



**Department of Veterans Affairs  
Office of Research and Development  
Guidance Document for VA Merit Projects with access to MVP data  
March 5, 2021**

## **Introduction**

The **Million Veteran Program (MVP)** is a national genetics research initiative of the Department of Veteran Affairs Office of Research and Development (ORD). The purpose of MVP is to create a longitudinal cohort of at least one million Veterans to understand better how genes, lifestyle behaviors, and military exposures impact health and illness. MVP will promote genomic discoveries and bring personalized medicine to VA health care. By volunteering to join one of the world's largest research projects focused solely on genetics and health, Veterans can contribute to genomic and epidemiological studies to better inform health care delivery. Participants who volunteer in MVP provide access to their medical records, complete a baseline survey, an optional lifestyle survey, and provide a blood specimen to complete their enrollment into the program. Currently, MVP has over 832,000 Veterans participating.

Since 2015, VA has funded over 30 VA research projects using MVP data. These projects were considered the alpha, beta, and gamma test projects, and represented VA investigators from all four ORD research services and the Cooperative Studies Program. The project teams have helped MVP test the computational infrastructure, and the regulatory and administrative frameworks around data access in addition to increasing the scientific knowledge regarding the genetics of various chronic illnesses and traits impacting US Veterans. Now it is time to allow for broader access to the MVP data resources, **particularly to VA investigators who have not previously had access to this data.**

This guidance document outlines how VA investigators can apply for Merit Awards that include access to MVP data across the four ORD research services. MVP data will be available for VA investigators for Merit projects beginning the Fall 2021 cycle for Biomedical Laboratory Research and Development (BLR&D) and Clinical Science Research and Development Service (CSR&D) and the Winter 2022 cycle for the Health Services Research and Development (HSR&D), and Rehabilitation Research and Development (RR&D).

**NOTE: CDA-2 Career Development Applicants (BLRD/CSR&D) can apply for MVP access, but this guidance document does not apply. Please refer to <https://www.research.va.gov/funding/cdp.cfm>**

## Available MVP data and Computing Environment:

All data analysis using MVP data will take place behind the VA firewall in the Genomic Information System for Integrative Sciences (**GENISIS**) research environment. **GENISIS** serves as the MVP informatics and computing platform. In addition, **GENISIS** also supports recruitment and enrollment module, and the Biorepository Laboratory Information Management System (LIMS). The MVP data resources include electronic health records extracted from the VA Corporate Data Warehouse (**CDW**) through the Veterans Informatics and Computing Infrastructure (**VINCI**), curated self-reported survey data and genomic data, and a High-Performance Computing (HPC) cluster with analytical tools. Researchers will have access to data, computing resources, and analytical tools within this secure study-specific study mart in **GENISIS**. The Data and Computational Sciences (**DACS**) Core team builds and manages the protected data and computing infrastructure for MVP behind the VA firewall. Researchers will also have access to the Centralized Interactive Phenomics Resource (CIPHER), the VA Phenotype library with a catalog of phenotype descriptions and associated metadata.

The following MVP data will be available for approved projects:

- 1) Electronic Health Records (EHR) data on **~832,000 MVP participants**, extracted from the CDW through the Veterans Informatics and Computing Infrastructure (VINCI).
- 2) Data from two surveys completed by the MVP participants. The first is a “Baseline Survey” on ~75% of the participants, focusing on demographic characteristics, medical and family history, health status, and lifestyle habits. The second is an optional “Lifestyle Survey” designed to gather detailed military and environmental exposure, dietary habits, and other behavior data, available on ~60% of the MVP participants. More information can be found in Genhub resource.
- 3) Genotype data on **~650,000 MVP participants**, generated by a custom designed Affymetrix genotyping array designed to maximize genomic coverage of common and rare SNPs as well as markers with clinical significance. The custom MVP Affymetrix chip utilizes the Affymetrix Biobank Array backbone. There are about ~800,000 SNPs on the array. More information can be found in Genhub resource.

