U.S. Department of Veterans Affairs

Office of Research and Development

Pain and Opioid AMP Updates for Fiscal Year 2025

September 26, 2024

POU AMP FEATURES

Pain and Opioid Use AMP

Team-Led AMP

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

WHAT IS NEW

- **Updated priorities**
- **Transformation to Portfolio-based Organization**
- **RFAs and NOSIs**
- **Application and funding processes**

ISRM'S TRANSITION FROM SERVICES-BASED RESEARCH TO PORTFOLIOS

The Four Services of Research Disciplines

- Clinical Science R & D
- Rehab R & D
- Health Services R & D
- Bio-medical Lab R & D

ORD Budget:

$581 M → $882M

2011 2022

Actively Managed Portfolios & Broad Portfolios

- Health Systems Research
- Brain Behavioral Mental Health
- Pain/ Opioid Use AMP
- Precision Oncology AMP
- Military Exposures AMP
- Medical Health Research
- Rehab Research & Translation
- TBI AMP
- Suicide Prevention AMP

Each Portfolio will be developed in a way that encourages collaboration, prevents duplication of research, and improves care to Veterans

KEY BENEFITS OF TRANSITIONING FROM SERVICES TO PORTFOLIOS

- **Tailored support for Veteran needs:** ISRM will transition to a Portfolio-based structure, aligning research funding with specific Veteran health priorities
- **Accelerated research impact:** Actively Managed Portfolios will focus resources on critical areas, driving faster advancements in Veteran care
- **Continued breadth of support:** Broad Portfolios will maintain funding for a diverse range of research, including early-stage discovery, translational studies, and investigator development
- **Enhanced investigator experience**: The new structure will provide streamlined support and resources to facilitate research and innovation

In order to address the issues that we have seen in the current process and the challenges they cause for ORD, ISRM proposed a revision to the application review process that has 5 components.

1. **Cross-Portfolio RFAs**
2. **Notices of Special Interest (NOSI)**
3. **RFA Standardization**
4. **Pre-Applications**

NEW CROSS-PORTFOLIO RFAS

RFAs

Research not including a clinical trial (I01)

Research including a clinical trial site (single or multisite (I01)

Pilot Research (I21)

Career Development Award 1 (IK1)

Career Development Award 2 (IK2)

Research Career Scientist (IK6)

Technology Development 1 (I01)

Pre-Application – Merit Clinical Trial (I01)

Pre-Application – Merit Non-Clinical Trials (I01)

Pre-Application – Pilot (I21)

Pre-Application – Career Development Award (IK1/IK2)

Pre-Application – Research Career Scientist (IK6)

PORTFOLIO NOTICES OF SPECIAL INTEREST

Based upon Portfolio purviews

Pain / Opioid Use Actively Managed Portfolio

Brain, Behavior, and Mental Health Broad Portfolio

Health Systems Broad Portfolio

Medical Health Broad Portfolio

Rehabilitation Broad Portfolio

Military Exposure Actively Managed Portfolio

Precision Oncology Actively Managed Portfolio

Suicide Prevention Actively Managed Portfolio

Traumatic Brain Injury Actively Managed Portfolio

Critical Research Areas/Cross Portfolio

Women's Health

Durability of Rehabilitation Interventions for Veterans

Chronic Effects of Neurotrauma

Studies on Lethal Means Safety Approaches to Suicide Prevention

NOT-RD-01-POU (NOTICE OF SPECIAL INTEREST - NOSI)

- **Primary outcome measure must be pain and/or opioid use**
- **Study has to fall under the Pain Opioid Use AMP purview**

https://www.research.va.gov/services/amp/pain_opiod.cfm

01-POU NOSI PRIORITIES

- 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, approaches, and methods to enhance pain services, and evaluation of quality and safety of pain care, 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.

01-POU NOSI PRIORITIES (CONTINUED)

- Clinical trials and observational 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.
- Clinical trials 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.

