U.S. Department of Veterans Affairs

Office of Research and Development

Pain Opioid Actively Managed Portfolio (POp AMP)

Request for Applications Summer 2023

April 18, 2023

POP AMP FEATURES

Pain Opioid AMP

Rotational leadership model

Proactively interact with relevant VA clinical/operations and NIH/DoD/other funder contacts

Ensure that ORD is not funding the same work as clinical/operations partners

Proactive management of the portfolio community, including bringing together researchers and/or other stakeholders to accomplish goals

The ability to stand up agile funding mechanisms when required

POP AMP BROAD RFAS

- **Companion Pre-Application (I02)**
- **Parent RFA**
  - **Pre-clinical, observational and epidemiological studies**
- **Clinical Trial RFA**
  - **Single and Multi-site Clinical Trials**

POP AMP PURVIEW

1. Clinical studies of the genetic, anatomical, and behavioral basis of algesia (pain), or tolerance, addiction, opioid metabolism, and tapering of opioid medication in acute and chronic painful conditions.
2. Clinical treatments emphasizing non-opioid medications and complementary and integrative approaches.
3. Implementation of treatments and approaches across VAMCs, evaluation of methods to enhance pain services, and evaluation of the quality and safety of pain care.
4. Preclinical development and translation of non-opioid therapies; and the accompanying anatomical, molecular, biochemical, behavioral, and genetic mechanism(s).

POP AMP PURVIEW

5. Studies identifying therapeutic targets for algesia (pain), tolerance and/or addiction to opioid medication in acute and chronic painful conditions.
6. Interventional and observational research of interventions to improve outcomes in opioid use disorder, including new models for OUD care, medication and behavioral therapy for OUD, use of overdose rescue medication.
7. Examination of pharmacology, pharmacotherapeutics, pharmacogenomics, and phenotype as well as the use of functional outcomes (e.g., correlating subjective pain measures with objective measures of function such as ADL, gait kinetics and kinematics, range of motion, and QoL or activity measures, etc.).

ELIGIBILITY-PI & MEDICAL CENTER

- PI must have a MD, PhD, or equivalent doctoral degree in a medical, biological, or behavioral science field.
- PI must have a VA paid appointment of at least 25 hours/week (5/8th FTE) in place before funding can begin
- Directors letter must confirm a commitment for a 5/8 appointment if funded.
  - Investigators with less than a 5/8th VA paid appointment must obtain approval of a waiver of the 5/8th FTE eligibility requirement for inclusion with their application for funding.
- All VA medical centers with an active research program are eligible.
- Each VA medical center must be registered as an applicant organization in Grants.gov and eRA Commons before any proposals can be submitted.

ELIGIBILITY-CO-I & BUDGET

- A Site PI must meet the same qualifications as a PI and be registered in ePromise at their current site.
- Non-VA investigators who have an MD/PhD equivalent are eligible to serve in the role of Co-investigator
- They cannot be listed as such on the budget forms. The Co-investigator role may be described in the proposal narrative and in the written budget justification.
- On the budget forms they should be reflected as a consultant or as having an Intergovernmental Personnel Act (IPA) assignment, if appropriate.
- If providing research services to the VA through a contract, the cost of the contract should be included on the budget forms under “All Other” expenses.
- Non-U.S. collaborators may only serve as unpaid consultants.

WAIVERS

- **Non-Veteran Enrollment Waiver**
  - **see VHA Directive 1200.01**
- **Eligibility Waiver see: Program Guide 1200.15**
- **Off Site Waiver see: Program Guide 1200.16**

Waivers are project specific.

- **Waiver Categories:**
  - **Offsite Research**
  - **Exceeding Duration or Budget Cap**
  - **Inclusion of Videos,**
  - **PI Eligibility,**
  - **Resubmissions**
  - **IPAs Make up a Large Percentage of Budget**
- **Deadline: May 1, 2023 (see RFAs)**

WAIVERS

- Copy of waiver approval letters must be included in the "Letters of Support" section of the application.

- Missing letters are considered fatal errors.

