed by the CDA recipient.

VII. APPLICANT ELIGIBILITY

Investigators may **only be approved for one BLR&D or CSR&D Career Development LOI** over their entire career. Therefore, once approved, applicants may **not** submit a new LOI.

A. Citizenship: All applicants must be US citizens or lawful permanent residents who have **successfully** applied for U S citizenship (and have a citizenship swearing in ceremony scheduled).

B. Education, Training and Research Experience

CDA-1: Applicants must be no more than 2 years beyond award of their terminal degree or clinical training immediately following (i.e., residency, fellowship, post-doc) as of the LOI submission deadline, **and** must not have served as PI or co-PI on a post-doctoral, peer-reviewed independent research project supported by a national, public, or private organization.

CDA-2:

- Non-clinicians must be no more than 5 years beyond award of their terminal degree as of the LOI submission deadline.
- Clinicians (licensed to practice in the US and eligible for a VA-paid clinical appointment) must be no more than 10 years beyond award of their clinical doctoral degree **and** no more than 5 years beyond their last clinical training (e.g., residency, internship, clinical fellowship) as of the LOI submission deadline.

- Applicants must not have served as PI, MPI, or co-PI on a post-doctoral, peer-reviewed independent research project supported by a national, public, or private organization.
- Applicants should have at least one senior author (first- or last-author, depending on the field) publication. Successful CDA-2 applicants typically have two to three senior-authored manuscripts, as well as postdoctoral or research fellowship experience.

C. VA Research Appointment

Applicants need not be VA employees to submit an LOI or funding application. However, a VA-paid appointment must be obtained before funds may be released.

Non-clinician applicants must have at least 6/8ths VA appointment, with 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 will require submission of a Memorandum of Understanding (MOU) describing time and effort (ensuring no potential for dual compensation) prior to release of funds.

Clinician applicants must have at least 6/8ths VA appointment. The table below outlines the expected breakdown of effort and salary support.

Calendar Months' Salary Support		
VA Appointment	CDA-1 / CDA-2	Clinical Care
8/8ths	9	3
7/8ths	7.5	3
6/8ths	6	3

Licensed clinicians who are not physicians (e.g., clinical psychologist, audiologist, etc.) may apply as either clinicians or non-clinicians, provided the local VA Medical Center is prepared to support a corresponding appointment. Non-clinicians CDA recipients may not have any 8ths of VA-paid clinical appointment.

VIII. DEADLINES AND REQUIRED LOI COMPONENTS

LOIs submitted to BLR&D or CSR&D are due on either **May 1** (for funding applications the following Fall round) or **November 1** (for applications the following Spring round) and must be submitted **by the local research office** to our Career Development program mailbox: vhacadereview@va.gov. If the deadline falls on a weekend or holiday, submissions must be received the following business day.

The items listed here must be included in the LOI submission, in the following order:

- A.** Completed ORD LOI cover page (Form 10-1313-13).
- B.** Brief statement on budget & study duration.
- C.** Brief description of the applicant's prior training and research experience (include number of years since clinical training and number of years of research experience).

- D. Brief description of the applicant and mentor(s)' qualifications (indicate which mentors have current VA Merit Review funding).

Items B, C, and D must be no more than 1 page, combined.

- E. Description of the proposed study or research plan. This should include a summary of the rationale and significance of the proposed work, program objectives, specific aims, project design and methods, description of any interventions/treatments, statement of disclosure, and acknowledgement of the VA policy on inclusion of women and minorities in research, as applicable.
- F. For proposals including a clinical trial, the description of the proposed study must address the additional prompts found in the supplemental instructions for Career Development clinical trials (see **Attachment 1**).

The description of the proposed study must be no more than 2 pages, or 4 pages for clinical trials.