01-POU NOSI PRIORITIES (CONTINUED)

- Pragmatic clinical trials for treatment of painful conditions using non-pharmacological approaches including Whole Health, complementary and integrative health, and biobehavioral approaches, on specialty populations including long-term opioid therapy, opioid use disorder, aged, minoritized persons, women, and overlapping painful conditions.
- Development and validation of predictive analytics and biomarkers to identify Veterans with high impact chronic pain, or who are at risk of developing chronic pain or opioid use disorder (OUD), as well as the effectiveness of pain or OUD therapies and opioid tapering, to guide clinical care for these individuals and those living with chronic pain. Studies of interest are limited to data mining and analysis of Million Veteran Program (MVP) and/or EHR, and clinical studies involving human subjects.

01-POU NOSI PRIORITIES (CONTINUED)

- Identification and evaluation of environmental, social, and policy changes addressing social determinants to prevent opioid misuse (including policies related to telehealth/virtual care, Veterans benefits, jail diversion programs, etc.).
- Where appropriate, applications should include outcome measurements that go beyond symptom-based assessments to consider the functioning and well-being of the whole person.

01-POU NOSI PRIORITIES (CONTINUED)

- Studies of fentanyl adulterated with xylazine. Proposed studies must be responsive to the Office of National Drug Control Policy (ONDCP) Fentanyl Adulterated or Associated with Xylazine Response Plan (FENTANYL-ADULTERATED-OR-ASSOCIATED-WITH-XYLAZINE-EMERGING-THREAT-RESPONSE-PLAN-Report-July-2023.pdf (whitehouse.gov).
- Harm reduction services and treatment programs that reduce pain medication usage but not complete abstinence, including:
  - Identification and evaluation of effective harms reduction strategies for individuals with OUD.
  - Identification and evaluation of effective harms reduction strategies in the different care settings (e.g., primary care, specialty care, etc.).
  - Effective communication strategies with individuals living with chronic pain based on experiences and sensitivities.
  - Evaluation of the syringe service project.

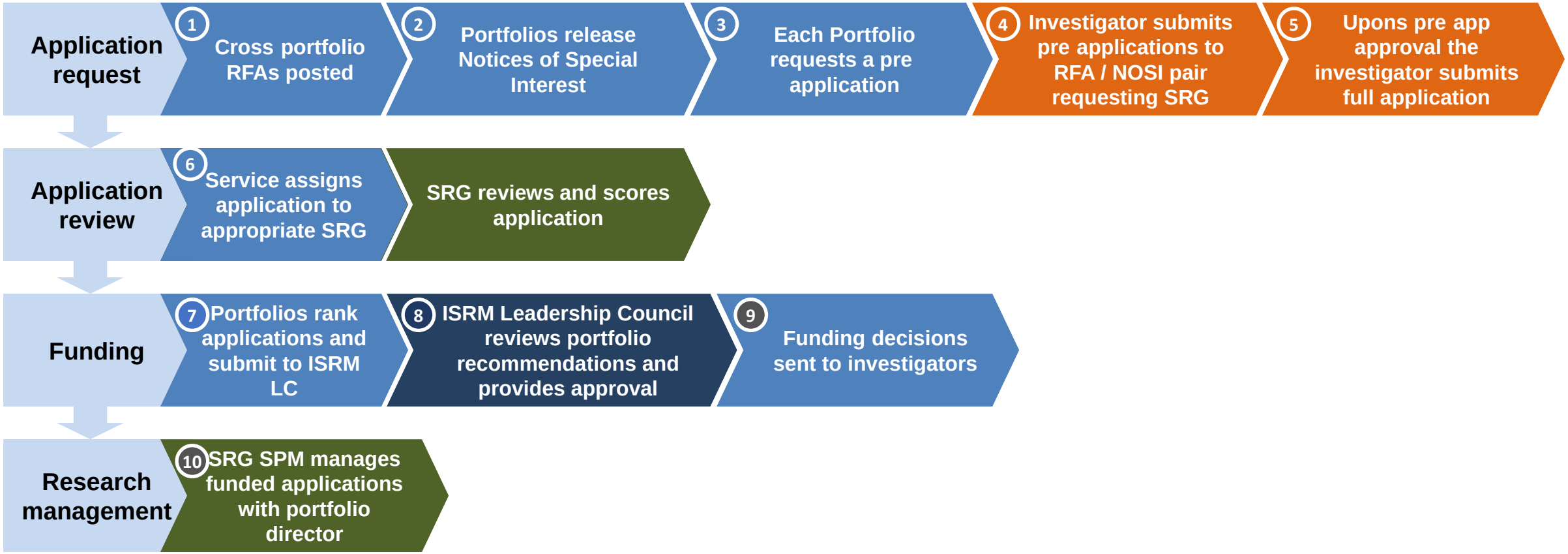
WHAT PAIN OUTCOMES SHOULD BE MEASURED?