Notes:

- **Applicants may not request access to MVP biospecimens or re-contact of MVP participants as part of the proposal.**
- **MVP sample collection and processing are not currently CLIA certified, and resulting data cannot be used to make clinical decisions.** Studies should not include procedures that would require communicating genomic results back to the MVP participants.
- **Applicants interested in the opportunity to access MVP data for Merit projects should register for an account in Genhub where they can view aggregate data**

from the MVP cohort to help prepare their letters of intent and applications. (<https://vawww.genisis.med.va.gov/genhub> ).

- **There will be no concierge service for MVP data not readily available through the Genhub portal.**
- *Interested applicants should note that MVP is an iterative data resource for VA and the broader research community. Tools and final data sets remain inside the **GENISIS** computing environment for future query and research by other researchers following an initial embargo period.*
- *Any new phenotypes created and validated as a result of an MVP Merit Award will be required to be submitted to the VA Phenotype library, CIPHER (the Centralized Interactive Phenomics Resource) which can be found at this link [https://vhacdwdwhweb100.vha.med.va.gov/phenotype/index.php/Centralized\\_Interactive\\_Phenomics\\_Resource\\_\(CIPHER\)\\_Centralized\\_Interactive\\_Phenomics\\_Resource\\_\(CIPHER\)\\_-VA\\_Phenomics\\_Library](https://vhacdwdwhweb100.vha.med.va.gov/phenotype/index.php/Centralized_Interactive_Phenomics_Resource_(CIPHER)_Centralized_Interactive_Phenomics_Resource_(CIPHER)_-VA_Phenomics_Library).*

#### **Applicant requirements:**

1. In the spirit of increasing new access to the data, the applicant PD/PI and/or MPI cannot be personnel on a current or previous MVP project. *This requirement may be relaxed in future review cycles.*
2. The applicant PD/PI and or MPI (if applicable) should be VA employee(s) and should meet eligibility requirements of the Service to which they are applying. All other named personnel on the application should meet the eligibility requirements of the Service to which they are applying.
3. Any person on the application requiring access to the MVP data must have a VA appointment OR a without compensation (WOC) VA appointment.

*Note: Collaborative research teams with expertise in genomics, phenomics and data science are encouraged.*

#### **Request for Application (RFA information)**

Approval for working with MVP data is a multistep process requiring 1. Registration in GENHUB for Preparatory to Research Access; 2. Submission of an LOI/ITS to the specific service (BLR&D, CSR&D, HSR&D, or RR&D) and obtaining approval; and 3. Submitting an application to BLR&D, CSR&D, HSR&D, or RR&D service Parent I01 or other relevant RFA and obtaining funding approval. **There is not a separate MVP RFA.**

Applicants can apply to any relevant RFA across any ORD research services (see appendix A for more information). Applicants must follow all the rules and requirements of the specific RFA to which they are applying. Budgets, project duration, and eligibility are Service and RFA specific.

## Letter of Intent (LOI) and Application information:

*Before applying, applicants should review existing MVP research projects (<https://www.mvp.va.gov/webapp/mvp-web-participant/#/public/science>) to ensure their proposal does not duplicate current research studies.*

Briefly, steps involved in applying to access to MVP data are described below:

### Step 1: Registration in GENHUB and Preparatory to Research Access

- <https://vaww.genisis.med.va.gov/genhub>
- Explore MVP aggregate data with the cohort builder and results explorer tools in Genhub.
- Ensure that the MVP cohort numbers and data are available to support PD/PI's research questions.