- G. Up to five reference citations relevant to the proposed project (optional)
- H. Completed and signed CDA Citizenship Certification (available at <https://www.research.va.gov/funding/CADE-CitizenshipCertification.pdf>).
Do not include any source material, only the certification form.
- I. For clinician applicants only: A letter from the Medical Center Director outlining their commitment to provide a VA-paid clinical appointment during and at the end of the CDA award.
- J. Biographical sketches for the applicant and all mentors. In addition to highlighting the most recent publications, presentations, and activities relevant to the application, all pending, current, and previous (within the past 4 years) research support must be listed. Include the role, title, supporting agency, performance period, and level of funding for each award.
- K. For mentors only: Using a table format, list all VA Career Development 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, etc.). Indicate whether the awardee transitioned to independent research funding and/or advancement in their academic position. This may be included in the biosketch or as a separate document. Mentors who have not collaborated with VA Career Development awardees before may list non-VA mentorship experience or include a statement indicating as such.

LOIs will be screened for completeness and compliance upon receipt and may be returned without review if submitted late or if any applicable policies are not satisfied. Applicants and research office personnel are encouraged to use the administrative screening checklist in Attachment 2 of this document as a guide.

IX. LOI APPROVALS, REVISIONS, AND WAIVERS

- A. **CDA-1** LOIs are approved for a maximum of three application submissions (initial and up to two resubmissions) during the three consecutive scientific review cycles immediately following LOI approval.
- B. **CDA-2** LOIs are approved for a maximum of three application submissions (initial and up to two resubmissions) during the four consecutive review cycles immediately following the LOI approval.

- C. **Title changes** after an LOI is approved are allowed provided the application remains within the scope of work proposed in the approved LOI.
- D. **Changes to the mentoring team** require approval. The local research office may request this change by submitting a memo from the Associate Chief of Staff for Research (ACOS/R) to the director of the appropriate funding service. Include text explaining why the changes are being made and attach a biosketch for any mentor(s) being added.
- E. Applicants may make minor changes to their specific aims, especially in response to reviewer critiques. However, **if there is a change in the scope of work being proposed**, a revised LOI must be submitted. This is done via the regular LOI submission process. If there is any question as to whether a revised LOI is required, please contact the BLR&D/CSR&D Career Development program mailbox. Approval of a revised LOI will not change the original expiration date of approval or number of submissions remaining on the original LOI.

F. POLICY WAIVERS

BLR&D and CSR&D will consider requests for waiver of CDA policies. Requests must be submitted **by the local research office** to our Career Development program mailbox: vhacadereview@va.gov, and should take the form of a memo from the ACOS/R to the Service Director describing the situation at hand as well as any extenuating circumstances to be factored into the decision.

Applicant Eligibility

We accept policy waiver requests at any time prior to, or along with, the LOI submission. If the waiver is requested in advance of LOI submission, include the applicant's biographical sketch or CV, a summary of the research being proposed, and make clear for which round the LOI will be submitted.

LOI Extensions

Requests to extend the timeline for an approved LOI should be submitted prior to its expiration.

Other Policy Waivers

Requests for waivers of other program policies may be considered. Please contact the Career Development program mailbox for more information.

XI. ADDITIONAL GUIDANCE

If applicants, mentors, or research office personnel require additional information or guidance, they are encouraged to communicate with their ACOS/R and their VA mentor. Applicants may also contact BLR&D/CSR&D (Career Development program mailbox and/or the Scientific Portfolio Manager for their topic area) but are advised to involve their research office in such discussions.

Contact information for BLR&D and CSR&D personnel may be found online at: https://www.research.va.gov/services/shared_docs/contacts.cfm.

Attachment 1

Supplemental Instructions for Submitting a Career Development (CDA-2) Clinical Trial Letter of Intent

This attachment applies only Letters of Intent submitted to Clinical Science Research and Development (CSR&D) that include a clinical trial.

The definition of a clinical trial may be found in VHA Directive 1200.05(2) (available at <https://www.va.gov/vhapublications/>).

CDA-2 LOIs submitted to CSR&D that include a clinical trial must address the items below in the **Description of Proposed Study/Research Plan** and may use **up to four pages to do so**.