Domain	Measure	# of Items
Subjective Health Status	Self-Rated Health (SRH)	1
Pain Intensity/Interference	**P**ain Intensity, Interference with **E**njoyment, Interference with **G**eneral Activity	3
Self-Efficacy	Pain Self-Efficacy Questionnaire, 2 Item (PSEQ-2)	2
Unhelpful Pain Thoughts (catastrophizing)	UW Concerns About Pain, 2 Item (CAP-2)	2
Sleep	Sleep Quality Scale (SQS)	1
Depression	Pain Health Questionnaire, 2 Item (PHQ-2)	2
Anxiety	Generalized Anxiety Disorder, 2 Item (GAD-2)	2
General Well-Being	Well-Being Signs Tool (WBS)	3
	TOTAL	**16**
Perceived Treatment Impact	Patient Global Impression of Change (PGIC Scale) – **FOLLOW-UP ONLY**	1
	TOTAL	**17**

REVISED RESEARCH APPLICATION PROCESS

Key

- *Portfolio actions*
- *Investigator actions*
- *Scientific Review Group (SRG) actions*
- *ISRM Leadership Council actions*



HOW TO APPLY TO POU AMP

- Align with POU AMP priorities in NOSI(s)
- Identify the SRG
- Consult with POU AMP SPMs
- Identify best RFA and due dates
- Submit preapplication
- Submit full application if preapplication approved

RFAs accepted by POU AMP:

- Parent Merit Review Award (RD-01-MRA)
  - Preapplication RFA: (RD-01-PREM)
- Merit Review Award for Clinical Trials (RD-01-MRCT)
  - Preapplication RFA: (RD-01-PRET)

RFA REQUIREMENTS

- Eligibility requirements:
  - 5/8 VA at time of funding
  - Work conducted fully in VA or VA-leased space
  - Limit on new non-clinicians for Spring/Fall review cycle
  - Waivers granted by the ISRM Leadership Council
- Budget caps:
  - Parent Merit: Non-clinician PI salary- 3/8 support above the cap for contact PI
  - Any additional salary support required by the non-clinician PI would be included in the budget, including multi-PI salary.
  - Standard research budget caps based on research type

PARENT MERIT REVIEW AWARD: RD-01-MRA

- Contact PD/PI can request up to 3/8ths salary above the cap.
- Can request more 8ths of salary support from the $200,000 budget cap.
- PD/PIs paid from the clinical appropriation or who have full VA salary support from another source should not request salary through this award.

	Budget Cap and Duration
Budget Cap	$200,000 per year
Duration	Up to four (4) years

CLINICAL TRIAL RFA: RD-01-MRCT

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 For a 3 or more sites a total: • Additional $100,000 per site per year for each additional site added to total budget cap
Duration	Up to four (4) years	Up to five (5) years

PRE-APPLICATION RFAs

- **Clinical Trials**
  - **Pre-apps due 12 weeks before full application due date**
  - **Administrative + Scientific review with feedback**
  - **Stations notified of concerns/disapprovals**

- **Parent Merit**
  - **Pre-Apps due six weeks before full application due date**
  - **Administrative review with optional scientific review and feedback**
  - **Stations notified of concerns/disapprovals**

PREAPPLICATION ATTACHMENT– COVER PAGE - PAGE LIMIT 1

a) Notice of Special Interest (NOSI) and Companion RFA

b) Portfolio Identifier: as noted in each NOSI

c) Resubmissions ONLY: eRA award number and title of research application (I01)

d) Scientific Review Group (SRG) Preference

e) PD/PI Data: Basic information contained on SF 424 Cover.

- U.S. Citizen? Clinician/Non-Clinician? Early Investigator? Prior CDA Awardee?

f) Population Description: Any proposed enrollment of non-Veterans must be described in this section.

g) Key Words: Provide 3 – 5 keywords

h) Million Veteran Program (MVP): Whether the proposed study uses MVP data. MVP Requests should be submitted at least four (4) weeks in advance of the Pre-application submission deadline.