**\*\*We will be providing a Q and A sessions on how to use Genhub in March 2021\*\***

### Step 2: Write and Submit Letter of Intent (LOI)

#### A. LOI Submission Process for BLR&D, CSR&D and HSR&D

- An LOI is required for every project requesting MVP data access, even if the RFA to which one is applying does NOT usually require it. Please see the attached template in Appendix B for requirements.
- If the RFA to which one is applying ALREADY requires an LOI (e.g., CSR&D clinical trial), please, complete the MVP LOI.
- HSR&D applicants will be required to complete an LOI and an Intent to Submit (ITS) at the same time.
  - HSR&D requires Intent to Submit (ITS) notification through HSR&D's ART website.
  - The ITS is required for this funding opportunity and is a process separate from the requirements for Grants.gov submission. The ITS is a key step in the proposal submission process and assists HSR&D by ensuring that the proposed research is appropriate to the goals of HSR&D and VA. The ITS is submitted electronically at <http://art.puget-sound.med.va.gov/IntentSubmitIntro.cfm>. The deadlines for ITS may be found in Table 4 of the RFAs.
  - Applications submitted to Grants.gov without a completed ITS will not be accepted or reviewed.
  - NOTE: The ITS title and the full proposal title must match. Once an ITS has been approved by the ACOS, titles may NOT be changed without a formal request from the ACOS to the Director of HSR&D. Title change requests

must be submitted to [vhacoscirev@va.gov](mailto:vhacoscirev@va.gov) by the deadline found in Table 4 of the RFAs.

- *HSR&D LOIs will be approved unless the proposed PD/PI and or MPI are personnel on current or past MVP projects.*

B. **RR&D:** A Letter of Intent must be submitted using the RR&D Pre-Application (I02) RFA RX-21-100 available at <https://vaww.research.va.gov/funding/rfa.cfm#rrd>.

C. **Review of LOIs will be done by the appropriate ORD Services.**

### **Step 3: Submission of Proposals**

After receiving *notification of their LOI approval*, investigator groups can seek funding and approval with a full proposal according to the dates and requirements of the Service and RFA to which they are applying. The corresponding peer-review process will occur using existing ORD-based scientific and administrative review mechanisms. Specifically, the preparation, submission, and review of applications for peer-review will utilize existing RFAs and service processes.

Approved LOI must be submitted with the full proposal.

Approval of proposals and final funding decisions will be communicated to the PD/PIs via the usual service-specific mechanisms.

#### **Timelines:**

##### **BLR&D/CSR&D:**

1-May 2021—LOIs Due  
30-June 2021 --LOI decisions returned  
10-September 2021--Deadline for proposals  
November-December 2021—Scientific Review meetings  
February 2022—Final Funding Decisions  
February-July 2022---JIT and Regulatory approvals  
May-July 2022 –Earliest access to MVP data in GENISIS

##### **HSR&D**

4-Nov 2021 LOIs and ITS due  
10-Dec 2021 Deadline for Proposals  
February 2022 -Scientific Review Meetings  
March 2022- Final Funding Decisions  
April-August 2022- JIT and regulatory approvals  
June-August 2022- Earliest access to MVP data in GENISIS

**RR&D**

Refer to the applicable RFA for the number of resubmissions, and timing of submission steps required to meet the application deadline, as well as review and award dates.

**Contact**

Please submit General Questions to [MVPLOI@va.gov](mailto:MVPLOI@va.gov). Service or RFA specific questions should go to the contact for the appropriate services listed in Appendix A.

**Appendices**

- A. ORD service purviews and scientific research areas of interest**
- B. LOI template for BLR&D, CSR&D, HSR&D**

## APPENDIX A:

Below is a brief description of each Research Service's purview and research areas of interest.

**BLR&D (BX):** BLRD funds preclinical biomedical and behavioral studies of disorders and diseases of importance to the health of Veterans. The BLRD purview includes *in vitro* and *in vivo* studies using tissue cultures, animal models, or human biological samples collected using minimally invasive procedures (blood, urine, buccal swabs) or from tissues acquired without direct contact with subjects (e.g., from tissue banks or pathology material). BLRD will fund discovery research involving -omic data including related phenotypic data in studies to genetic risk factors, pathophysiological pathways, treatment target identification and biomarker discovery. The VA will not fund studies of human fetal tissue. Applications that seek to administer surveys or questionnaires (e.g. new clinical data collection) or perform medical procedures and treatments (including biopsies) or observational studies should be submitted to the Clinical Sciences R&D Service (CSR&D) RFAs.

