

**Department of Veterans Affairs**

**Clinical Science Research & Development Service**

**Call for Letters of Intent Proposing Clinical Trials**

**For SARS-CoV2 Infection/COVID-19**

**Under the VA CURES Program of Master Protocols**

**November 6, 2020**

**CSRD is soliciting Letters of Intent for clinical trial studies that could be aligned under VA CURES, a program of master protocols for COVID-19.**

**The first deadline is December 14, 2020.**

**Background**

As soon as the urgent need for proven SARS-CoV2 treatments was identified, the VA Office of Research and Development organized a new program to develop clinical trial priorities under a program of master protocols with multiple investigational lanes addressing prevention and treatment strategies by disease severity. The program is known as VA CURES (**C**oronavir**U**s **R**esearch & **E**fficacy **S**tudies), and the first protocol approved is called CURES-1. This first protocol covers the COVID-19 symptomatic inpatient therapeutic lane. VA CURES-1 will test the benefits of convalescent plasma in reducing the need for mechanical ventilation and preventing death from COVID-19. Participant enrollment to VA CURES-1 will begin in November 2020. Additionally, the VA CURES Program is developing master protocols both for prophylaxis/prevention, and for treatment of symptomatic outpatients. Thus, the three interventional lanes under VA CURES will be: (1) prophylaxis/prevention, (2) outpatient therapeutics, and (3) inpatient therapeutics. Each of these lanes will be considering the next candidate interventions going forward, which will be ranked to determine inclusion in lane-specific randomized controlled trials (RCTs) in an ongoing adaptive process. Modalities validated by a VA CURES RCT will become the basis of care in subsequent trials testing new agents in that therapeutic lane, and so on, while the evidence continues to build.

The VA CURES Program is now accepting Letters of Intent (LOIs) for clinical trials to be considered for the outpatient and inpatient therapeutic lanes for these priorities:

* Potential **therapeutic compounds for symptomatic/COVID+ outpatients** not requiring hospitalization. Note: the outpatient master protocol has not yet been developed, thus, this is a particularly high area of interest. The team developing the outpatient therapeutic arm will benefit from collaborating with the two other protocol teams during study planning.
* Potential **therapeutic compounds to be considered for inpatient therapeutics** to be tested once CURES-1 results on convalescent plasma are known.

A high interest for VA CURES is on repurposing agents with a known safety profile, as well as drug availability. After this initial call for LOIs, the CURES Program will continue to specify future deadlines and updated priorities including for example, an LOI opportunity to be presented in the future for the prophylaxis/prevention protocol.

Clinical trial LOIs submitted but not approved for CURES will be provided guidance as to whether any other mechanism may be used (e.g., standard Merit Review).

The clinical trial LOIs will be evaluated for both scientific rationale and prioritized for fit within the specific interventional lanes: (1) outpatient therapeutics or (2) inpatient therapeutics. Because of the planned adaptive nature of VA CURES, we invite as many ideas as possible, as soon as possible. Input from the field will allow the program to continuously rank ideas for prioritization within CURES.

**Process**

VA investigators should consider submitting Letters of Intent describing the rationale and evidence to support a compound for testing that fits within one of the VA CURES Program lanes: outpatient therapeutics or inpatient therapeutics. The first section of the LOI should indicate the appropriate VA CURES Program lane.

LOIs will be evaluated to ensure that requested elements are fully described, and the potential investigator is eligible to submit. Note that any eligible VA scientists may submit an LOI to VA CURES even if they have another clinical trial funded by CSRD. Scientific evidence, drug availability and feasibility will also be reviewed within CSRD and by the CURES Program Executive Steering Committee.

LOIs of high interest will undergo an expedited prioritization review. Thus, as aligned with VA CURES goals, we will advance each compound to testing as quickly as possible, ideally already having the next compound/s to be tested identified as ongoing trials are completed.

Deadline for new LOIs to be considered in the first prioritization is **December 14, 2020.** Review of LOIs will result in four possible outcomes: (a) acceptance as a potent­ial CURES study in a specific intervention lane; (b) a referral to another mechanism (e.g., standard Merit Review); (c) encouragement of closely related concepts to be merged for resubmission; (d) or disapproval of the LOI.

If approved under CURES, the PI and the CURES Executive Steering Committee will work together on planning the trial application, taking advantage of existing resources and capabilities under the master protocol program. The PI would then submit the trial application for peer review by CSRD to evaluate the application. A decision for funding support will be made following peer review.