PRE-APPLICATION TEXT: SEE RFA

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

b) Background: The scientific rationale for the proposed research and its relationship to other major research findings. Describe the significance of the research and how it relates to the goals of the ISRM Broad or Actively Managed Portfolio. Indicate how this research directly benefits Veterans and how it contributes to the quality of services provided by VA.

c) Gaps Addressed: Briefly describe knowledge and practices.

PRE-APPLICATION - LOI TEXT

d) Methods and Research Plan: An outline of the proposed study design, methods and innovation. 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. Indicate implications for technology transfer and potential for replication.

e) Outcomes: Briefly describe the primary outcomes and endpoints and the sustainability of the proposed project, i.e., clinical program office and plans.

PRE-APPLICATION - LOI TEXT

f) 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 only writers of support letters here using the format in Table 1: Name Institution(s) Role and Percent Effort Expertise

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

h) Project History: Indicate whether this study is new, a continuation of an existing project (Renewal, include years funded) or related to a previously unfunded project.

PRE-APPLICATION - LOI TEXT

i) **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).

j) Cited References: Limit to one (1) page.

Note: For Clinical Trial Preapplication – see RFA for additional requirements:

Outcomes

Investigator Qualifications

Regulatory Considerations, etc.

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: 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

MILLION VETERAN PROGRAM (MVP)

NEW: MVP Data Use Request

Goal– ensure that investigators are submitting project proposals that can be done with the MVP data and environment available before the scientific review process

- **MVP data use request form is in the appendix of the current MVP guidance**
  - Brief description of aims
  - Required data types for project
  - Additional software/tools request
  - Which service/portfolio/RFA do you plan on submitting to
- **Rolling submission**
  - Ensure that you submit your MVP data use request several weeks prior to the due date for your LOI/preapplication/ITS or full submission. Remember that you may want to leave time for discussion with MVP.
  - MVP staff will review your application for feasibility and provide an approval memo
- **Attach the MVP approval memo to your LOI/ITS/pre-application or full application**
- **Any LOI/ITS/Pre-Application or Merit application with MVP aims that does not have an Approval Memo will be administratively rejected**
- Detailed guidance available as of 9/19/2023 here: Community - File : GenHub (va.gov)

- Questions can be sent to MVPLOI@va.gov

MVP Data Use Request Form

PI Name(s):

VA Station(s):

Proposed title:

Does your proposal also include non-MVP aims? ☐ yes ☐ no

Brief description of proposal aims (no more than 1 page total)

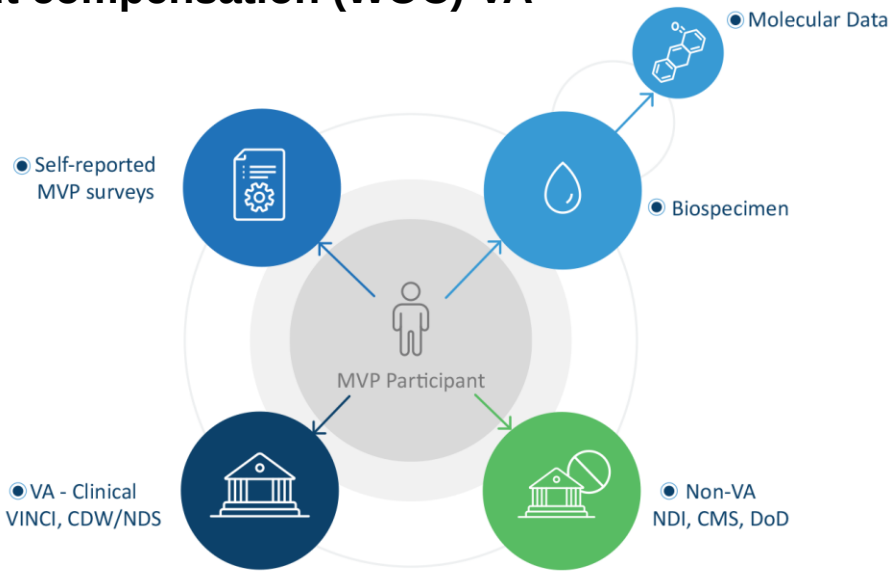
Please include information/numbers from the Data Explorer Tool in GenHub

https://genhub.va.gov

MVP DATA ACCESS GUIDANCE

1. MVP access is for VA investigators with VA funded research projects with MVP aims
   - The applicant PI and/or MPI (if applicable) should be VA employee(s) and should meet eligibility requirements of the Service/portfolio to which they are applying.
   - Any person on the application requiring access to the MVP data must be research credentialed with a VA appointment OR a without compensation (WOC) VA appointment.