BLRD applicants are encouraged to submit innovative and clinically relevant research projects with the potential to lead to significant advances in healthcare for Veterans. Priority research areas of specific interest to BLRD include (but are not limited to):

- Posttraumatic stress disorder
- Traumatic Brain Injury (TBI)
  
- Suicide prevention research (with emphasis on biological markers)
- Modifiable risk factors (e.g., smoking, substance abuse)
- Military service or deployment-related occupational exposures
- Women Veteran's health
- Genomic and personalized/precision medicine
- Pain and neurological disorders

**NOTE: BLR&D applicants will still be limited to one project per RFA unless granted a waiver by the director.**

**The following BLR&D RFAs are open for MVP proposals:**

1. BLRD Parent RFA (BX-21-001),
2. Data Science RFA (BX-21-008),
3. BLRD Merit Review Award for Research on Amyotrophic Lateral Sclerosis (I01) (BX-21-004)
4. BLRD Merit Review Pilot Project Awards for Research on Amyotrophic Lateral Sclerosis (I21) (BX-21-040)

**CONTACT** for further information [VHABLRD-CSR&D@va.gov](mailto:VHABLRD-CSR&D@va.gov)

**CSR&D (CX):** CSR&D funds clinical, behavioral, and epidemiological research on disorders and diseases of importance to the health of Veterans. Studies supported under this Program include experimental and observational studies involving human subjects for research purposes, and methodological studies focused on research with human subjects. Proposals using MVP data may be submitted to CSR&D when there will be new clinical data/assessments collected in the

proposed study (e.g. through administration of surveys or questionnaires, observational studies with new subjects, or while performing medical procedures and treatments, such as biopsies). If new data are only generated from pre-existing records, from biological samples collected using minimally invasive procedures (blood, urine, buccal swabs) or from tissues acquired without direct contact with subjects (e.g., from tissue banks or pathology material), the project should be submitted to the Biomedical Laboratory R&D Service (BLR&D) RFAs. Note that CSRD will support interventional clinical trials only if a Letter of Intent (LOI) is approved in advance and those applications are submitted only using RFA CX-20-006 or CX-20-005.

Eligible applicants are encouraged to submit innovative or highly impactful clinically relevant research with the potential to lead to significant advances in healthcare for Veterans particularly as related to translational capability. Priority areas described below are considered when funding decisions are made. Examples of priority research areas of specific interest to CSRD include focus on:

- Psychiatric, behavioral and cognitive disorders prevalent in Veterans including, but not limited to:
  - Suicide
  - Posttraumatic stress disorder (PTSD) including commonly occurring co-morbidities
  - Health-risk behaviors (e.g., substance abuse, addictive disorders)
- Pain mechanisms and treatment alternatives to opioids
- Traumatic brain injury, specifically diagnosis and treatment
- Women Veteran's health
- Deployment health, e.g. OIF/OEF/OND and related consequences of military Service (Military Exposures research)
- Precision medicine especially individual treatment response

**CONTACT** for further information: [VHABLRD-CSR@va.gov](mailto:VHABLRD-CSR@va.gov)

**HSR&D:** Proposals submitted to HSR&D should use MVP genotype and survey data, EHR data, administrative data, and other relevant data sources to advance analytics methods and/or develop algorithms, tools, or models that will contribute to the implementation of personalized medicine in VHA; improvements in the delivery of high value and quality healthcare; and the design and implementation of innovative interventions to improve population health.