This LOI announcement is restricted to COVID-19 trial ideas under CURES. Recurring reviews of LOIs beyond this initial call will be conducted on a rolling/as-received basis; however, the process of prioritization will still be applied. Updates about VA CURES priorities will be available on both the CSRD webpage (<https://www.research.va.gov/services/csrd/> ) and the VA COVID19 webpage ([https://www.research.va.gov/covid-19.cfm](https://gcc01.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.research.va.gov%2Fcovid-19.cfm&data=04%7C01%7C%7Cd78d962ca2284ea9d8a708d88266a6d9%7Ce95f1b23abaf45ee821db7ab251ab3bf%7C0%7C0%7C637402724675416017%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C1000&sdata=l3B9tHa6nX7qbEwELLROvdniCb5WZiFFipMv3WStZLk%3D&reserved=0) ).

Clinical trial work as well as subsequent studies under CURES will be highly collaborative, as we are working together to drive efficient evidence building for effective therapeutics for COVID-19.

Instructions for Submission are described in Appendix A. LOI templates are located on our webpage: <https://www.research.va.gov/services/shared_docs/resources.cfm#4> (See Section IV, #3 (Merit Review Clinical Trial).

CONTACT: clin-review@va.gov

**Clinical Science Research & Development Service**

**Guidance for Submission of a Letter of Intent for a Clinical Trial**

**For SARS-CoV2 Infection/COVID-19**

**Under the VA CURES Program of Master Protocols**

**APPENDIX 1, LOI Instructions**

1. **Components of the LOI Submission**. LOIs must include the following components (A-C):
2. **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 (<https://www.research.va.gov/funding/>).
3. **LOI. Attach word document to VHA Form 10-1313-13 describing the** following in a maximum of four pages:

1. **Focus**: LOIs submitted to VA CURES Program must address one of the interventional master protocols:
* outpatient therapeutics (newest protocol to be added, all ideas are welcome)
* inpatient therapeutics (building upon/after CURES1 trial of convalescent plasma is complete)
1. **Design**: An LOI must include and describe the following:
2. An appropriate study design statistically powered with a sufficient sample size to determine the effect of the proposed intervention;
3. Primary outcome measure should be described. Note that CURES has specified outcome measures for prophylaxis/prevention and inpatient therapeutic protocols; individuals proposing outpatient therapeutics should propose a clinically meaningful outcome measure.
4. Evidence to justify the application of the drug to the proposed population and a description of the strength of the evidence. Briefly describe known safety profile.
5. Appropriate control groups;
6. Rationale for the significance tests to be used;
7. Sufficient evidence supporting the feasibility of enrolling the target Veteran population;
8. Proposed size, scope and duration of trial
9. Describe other similar clinical trials or competing trials
10. **FDA Documentation.** If the proposed trial will require an Investigational New Drug (IND) or Investigational Device Exemption (IDE) with the FDA, documentation of status of IND/IDE application should be included with the LOI or a description of FDA status.
11. **Availability/Access Documentation.** Attach documentation of availability and access to pharmaceutical compounds or agents, biologics, treatments, or devices. Note: the quality of the agent/product should be consistent with FDA manufacturing standards.
12. **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. Please indicate specific clinical trials experience by highlighting work in the biosketch.
13. **Submission of the LOI.** CSRD will review and respond to submitted LOIs at any time; however, an LOI must be submitted no later than December 14 for this initial prioritization exercise. LOIs must be e-mailed to CLIN-Review@va.gov by the local VA facility research office. Applicants may not upload LOIs directly to the mailbox themselves.
14. Questions relating to the LOI preparation and submission process may also be directed to CLIN-Review@va.gov .
15. 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.

1. LOIs meeting all administrative requirements will be reviewed on the following criteria:
* Strength of the evidence for therapeutic effect on COVID19 infection
* Drug availability and safety profile
* Area is not overly represented by ongoing funded clinical trials
* Feasibility of recruitment
* Falls within the purview of CSRD and the indicated VA CURES Program

**VI. Approval.** After consultation with the CURES Program Executive Steering Committee, CSRD review of LOIs will result in four possible outcomes: (a) acceptance as a potent­ial CURES study in a specific intervention lane; (b) a referral to another mechanism (e.g., standard Merit Review); (c) encouragement of closely related concepts to be merged for resubmission; (d) or disapproval of the LOI. If an LOI is accepted, the PI will work closely with the CURES Program to plan the study and submit the application for peer review. If the study is then approved for funding, the PI will also join the VA CURES Program Steering Committee.