- Recruitment of Non-Veterans:

  Approved Enrollment of non-Veterans in ORD funded research required for all projects with non-Veterans (including VA employees) if awarded

REQUIREMENTS

MANDATORY REQUIREMENT:

Completion of the Involved Personnel and Collaborators information.

- **A List of ALL named personnel and collaborators with their VA and non-VA institutions, city, and state must be included in the letters of support section.**

This includes: ***PD/PI(s), co-investigators***
personnel with ANY role in the study
IPAs, consultants
mentors, collaborators,
advisory panel members, letter writers,
active partners (Program offices).

Note: If only named in the bibliography or Biographical Sketch section, they do not need to be included.

REQUIREMENTS

MANDATORY REQUIREMENT:

Completed for each Involved Personnel/Collaborator/Named person:

- **Name (Last, First)**
- **Degree**
- **Project Role**
- **VA Medical Center, City, State or VA CBOC, City, State (as applicable) (NOTE: listing just VHA is not sufficient)**
- **Academic Institution(s) or Non-VA Organization Name(s), City, State (as applicable)**

- **If individual has a joint VA and academic appointment, both must be listed**

REQUIREMENTS

MANDATORY REQUIREMENT:

A table of contents for the letters of support that lists each letter writer's

- **Name**
- **Position**
- **Office/institution**

- **Director's Letter must include language supporting protected time for clinician researchers**

LETTERS OF SUPPORT

- **A single letter of support from all individuals at the same institution is OK**
  - **if all individuals at the institution sign the letter.**
  - **Individual letters are still acceptable.**
    - **PD/P**
    - **Co-investigators**
    - **Collaborators & consultants (VA & non-VA)**
    - **Program Offices**
    - **Other Stakeholders**

PRE-APPLICATION

A Pre-Application is required and will be submitted through eRA Commons using the I02 Pre-Application form.

Pre-Application are due May 1, 2023.
See RFAs for future dates

All waivers must be submitted with the pre-application.

PRE-APPLICATION - LOI TEXT

Purpose: goals and specific objectives of the proposed research; question to be addressed, hypothesis to be tested, methods, concepts, systems or devices to be developed or evaluated.

Background: The scientific rationale for the proposed research and its relationship to other major research findings. Explain how this research will advance knowledge in POp-AMP research. Describe the significance of the research and how it relates to POp-AMP priority areas. Indicate how this research directly benefits Veterans and how it contributes to the quality of services provided by VA.

Innovation and Impact: Summarize the innovative aspects of the project and why they are likely to improve care if the project is successful.

PRE-APPLICATION - LOI TEXT

Specific Aims: Provide a numbered list of the specific aims and describe the component of the study relevant to each one

Methods and Research Plan: An outline of the proposed study design and methods. Identify Veteran subject population, sample size and rationale for inclusion or exclusion of population served (It is required that women and members of diverse ethnic and racial groups be recruited, unless contraindicated due to the study's aims.), and include data sources. Identify key issues that may have an impact on the success of the proposed project, such as: subject recruitment, participation of specialized personnel, orphan companies, space and budget. Specify if the proposed research will involve animals and, if so, the time frame to clinical application.

PRE-APPLICATION - LOI TEXT

Primary Outcomes/Endpoints: Provide a list of the anticipated primary outcomes and endpoints of the study.

Resources needed for the study with associated costs: Provide budget details. Refer to the companion FOA/RFA for project duration and budget caps.

Project History: Indicate whether this study is new, a continuation of an existing project (include years funded) or related to a previously unfunded project. Indicate the project/eRA grant number, title and date of the previous related submission.

PRE-APPLICATION - LOI TEXT

Research Site: State the name of the lead facility where the research (subject and laboratory work) will take place. If a portion of the project will be performed at any other site(s), identify the site location(s).

Cited References: Limit to one (1) page.

Key Personnel: The *Research & Related Senior/Key Person Profile(s)* is required in the Pre-application (I02) package (see Research & Related Senior/Key Person Profile(s) section below). Include all named individuals on the projects, including writers of support letters here using the Table format.