2. MVP data available for request includes:
   - EHR data from VINCI
   - MVP surveys
   - Genotypes (650k), Whole genome sequences (100k), methylation (40k)
   - Nutrition data



3. Regulatory notes:
   - MVP projects are submitted to Central IRB
   - Access to MVP data is project specific
   - MVP data cannot be requested for existing VA projects or non-VA funded projects
   - Bringing in outside data into MVP can be done under certain circumstances and requires a DUA
4. Phenotypes generated through MVP projects should be deposited into CIPHER

CIPHER Program

Centralized Interactive Phenomics Resource

Overview

- Collection of phenotypes began as part of the Million Veteran Program (MVP)
- Formal VA Office of Research and Development (ORD) funding started FY20
- CIPHER's directive from VA ORD is to reach 10K phenotypes over 5 years

Mission

To provide an encyclopedia of VHA EHR-based phenotyping through integration of phenomics work across the VA, to optimize and expedite VA data use for both research and clinical operations and to serve the VA community

https://vhacdwdwhweb100.vha.med.va.gov/phenotype/index.php/VA_Phenomics_Library__Centralized_Interactive_Phenomics_Resource_(CIPHER)

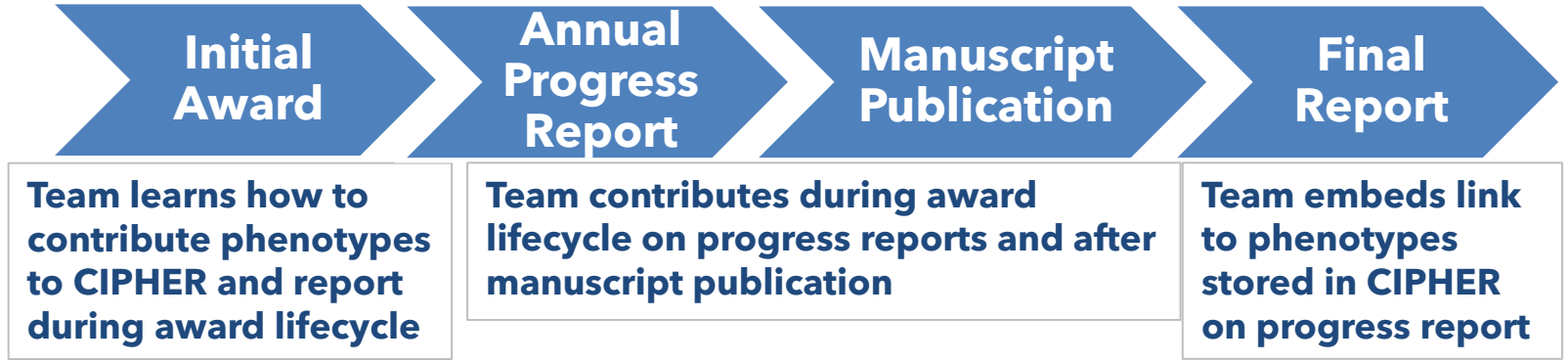
- ✓ Scalability
- ✓ Reusability
- ✓ Efficiency
- ✓ Communication
- ✓ Collaboration

CIPHER as a VA-Wide Resource

- Part of an enterprise-wide approach to provide a phenotyping resource for ORD supported research
- CIPHER collects phenotypes from VA programs and projects, including key partners *(MVP, VINCI, CSP & others)*
- Support of priority programs
  - Office of Mental Health and Suicide Prevention
  - Precision oncology
  - Military exposures
  - Traumatic brain injury
  - EHR modernization and interoperability

CIPHER

VA Awardees Phenotype Contribution During the Award Lifecycle



- **Messaging to VA awardees**
  - **Importance of participating in VA-wide expansion of phenomics knowledgebase**
  - **Benefits of contributing phenotype algorithms to VA's central knowledgebase including visibility of research, more citations of published work, and enhance collaboration**
  - **Becoming a VA SME partner for current and future CIPHER resources and innovation**
  - **Access to project specific phenomics metadata for tracking, reporting and dissemination purposes**
- **Note that CIPHER language is already in the current HSRD Merit RFA**

