POU AMP FEATURES

Pain Opioid 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

- **Updated priorities**
- **New Focus areas**
- **New RFA on pharmacogenomics/ biomarkers**
- **New CIPHER and Million Veteran Program requirements**

- **Parent RFA: Pre-clinical, observational and epidemiological studies**

- **Clinical Trial RFA: Single and Multi-site Clinical Trials**

- **Focused RFA for Pharmacogenomics/Biomarker Studies**

- **Companion Pre-Application (I02)**

- **Primary outcome measures have to include a measurement of pain/opioid use**

- **Study has to fall under the Pain Opioid Use AMP purview**

- **Studies identifying therapeutic targets for pain or identifying mechanisms and modifiable targets related to opioid tolerance, withdrawal, etc.**

- **Preclinical and observational clinical research of interventions to improve outcomes in opioid use disorder, incorporating a Whole Health approach.**

- **Studies using electronic health record/Million Veteran Program (MVP), and similar Veteran data to conduct retrospective studies and data analyses to improve understanding of pain chronicity and response to opioids.**

- **Clinical studies - genetic, anatomical, and behavioral basis of pain, opioid tolerance, opioid dependence or addiction, opioid metabolism. (NO interventions).**

- **Implementation and evaluation of treatments and approaches across VAMCs relating to the quality and safety of pain and opioid use disorder care, and tapering of opioid medication.**

- **Preclinical development and translation of non-opioid therapies and reversal of xylazine intoxication.**

- **Investigations that will yield new biomarkers for pain.**

Parent and Clinical Trial POU AMP RFAs

- **Studies of fentanyl adulterated with xylazine**

- **Harm reduction services and treatment programs**

- **Development of pharmacological alternatives for treatment of pain and xylazine reversal**

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

Focus:

The development and validation of *predictive analytics and biomarkers* to identify Veterans with High Impact Chronic Pain (HICP; i.e., the Center for Disease Control definition of chronic pain that is experienced on most days or everyday, and limited daily life or work activities on most days or every day during the previous 3 months), or who are at risk of developing HICP or opioid use disorder (OUD), and to guide clinical care for these individuals and those living with chronic pain.

PHARMACOGENOMIC/BIOMARKER RFA

- **Machine learning and AI methods to extract data from EHR, etc., to determine best course of treatment, or development of chronic pain.**

- **Studies identifying behavioral, clinical, genetic, and epigenetic risk factors to identify: 1) Individuals with high impact chronic pain (HICP); 2) Individuals at risk of progressing to HICP; 3) Individuals at risk of developing OUD as a result of prescribed opioids.**

- **Studies identifying factors that may predict responsiveness to specific pharmacologic or nonpharmacologic treatments for chronic painful conditions.**

- **Prospective studies validating biomarkers etc. to predict treatment approaches for individuals with HICP.**

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**

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

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

Pre-Application are due November 1, 2023 for Winter 2024 review cycle.
See RFAs for future dates.

All waivers must be submitted with the pre-application as well as MVP data use.

Purpose: Goals and specific objectives of the proposed research. (Hypotheses, methods, concepts, questions to be addressed.)

Background: The scientific rationale for the proposed research and its relationship to other major research findings. (How the research will benefit Veterans. How does the study relate to POU AMP priority areas.)

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

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. (Veteran subject population, sample size and rationale for inclusion or exclusion of population served 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.

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.

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.

- 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.

- **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**
  <mark>**Waivers are project specific.**</mark>
- **Waiver Categories:**
  - **Offsite Research**
  - **Exceeding Duration or Budget Cap**
  - **Inclusion of Videos,**
  - **PI Eligibility,**
  - **Resubmissions**
  - **IPAs Make up a Large Percentage of Budget**
- <mark>**Deadline: November 1, 2024 for HSRD and RRD (see RFAs)**</mark>