NOTABLE SECTIONS IN RFAS

Engagement of Veterans in the Design and Implementation of Research

If recruiting human subjects:

- Veterans and their caregivers can provide important insights into what outcomes matter most and the feasibility and acceptance of proposed interventions and study designs.

- Options for obtaining input include interaction with Veteran engagement panels or Veteran advisory groups as well as including Veterans on the research team.

CyberSeminar: How to Integrate Veteran Engagement from Research Plan to Publication

Toolkit: Strengthening Excellence in Research through Veteran Engagement (SERVE) Toolkit 2.0

PAIN OPIOID CORE VETERAN ENGAGEMENT

- Twelve member national panel (40% women)
- Diverse in terms of age, race/ethnicity, professional experience, location
- All have experience with chronic pain, opioid pain medications, or opioid addiction or suboxone
- Provide support throughout the research life cycle, from project proposal through publication

CORE VEP webpage: https://pain-opioid-research.umn.edu/veteran-engagement

Additional resource: GROVE https://www.hsrd.research.va.gov/publications/vets_perspectives/1221-Growing-Rural-Outreach-through-Veteran-Engagement.cfm

VETERAN ENGAGEMENT PANEL PROCESS

Initial planning

Researcher/Partner & CORE staff meet & work together to develop key questions for VEP

VEP session prep

CORE staff writes facilitation guide

Researcher/Partner & CORE staff do dry run, finalize materials

VEP meeting

CORE staff facilitates and researcher/partner attends

CORE staff provides notes/executive summary to researcher/partner

Contact Tracy Sides at tracy.sides@va.gov to learn more;
Currently scheduling in December

NOTABLE SECTIONS IN RFAS

Human Subjects Recruitment

- A large proportion of studies fail to meet recruitment goals.
- Trials need to explicitly justify the data used to estimate recruitment --
  - e.g., pilot data, prior studies, etc.
  - comment on mitigation strategies if recruitment lags.
- We expect you to include a **PLAN B** as part of your proposed recruitment strategy.

Implementation and Dissemination Plan - For HSRD Studies

Dissemination in manuscripts and to partners is insufficient.

- **Explicitly discuss next steps after project is completed. What is the path to making a difference in VA care?**
- **Need to consider who "owns" the problem the study is attempting to solve**
  - **potential barriers to implementation, and how to overcome**
  - **Who will be the partner to implement the project?**
- **Studies of interventions should consider how they can collect information relevant to implementation during the efficacy/effectiveness study (e.g., use of hybrid designs).**

PARENT RFA

- Clinical studies of the genetic, anatomical, and behavioral basis of pain, opioid tolerance, opioid dependence or addiction, opioid metabolism, in acute and chronic painful conditions that do not propose interventional treatment regimens in humans in any of the specific aims.
- Implementation of treatments and approaches across VAMCs, evaluation of methods to enhance pain services, and evaluation of the quality and safety of pain care and opioid use disorder care, and tapering of opioid medication.
- Preclinical development and translation of non-opioid therapies; and accompanying anatomical, molecular, biochemical, behavioral, and genetic mechanism(s) of pain or opioid tolerance.

PARENT RFA

- Studies identifying therapeutic targets for pain in acute and chronic painful conditions or identifying mechanisms and modifiable targets related to opioid tolerance, withdrawal, or other harmful physiological adaptations to opioid use
- Preclinical and observational research of interventions to improve outcomes in opioid use disorder, including new models for opioid use disorder (OUD) care, medication and behavioral therapies for OUD (including the role of whole health and CIH approaches), overdose prevention and treatment, and the role of Whole Health and complementary and integrative approaches.
- Investigations that will yield new biomarkers for pain.
- Studies using electronic health record/Million Veteran Program (MVP), and similar Veteran data to conduct retrospective studies and data analyses to improve understanding of basis of pain, opioid tolerance, opioid dependence/addiction, opioid metabolism, progression, genetic susceptibilities, effectiveness of pain or OUD therapies and of opioid tapering.