1. Clearly specify the type of clinical trial to be conducted, including phase or class that is being proposed. (Note, only Phase II and/or III trials are allowed by CSR&D for CDA-2).
2. Provide a description of the purpose and objectives of the proposed clinical trial and the hypothesis to be tested. Clearly state the specific aims. The proposed study and intervention should be based on sound scientific rationale, logical reasoning, and critical review of the literature. The trial should be the primary focus and aim of the proposal; additional aims should be limited to (a) initial programmatic/refinement or modification of existing protocol, manual related to the clinical trial that will provide additional publications for the applicant, or (b) secondary mechanistic approaches to understand clinical results/mechanism of action.
3. Describe the proposed intervention, treatment, device, and control(s), as applicable.
4. Provide an overview of the background, preliminary studies, and data supporting the proposed application. Provide references for any published results.
5. State whether documentation exists for an Investigational New Drug (IND)/ Investigational Device Exemption (IDE) (as applicable) for agents not already approved by the Food and Drug Administration (FDA) for the specific investigational use. Note, the quality of the agent/product should be consistent with FDA manufacturing standards.
6. Describe the availability of and access to the pharmaceutical compounds, agents, biologics (including any matched placebos), treatments or devices. Include discussion of any agreement with companies providing the intervention.
7. Describe subject screening/recruitment methods and projected recruitment rate. As evidence of feasibility, provide data describing the size of the subject population available at the recruiting site that would satisfy the planned inclusion/exclusion criteria, and verification of access to the appropriate Veteran population.
8. Clearly describe the defined and appropriate clinically relevant endpoints to be tested and how they will be measured
9. Provide your sample size and briefly describe the statistical analysis plan including power analysis to demonstrate that the sample size projection is appropriate to meet the trial objectives.
10. Provide a list of any local or national competing trials on this topic that would draw subjects from the same Veteran population. If competing trials exist, the distinction from the proposed trial must be accurately described. If no competing trials are underway, please indicate so. See www.clinicaltrials.gov as one source for this information.

11. Provide a discussion of any unique problems or challenges that are anticipated that would prohibit the trial from commencing immediately once an award is made (including whether the study will be FDA regulated and/or will require agreements with industry or other non-VA entity, patents/licensing, etc.)
12. Describe how the results will impact clinical practice and/or plans for future studies. Specifically, what are the expected changes that will take place because of this trial (e.g., clinical management, policy, new phase trial, additional research)?

LOIs that describe a clinical trial may include the following supplemental documents:

1. Documentation of approved IND or IDE, if applicable
2. Documentation of supplemental funds from other sources to support the clinical trial to completion, if applicable.

Attachment 2

Administrative Screening Checklist for CDA-1 and CDA-2 LOIs (BLR&D/CSR&D)

	Y	N
Applicant Eligibility		
Applicant is a US citizen or permanent resident with swearing in ceremony scheduled?		
CDA-1 (All Applicants)		
Applicant is < 2 years beyond the terminal degree or training immediately following?		
Applicant or proposed work corresponds to a current, published BLR&D/CSR&D CDA-1 RFA?		
CDA-2 Non-Clinician Investigator		
Applicant is < 5 years beyond award of terminal degree?		
CDA-2: Clinician Investigator		
Applicant is < 10 years beyond award of clinical doctoral degree?		
Applicant is < 5 years beyond most recent clinical training?		
Expected VA appointment is at least 6/8ths?		
(Clinician applicants only) Expected clinical salary support is equal to 2/8ths?		
If any eligibility criteria above not met, is an approved waiver or waiver request included?		
Mentoring Team		
Does at least one member of mentoring team have current VA Merit Review (I01) funding?		
Required LOI Components		
A. Completed/signed ORD LOI cover page (Form 10-1313-13)		
B. Statement on Budget & Study Duration		
C. Brief description of the applicant's prior training and research experience		
D. Brief description of the applicant and mentor(s)' qualifications		
Items B, C, and D above are no more than 1 page, combined		
E. Description of proposed study/research plan (no more than 2 pgs. / 4 pgs. If clinical trial)		
F. (Clinical trials only) Item E addresses additional prompts in the supplemental instructions?		
G. Up to 5 reference citations (optional)		
H. Completed/signed CDA Citizenship Certification Form (without source documents)		
I. (Clinician applicants only) Letter from the medical center director outlining their commitment to provide a VA-paid clinical appointment during/at the end of the CDA		
J. Biographical sketch for applicant and all mentors		
K. Table showing prior collaboration with VA CDA awardees (or statement indicating no such collaboration) for each mentor		