WAIVERS

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

- **<mark>Missing letters are considered fatal errors.</mark>**

- **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

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
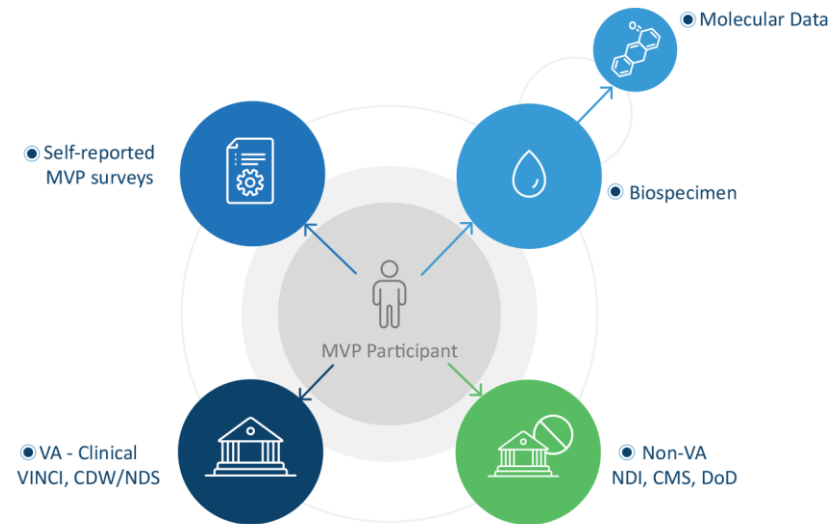
https://genhub.va.gov

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**

Self-reported MVP surveys · Molecular Data · Biospecimen · MVP Participant · VA - Clinical VINCI, CDW/NDS · Non-VA NDI, CMS, DoD

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**

> ✓ **Scalability**
> ✓ **Reusability**
> ✓ **Efficiency**
> ✓ **Communication**
> ✓ **Collaboration**

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)
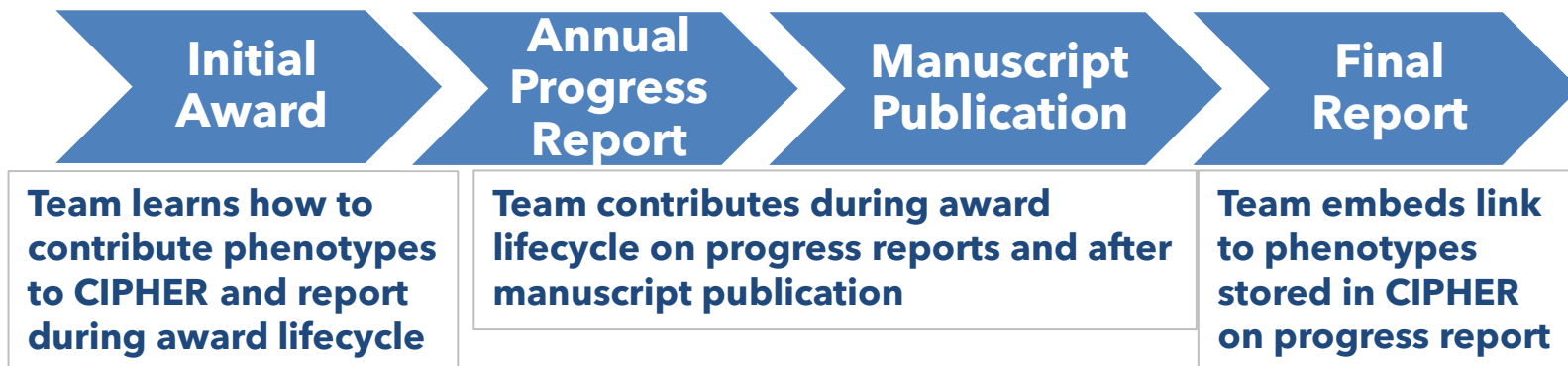
CIPHER as a VA-Wide Resource

- **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**

Initial Award	Annual Progress Report	Manuscript Publication	Final Report
Team learns how to contribute phenotypes to CIPHER and report during award lifecycle	Team contributes during award lifecycle on progress reports and after manuscript publication		Team embeds link to phenotypes stored in CIPHER on progress report

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

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.

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**

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**

- **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**

Engagement of Veterans in the Design and Implementation of Research (Scored for HSRD)

- **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

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.**

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? 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).

- **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 (if applicable)**
- **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**

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 15	June 15	September 15
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 can be downloaded from the VA ORD intranet site:
https://vaww.research.va.gov/funding/rfa.cfm
(VA network access only).
Look under ORD-Wide RFAs

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

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

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

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

Please reach out early and often!

RFAs:

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

- **What is the POU AMP?**

Answer: The Pain/Opioid Use Actively Managed Portfolio (POU AMP) has been established as a shared cross-service portfolio with representation from BLR&D, CSR&D, HSR&D and RR&D. The focus of the POU AMP will be to review preclinical, translational, clinical, rehabilitation, and health services/implementation research applications where pain and opioid use, and the consequences of opioid use, are the primary outcome(s) of the study.

