Program Announcement

for the

Department of Defense

Defense Health Program

Congressionally Directed Medical Research Programs

Peer Reviewed Medical Research Program

Technology/Therapeutic Development Award

Funding Opportunity Number: W81XWH-16-PRMRP-TTDA

Catalog of Federal Domestic Assistance Number: 12.420 Military Medical Research and Development

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-Application Submission Deadline:** 5:00 p.m. Eastern time (ET), June 23, 2016
- **Invitation to Submit an Application:** August 2016
- **Application Submission Deadline:** 11:59 p.m. ET, October 19, 2016
- **End of Application Verification Period:** 5:00 p.m. ET, October 24, 2016
- **Peer Review:** December 2016
- **Programmatic Review:** February 2017

This Program Announcement/Funding Opportunity is one of two documents with instructions to prepare and submit an application for this funding opportunity. The second document, the General Application Instructions, is available for downloading from Grants.gov.

TABLE OF CONTENTS

I. FUNDING OPPORTUNITY DESCRIPTION

A. Program Description

Applications to the Fiscal Year 2016 (FY16) Peer Reviewed Medical Research Program (PRMRP) are being solicited for the Defense Health Agency, Research, Development, and Acquisition (DHA RDA) Directorate, by the U.S. Army Medical Research Acquisition Activity (USAMRAA). As directed by the Office of the Assistant Secretary of Defense for Health Affairs (OASD[HA]), the DHA RDA Directorate manages the Defense Health Program (DHP) Research, Development, Test, and Evaluation (RDT&E) appropriation. The managing agent for this Program Announcement/Funding Opportunity is the Congressionally Directed Medical Research Programs (CDMRP). The PRMRP was initiated in 1999 to provide support for military health-related research of exceptional scientific merit. Appropriations for the PRMRP from FY99 through FY15 totaled $1.092 billion. The FY16 appropriation is $278.7 million (M).

The vision of the FY16 PRMRP is to improve the health and well-being of all military Service members, Veterans, and beneficiaries. The PRMRP challenges the scientific and clinical communities to address at least one of the FY16 Topic Areas with original ideas that foster new directions along the entire spectrum of research and clinical care. The program seeks applications in laboratory, clinical, behavioral, epidemiologic, and other areas of research to advance knowledge in disease etiology, improve prevention, detection, diagnosis, treatment, and quality of life for those affected by a relevant disease or condition, and to develop and validate clinical care or public health guidelines.

B. FY16 PRMRP Topic Areas

All applications for PRMRP funding must specifically address at least one of the Topic Areas as directed by Congress and must be directly relevant to the healthcare needs of military Service members, Veterans, and/or beneficiaries. If the proposed research does not specifically address at least one of the FY16 PRMRP Topic Areas, the Government will administratively withdraw the application. The Government reserves the right to reassign the application's Topic Area if submitted under an inappropriate Topic Area. The FY16 PRMRP Topic Areas are listed below.

- Acute Lung Injury
- Antimicrobial Resistance
- Chronic Migraine and Post-Traumatic Headache
- Congenital Heart Disease
- Constrictive Bronchiolitis
- Diabetes
- Dystonia
- Emerging Infectious Diseases
- Focal Segmental Glomerulosclerosis

- Fragile X Syndrome
- Hepatitis B
- Hereditary Angioedema
- Hydrocephalus
- Inflammatory Bowel Disease
- Influenza
- Integrative Medicine
- Interstitial Cystitis
- Lupus
- Malaria

- Metals Toxicology
- Mitochondrial Disease
- Nanomaterials for Bone Regeneration
- Non-Opioid Pain Management
- Pancreatitis
- Pathogen-Inactivated Dried Plasma
- Polycystic Kidney Disease
- Post-Traumatic Osteoarthritis
- Psychotropic Medications
- Pulmonary Fibrosis

- Respiratory Health
- Rett Syndrome
- Rheumatoid Arthritis
- Scleroderma
- Sleep Disorders
- Tinnitus
- Tuberculosis
- Vaccine Development for Infectious Disease
- Vascular Malformations
- Women's Heart Disease

Research relevant to one or more FY16 PRMRP Topic Areas may be considered for funding. ***Applicants should select the FY16 PRMRP Funding Opportunity most appropriate to the stage of the proposed research.*** Areas of Encouragement related to the FY16 PRMRP Topic Areas have been identified by the Department of Defense (DoD), the Department of Veterans Affairs (VA), and other relevant stakeholders (Appendix 1). Applicants are urged to read and consider these Areas of Encouragement before preparing their applications. ***The information provided is not exhaustive, and applicants are not restricted to submitting applications that address an Area of Encouragement on this list.***

C. Award Information

The PRMRP Technology/Therapeutic Development Award is a product-driven award mechanism intended to provide support for the translation of promising preclinical findings into products for clinical applications, including prevention, detection, diagnosis, treatment, or quality of life, in at least one of the Congressionally directed FY16 PRMRP Topic Areas. Products in development should be responsive to the healthcare needs of military Service members, Veterans, and/or beneficiaries.