For example:

- Development, validation, and application of computer and data sciences (e.g. Natural Language Processing, machine learning), innovative statistical approaches, and other engineering and mathematical modeling approaches to improve data standardization and ontologies, clinical knowledge, and decision-making involving genomic data.
- Advancement of clinical phenotyping, validation and improvement of accuracy of phenotyping using medical record data, and survey data.
- Development of computational and statistical algorithms, tools, or models for implementing personalized medicine in VHA Note: Because of the limits of the collection



process and consent in MVP, studies should not include procedures that would require communicating genomic results back to the MVP participants.

- Identification of personalized medicine care model based on genomic data and effective way to engage patients in treatment decision making (e.g. discussions on uncertainty of the proposed treatments, potential benefits and side effects of pharmacological therapies).
- Identification and validation of important behavioral phenotypes, such as those describing health risk behaviors (including drug, alcohol, and tobacco use; diet and nutrition; and physical activity). Examination of associations between these phenotypes, genotypes, and behavioral and health outcomes and the development of treatments or interventions to reduce risky behaviors, increase healthy behaviors, and improve health outcomes.
- Disease conditions of HSR&D's interest include but not limited to prostate cancer, colon cancer, opioid addiction, chronic pain, depressions, other mental health conditions, and traumatic brain injury.

All HSR&D RFAs are available for MVP data research projects. HSR&D applications must conform to the HX Parent RFA requirements, priorities, and review criteria. Please check the HSR&D research priorities at [Health Services Research and Development Updated Research Priorities \(va.gov\)](https://www.hsrd.research.va.gov/funding/PriorityDomains2019.pdf) <https://www.hsrd.research.va.gov/funding/PriorityDomains2019.pdf> .

**CONTACT** for further information: [yhacoscirev@va.gov](mailto:yhacoscirev@va.gov)

**RR&D:** Proposals submitted to RR&D should use MVP and related data sources to probe the underlying genetics of functional loss, recovery, and response to rehabilitation of Veterans with potentially disabling conditions. For example:

- Association between biomarkers of chronic inflammation and disability in neurodegenerative conditions or cardiovascular disease
- Identification of genetic influences on healing and regeneration of function following musculoskeletal or nervous system trauma
  - Identify genetic factors that promote wound healing and regeneration to maximize functional recovery.
- Identification of genetic factors associated with pain resilience following injury to the musculoskeletal and/or nervous system(s)
- Genetic mechanisms associated with poorer functional outcomes following injury to the central nervous system
- Genetic studies to identify adverse outcome pathways (e.g. susceptibility to develop ALS) from military exposure and response to rehabilitation.
- Identify genetic factors that predict development of neuropathic pain following injury/disease involving the PNS and CNS (e.g. chronic headaches, nerve pain).
- Genetic influences on responsiveness to rehabilitative therapies (e.g. genetic factors that limit or facilitate rehabilitation; e.g. BDNF Val/Met polymorphism).

- Genetic factors that distinguish Veterans at risk for long term progression of disability (e.g. transition from acute to chronic pain, TBI-related neurodegenerative conditions)
  - Identify genetic factors that impact the susceptibility to long-term COVID-19 symptomatology (e.g. exhaustion, pulmonary function) and response to rehabilitation strategies.
  - Genetic factors predicting development of chronic low back pain and osteoarthritis of the knee as a result of overuse/injury and response to rehabilitation.
  - Studies capitalizing upon newly identified genetic influences of PTSD to develop personalized rehabilitation approaches for Veterans.

**Priority conditions include:**

- Traumatic Brain Injury
- Spinal Cord Injury
- Post-traumatic Arthritis
- Chronic Painful conditions
- Alzheimer's Disease
- Multiple Sclerosis
- ALS
- Sensory Systems & Communication Disorders; hearing loss, visual loss, vestibular, and tinnitus

The following RR&D RFAs are available for MVP applications: RR&D Parent Merit Award

**CONTACT** for further information: <https://www.rehab.research.va.gov/staff/science1.html> or [rrdreviews@va.gov](mailto:rrdreviews@va.gov)