APPLICATION COMPONENTS

- Specific Aims
- Research Plan
  - Background and Significance
  - Preliminary Studies
  - Research Design and Methods
  - Next steps to implementation
- Progress Report (Renewals and CDA2 applicants for first Merit)
- Human Subjects and/or Vertebrate Animals
- Multiple PI Leadership Plan (if applicable)
- Director's Letter
- Letters of Support
- DMAP
- COI
- Appendix
  - Appendix 1 – Preapplication approval email
  - Appendix 2 – abbreviations
  - Appendix 3 – Translational Pipeline appendix
  - Others as required or needed (see RFAs)

NOTABLE SECTIONS IN RFAS

- **Engagement of Veterans in the Design and Implementation of Research**
  - **Veterans and their caregivers can provide important insights into what outcomes matter most, and the feasibility and acceptance of the 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**

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.
- Include a PLAN B as part of your proposed recruitment strategy.

NOTABLE SECTIONS IN RFAS

Implementation/ Dissemination

Dissemination in manuscripts and to partners is insufficient.

- **Explicitly discuss next steps after project is completed to move the research along the translational pathway and/or into practice**
- **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? Letters of support assist us with determining the commitment of partners.**
- **Studies of interventions should consider how they can collect information relevant to implementation during the efficacy/effectiveness study (e.g., use of hybrid designs).**

REQUIREMENTS FOR FULL APPLICATION

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/PI**
  - **Co-investigators**
  - **Collaborators & consultants (VA & non-VA)**
  - **Program Offices**
  - **Other Stakeholders**

CALENDAR FOR RD-01-MRA

Submission Cycles	Winter	Spring	Summer	Fall
Site Waivers for 2nd new non-clinician investigator slot	NA	October 15	NA	April 15
MVP Data Use Request	October 1	January 1	April 1	July 1
Pre-application (I02) – Letter of Intent & Waiver Request Submission Deadline	November 1	February 1	May 1	August 1
Begin Submitting Applications	November 15	February 15	May 15	August 15
Down-to-the-Wire Application Submission Deadline. After this date the full 2 day application viewing window cannot be used.	December 8	March 8	June 8	September 8
Application Submission Deadline to Grants.gov. Changed/corrected applications submitted after this date will be withdrawn.	December 10	March 10	June 10	September 10
Review and Award Cycles				
Scientific Merit Review	February – March	May - June	August - September	November - December
Administrative Review	March – April	July – August	September - October	January - February
Earliest Project Start Date	Upon Completion of JIT			

CALENDAR FOR RD-01-MRCT

Submission Cycles	Winter	Spring	Summer	Fall
Pre-application (I02) – Letter of Intent & Waiver Request Submission Deadline	August 1	November 1	February 1	May 1
Begin Submitting Applications	November 15	February 15	May 15	August 15
Down-to-the-Wire Application Submission Deadline. After this date the full 2-day application viewing window cannot be used.	December 8	March 8	June 8	September 8
Application Submission Deadline to Grants.gov. Changed/corrected applications submitted after this date will be withdrawn.	December 10	March 10	June 10	September 10
Review and Award Cycles				
Scientific Merit Review	February – March	May - June	August - September	November - December
Administrative Review	March – April	July – August	September - October	January - February
Earliest Project Start Date	Upon Completion of JIT			

RFAS AND NOSI

RFAs and NOSIs can be downloaded from the VA ORD intranet site:

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

(VA network access only).

Look under:

- **NOSIs – Actively Managed Portfolios and**
- **Requests for Applications (RFAs)**

CONTACTS

For general review questions/issues: vhaISRM@va.gov
Grants.gov/eRA Commons questions/issues: vhacordera.vhacordera@va.gov
Clinical trial questions: clin-review@va.gov
For questions about the POU AMP: VHACOORDPainAMP@va.gov

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Please reach out early and often!

QUESTIONS

RFAs:

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

VA | U.S. Department of Veterans Affairs

Thank you for your attendance.

We hope to review your application soon!