The product(s) to be developed may be a tangible item such as a pharmacologic agent (drugs or biologics) or device, or a knowledge-based product. A "Knowledge Product" is a non-materiel product that addresses an identified need in a Topic Area, is based on current evidence and research, aims to transition into medical practice, training, tools, or to support materiel solutions (systems to develop, acquire, provide, and sustain medical solutions and capabilities), and educates or impacts behavior throughout the continuum of care, including primary prevention of negative outcomes. The Principal Investigator (PI) must provide a transition plan (including potential funding and resources) showing how the product will progress to the next level of development (e.g., clinical trials, delivery to the military or civilian market) after the completion of the PRMRP award. PIs are encouraged to develop relationships with industry and/or other funding agencies to facilitate moving the product into the next phase of development.

Proof-of-concept demonstrating the potential utility of the proposed product, or a prototype/preliminary version of the proposed product, should already be established. ***Applications must include relevant data that support the rationale for the proposed study.*** These data may be unpublished and/or from the published literature. Investigators seeking to identify a product or demonstrate initial proof-of-concept should consider submitting to the FY16 PRMRP Investigator-Initiated Research Award (W81XWH-16-PRMRP-IIRA) or the FY16 PRMRP Discovery Award (W81XWH-16-PRMRP-DA), as appropriate.

Examples of the types of research that may be supported include, but are not limited to:

- Developing and validating clinical guidance/guidelines for standard of care
- Testing new therapeutic modalities (agents, delivery systems, and chemical modification of lead compounds) using established or validated preclinical systems
- Designing and implementing pilot or full-scale Good Manufacturing Practice (GMP) production of therapeutics and/or delivery systems for use in advanced preclinical and initial clinical trials
- Developing pharmacologic agents through absorption, distribution, metabolism, excretion, and toxicology (ADMET) studies
- Developing pharmacologic agents to Investigational New Drug (IND) stage for initiation of Phase I clinical trials
- Developing prototype devices to Investigational Device Exemption (IDE) stage or abbreviated IDE stage for initiation of clinical trials
- Optimizing diagnostic or treatment devices for field deployment

Research involving human subjects and human anatomical substances is permitted; however, this award may not be used to conduct clinical trials. A clinical trial is defined as a prospective accrual of human subjects where an intervention (e.g., device, drug, biologic, surgical procedure, rehabilitative modality, behavioral intervention, or other) is tested on a human subject for a measurable outcome with respect to safety, effectiveness, and/or efficacy. This outcome represents a direct effect on the human subject of that intervention or interaction. For more information on how to distinguish clinical research from clinical trials, see the Human Subject Resource Document at https://ebrap.org/eBRAP/public/Program PIs seeking funding for a clinical trial should apply to the FY16 PRMRP Clinical Trial Award mechanism (W81XWH-16-PRMRP-CTA).

Military Relevance: Relevance to the healthcare needs of military Service members, Veterans, and beneficiaries is a key feature of this award. Investigators are encouraged to consider the following characteristics as examples of how a project may demonstrate military relevance:

- Explanation of how the project addresses an aspect of the target disease/condition that has direct relevance to military Service members, Veterans, or other military health system beneficiaries
- Description of how the knowledge, information, products, or technologies gained from the proposed research could be implemented in a dual-use capacity to to benefit the civilian population and also address a military need

- Use of military or Veteran populations or datasets in the proposed research, if appropriate to the proposed research project
- Involvement of military consultants (Army, Air Force) or specialty leaders (Navy, Marine Corps) to the Surgeons General in a relevant specialty area

PIs are encouraged to integrate and/or align their research projects with DoD and/or VA research laboratories and programs. Collaboration with the DoD or VA is also encouraged. A list of websites that may be useful in identifying additional information about ongoing DoD and VA areas of research interest or potential opportunities for collaboration within the FY16 PRMRP Topic Areas can be found in Appendix 2.