- **What funding opportunities are available under the POU AMP?**

Answer: The POU AMP has 3 merit Request For Applications (RFAs):

1) The Broad Parent POU AMP RFA funds preclinical, translational, observational, behavioral, epidemiological, and health services/implementation research applications focusing on Pain and Opioid Use.

2) A companion Clinical Trial POU AMP RFA for investigator-initiated single and multi-site clinical trials on painful conditions and opioid use in Veterans.

3) A focused RFA on pharmacogenomics and biomarkers

Veteran engagement is part of the POU AMP RFAs for clinical research and trials as an unscored criteria for BX, RX and CX RFAs and a scored criteria for HSRD-focused applications.

- **When will I be able to apply? Are these RFAs offered for Future submission Rounds?**

Answer: Applications for Rehabilitation and Health Services Research will be accepted for the Winter round, with Pre-applications due on November 1 and full applications due in early December. POU AMP RFAs will continue to be available for future Merit submission rounds as well. Applications will follow the general service timelines (Spring/Fall for BLR&D and CSR&D, and Summer/Winter for HSR&D and RR&D oriented applications); however, they may not have the exact deadlines as the other Parent RFAs in all services. Please check the due dates in the POU AMP RFA

- **Is a Letter of Intent required?**

Answer: A pre-application is required. Pease refer to BX-23-200, CX-23-200, RX-23-200 and HX-23-200 (Pre-Application RFA for the POU AMP). A Pre-application is required for all POU AMP RFAs and must be submitted through eRA. Please check the due dates in the POU AMP RFAs and Pre-application.

- **Does this mean other HSR&D, BLR&D and CSR&D RFAs will require a pre-application (I02) through eRA? How about other requirements?**

Answer: No, currently, the only RFAs that require pre-applications are all RR&D RFAs and three cross-service Pain/Opioid AMP RFAs. Other HSR&D RFAs will still use the Intent to Submit process through ART and other BLR&D and CSR&D RFAs will follow the current LOI requirements for those services, if required by the RFA. Please see the submission requirements for each individual RFA.

- **What are the budget caps for the POU AMP RFAs?**

Answer:

1) Parent and focused RFA: 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

2) Clinical Trial RFA Budget:

Budget Item	Limit for Single Site	Limit for Multi-Site
Budget Cap	• For 2 years, $600,000 • For 3 years, $900,000 • For 4 years, $1,200,00	For a **2-site** total: • For 2 years, $600,000 • For 3 years, $1,125,000 • For 4 or 5 years, $1,500,000 • Additional $100,000 per site per year for each additional site.
Duration	Up to 4 years	Up to 5 years

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

- **Where can I find the RFAs?**

Answer: The RFAs are now posted on the RFA page of the ORD intranet site at https://vaww.research.va.gov/funding/rfa.cfm (available on the VA intranet, only). Look under the section for ORD Wide Requests for Applications

- **How do I decide which service/RFA to apply to?**

Answer: Please reach out to POU AMP Scientific POCs:

- **BLR&D:** Dr. Carol Fowler; Carol.fowler@va.gov

- **CSR&D:** Dr. Jayanthi Sankar; Jayanthi.sankar@va.gov

- **HSR&D:** Dr. Cathie Plouzek; Cathie.plouzek@va.gov

- **RR&D:** Dr. Audrey Kusiak; Audrey.kusiak@va.gov

- **Do we need to do a full preapplication for resubmission of proposals?**

Answer: Preapplications are required for both new projects and resubmissions. If you are resubmitting a proposal that **was previously reviewed on the POU AMP RFAs**, you would have to submit a pre-application for each submission. Please see the instructions in the Pre-Application RFAs (i.e. BX-23-200, CX-23-200, RX-23-200 or HX-23-200) for full instructions on resubmissions.

- **Are there any changes to non-VA investigators role - their salary and involvement?**

Answer: Please see the RFAs for more guidance, but briefly: Non-VA investigators who have an M.D./Ph.D. equivalent are eligible to serve in the role of Co-investigator, but they cannot be listed as such on the budget. The Co-investigator role may be described in the proposal narrative. On the budget they should be reflected as a consultant or as

- having an Intergovernmental Personnel Act (IPA) assignment, if appropriate. If they are providing research services to VA through a contract, the cost of the contract should be included on the budget forms under all other expenses. Collaborators from outside of the U.S. may only serve as unpaid consultants.

- A Site PI must meet the same qualifications as a Study PI; this includes a minimum of a 5/8th VA appointment or waiver of the 5/8th appointment eligibility requirement, a M.D./Ph.D. or equivalent.

- See Program Guide 1200.15: Eligibility for VA Research Support for additional guidance.