CLINICAL TRIAL RFA

RFA accepts applications that involve:

- **Clinical research that include treatment regimens in any of the specific aims**
- **Clinical trials (includes a control group) that include treatment regimens in any of the specific aims**
- **Pragmatic clinical trials that include an intervention**
- **Comparative-effectiveness clinical trials that compare different interventions**
- **Implementation of treatments and approaches**

PARENT & CLINICAL TRIAL RFAS

- Research Plan
  - Background and Significance
  - Preliminary Studies
  - Research Design and Methods
  - Implementation and Dissemination if HSRD
- Progress Report (not required for HSRD)
- Human Subjects
- Vertebrate Animals
- Multiple PI Leadership Plan
- Letters of Support
- Appendix
  - Appendix 1 Abbreviations
  - Appendix 2 Enrollment/Recruitment Table
  - Appendix 3 Recruitment and Retention Plan
  - Appendix 4 Multi-site Management Plan
  - Appendix 5 Milestones and Timeline
  - Appendix 6 Veteran Engagement Plan

PARENT MERIT REVIEW AWARD

PD/PIs may request funding for a maximum of four (4) years, based on the total project maximum amount outlined below.

There is no annual budget cap; thus, variable funding may be utilized as long as the overall budget cap (based on years requested) is maintained.

The salary for all personnel, including the contact PD/PI is included in this cap.

1 year = $300,000 max
2 years = $600,000 max
3 years = $900,000 max
4 years = $1,200,000 max

Clinical Trial Award Budget Cap and Duration

Budget Item	Limit for Single Site	Limit for Multi-VAMC Sites
Budget Cap	• For two (2) years, $600,000 • For three (3) years, $900,000 • For four (4) years, $1,200,000	For a 2-site a total: • For two (2) years, $600,000 • For three (3) years, $1,125,000 • For four (4) or five (5) years, $1,500,000 • Additional $100,000 per site per year for each additional site.
Duration	Up to four (4) years	Up to five (5) years

CALENDAR – SUMMER CYCLE

Date	Event
May 1, 2023	Pre-application deadline
May 1, 2023	Waiver deadline
May 15, 2023	Grants.gov opens
June 8, 2023	Down to the Wire Submission
June 12, 2023	Last Submission Date Grants.gov
June 15, 2023	Verification Deadline
August 2023	Scientific Merit Review

CALENDAR

Submission Cycles	Cycle I (Winter – HSR&D & RR&D)	Cycle II (Spring – BLR&D and CSR&D)	Cycle III (Summer – HSR&D & RR&D)	Cycle IV (Fall – BLR&D and CSR&D)
Pre-application (I02) – Letter of Intent & Waiver Request Submission Deadline	November 1	January 1 & November 1 for Clinical Trials	May 1	July 1 & May 1 for clinical trials
Begin Submitting Applications to RFA	November 15	February 1	May 15	August 1
Down-to-the-Wire Application Submission Deadline	5 business days prior to the Verification Deadline			
Application Submission Deadline to Grants.gov.	3 business days prior to the Verification Deadline 5:00 p.m. local time			
Verification Deadline in eRA	December 15	March 10	June 15	September 11
Review and Award Cycles	Cycle I (Winter – HSR&D & RR&D)	Cycle II (Spring – BLR&D & CSR&D)	Cycle III (Summer – HSR&D & RR&D)	Cycle III (Fall – BLR&D & CSR&D)
Scientific Merit Review	February	May - June	August	November - December
Administrative Review	March – April	July – August	August – September	January - February

RFAS

RFAs can be downloaded from the VA ORD intranet site:

https://vaww.research.va.gov/funding/rfa.cfm#hsrd

(VA network access only).

CONTACTS

RR&D
Audrey Kusiak
Audrey.Kusiak@va.gov

BLR&D
Carol Fowler
Carol.Fowler@va.gov

HSR&D
Cathie Plouzek
Cathie.Plouzek@va.gov

CSR&D
Jayanthi Sankar
Jayanthi.Sankar@va.gov

QUESTIONS

RFAs:

http://vaww.research.va.gov/funding/rfa.cfm

U.S. Department of Veterans Affairs

Thank you for your attendance.
Please stay safe.

We hope to review your application soon!