Use of Active Duty Military and VA Populations: If the proposed research plan involves access to active duty military and/or VA patient populations or resources, the PI is responsible for establishing such access. If possible, access to target active duty military and/or VA patient populations/resources should be confirmed at the time of application submission by inclusion of a letter of support, signed by the lowest ranking person with approval authority, for studies involving active duty military Service members, Veterans, military- and/or VA-controlled study materials, and military and/or VA databases. If access cannot be confirmed at the time of application submission, the Government reserves the right to withhold or revoke funding until the PI has demonstrated support for and access to the relevant population(s) and/or resources. Note that access to a Veteran population for clinical studies may only be obtained by either collaboration with a VA investigator where the VA investigator has a substantial role in the research or by advertising to the general public.

Research Involving Human Anatomical Substances, Human Subjects, or Human Cadavers: All DoD-funded research involving new and ongoing research with human anatomical substances, human subjects, or human cadavers must be reviewed and approved by the U.S. Army Medical Research and Materiel Command (USAMRMC) Office of Research Protections (ORP), Human Research Protection Office (HRPO) prior to research implementation. This administrative review requirement is in addition to the local Institutional Review Board (IRB) or Ethics Committee (EC) review. Local IRB/EC approval at the time of submission is *not* required. The HRPO is mandated to comply with specific laws and requirements governing all research involving human anatomical substances, human subjects, or human cadavers that is supported by the DoD. These laws and requirements will necessitate information in addition to that supplied to the IRB/EC. *Allow a minimum of 2 to 3 months for HRPO regulatory review and approval processes*. Refer to the General Application Instructions, Appendix 6, and the Human Subject Resource Document available on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) for additional information.

Guidelines for Animal Research: All projects should adhere to a core set of standards for rigorous study design and reporting to maximize the reproducibility and translational potential of preclinical research. The standards are described in Landis, S.C., et al. A call for transparent reporting to optimize the predictive value of preclinical research, *Nature* 2012, 490:187-191 (www.nature.com/nature/journal/v490/n7419/full/nature11556.html). While these standards are written for preclinical studies, the basic principles of randomization, blinding, sample-size estimation, and data handling derive from well-established best practices in clinical studies.

Applicants should consult the ARRIVE (Animal Research: Reporting *In Vivo* Experiments) guidelines to ensure relevant aspects of rigorous animal research are adequately planned for and, ultimately, reported. The ARRIVE guidelines can be found at https://www.elsevier.com/__data/promis_misc/622936arrive_guidelines.pdf.

All DoD-funded research involving new and ongoing research with animals must be reviewed and approved by the USAMRMC ORP Animal Care and Use Review Office (ACURO), in addition to the local Institutional Animal Care and Use Committee (IACUC) of record. IACUC approval at the time of submission is not required. Specific documents relating to the use of animals in the proposed research will be requested **if the application is selected for funding**. The ACURO must review and approve all animal use prior to the start of working with animals, including amendments to ongoing projects. PIs must submit the institutional animal use protocol, IACUC approval of that protocol, and a version of the animal use appendix titled "Research Involving Animals." *Allow at least 2 to 3 months for ACURO regulatory review and approval processes for animal studies.* Refer to General Application Instructions, Appendix 6, for additional information.

The CDMRP intends that information, data, and research resources generated under awards funded by this Program Announcement/Funding Opportunity be made available to the research community (which includes both scientific and consumer advocacy communities) and to the public at large. For additional guidance, refer to the General Application Instructions, Appendix 4, Section K.

D. Eligibility Information

- PIs at or above the level of Assistant Professor (or equivalent) are eligible to submit applications.

- Cost sharing/matching is not an eligibility requirement.

- Eligible investigators must apply through an organization. Organizations eligible to apply include Federal agencies, national, international, for-profit, nonprofit, public, and private organizations.

- An intramural investigator is defined as a DoD military or civilian employee working within a DoD laboratory or medical treatment facility, or working in a DoD activity embedded within a civilian medical center. Submissions from intramural (DoD) organizations are allowed and encouraged for this Program Announcement/Funding Opportunity. Applicants submitting through their intramural organizations are reminded to coordinate receipt and commitment of funds through their respective resource managers. *If an investigator at an intramural organization is named as a collaborator on an application submitted through an extramural organization, the application must include a letter from the collaborator's Commander or Commanding Officer at the intramural organization that authorizes the collaborator's involvement.*

- Refer to the General Application Instructions, Appendix 1, for general eligibility information.

E. Funding

- The maximum period of performance is **3** years.

- The anticipated direct costs budgeted for the entire period of performance will not exceed **$3M**. Indirect costs are to be budgeted in accordance with the organization's negotiated rate. No budget will be approved by the Government exceeding **$3M** direct costs or using an indirect rate exceeding the organization's negotiated rate.

- All direct and indirect costs of any subaward (subgrant or subcontract) must be included in the total direct costs of the primary award.

- The applicant may request the entire maximum funding amount for a project that has a period of performance less than the maximum **3** years.

For this award mechanism, direct costs may be requested for (not all-inclusive):

- Salary

- Research supplies

- Equipment

- Clinical research costs *(clinical trials are not allowed)*

- Support for multidisciplinary collaborations, including travel

- Travel costs for the PI to disseminate project results at one DoD sponsored meeting to be specified by the program office during award negotiations

- Travel costs for up to three investigators to travel to one scientific/technical meeting per year in addition to the DoD-sponsored meeting described above

Awards to extramural organizations will consist solely of assistance agreements (Cooperative Agreements and Grants). Awards to intramural (DoD) agencies and other Federal agencies may be managed through a direct fund transfer (e.g., the Military Interdepartmental Purchase Request [MIPR]; Funding Authorization Document [FAD] process; or DD Form 1144 Support Agreement). Direct transfer of funds from the recipient to a DoD agency is not allowed except under very limited circumstances. Refer to the General Application Instructions, Section II.C.4., for budget regulations and instructions for the Research & Related Budget. ***For Federal agencies or organizations collaborating with Federal agencies, budget restrictions apply as are noted in Section II.C.4. of the General Application Instructions***.

The CDMRP expects to allot approximately $45M of the $278.7M FY16 PRMRP appropriation(s) to fund approximately 10 Technology/Therapeutic Development Award applications, depending on the quality and number of applications received. Funding of applications received in response to this Program Announcement/Funding Opportunity is contingent upon the availability of Federal funds for this program.

II.   SUBMISSION INFORMATION

Submission of applications that are essentially identical or propose essentially the same research project to different Funding Opportunities within the same program and fiscal year is prohibited and will result in administrative withdrawal of the duplicative application(s).

Submission is a two-step process requiring both (1) pre-application submission through the electronic Biomedical Research Application Portal (eBRAP) (https://eBRAP.org/) and (2) application submission through Grants.gov (http://www.grants.gov/). Refer to the General Application Instructions, Section II.A., for registration and submission requirements for eBRAP and Grants.gov.

The pre-application and application submission process should be started early to avoid missing deadlines. There are no grace periods. Federal applicants must be familiar with Grants.gov requirements, including the need for an active System for Award Management (SAM) registration and a Data Universal Numbering System (DUNS) number. Refer to Appendix 3 of the General Application Instructions for further information regarding Grants.gov requirements.

eBRAP is a multifunctional web-based system that allows PIs to submit their pre-applications electronically through a secure connection, to view and edit the content of their pre-applications and full applications, to receive communications from the CDMRP, and to submit documentation during award negotiations and period of performance. A key feature of eBRAP is the ability of an organization's representatives and PIs to view and modify the Grants.gov application submissions associated with them. eBRAP will validate Grants.gov application files against the specific Program Announcement/Funding Opportunity requirements and discrepancies will be noted in an email to the PI and in the Full Application Files tab in eBRAP. It is the applicant's responsibility to review all application components for accuracy as well as ensure proper ordering as specified in this Program Announcement/Funding Opportunity.

The application title, eBRAP log number, and all information for the PI, Business Official(s), performing organization, and contracting organization must be consistent for the entire pre-application and application submission process. Inconsistencies may delay application processing and limit the ability to view, modify, and verify the application in eBRAP. If any changes need to be made, the applicant should contact the CDMRP Help Desk at help@eBRAP.org or 301-682-5507 prior to the application deadline.

Application viewing, modification, and verification in eBRAP is strongly recommended, but not required. *The Project Narrative and Budget cannot be changed after the application submission deadline.* Prior to the full application deadline, a corrected or modified full application package may be submitted. Other application components may be changed until the end of the application verification period. After the end of the application verification period, the full application cannot be modified.

A.   Where to Obtain the Grants.gov Application Package

To obtain the Grants.gov application package, including all required forms, perform a basic search using the Funding Opportunity Number W81XWH-16-PRMRP-TTDA in Grants.gov (http://www.grants.gov/).

B.   Pre-Application Submission Content

The pre-application process should be started early to avoid missing deadlines. There are no grace periods. During the pre-application process, each submission is assigned a unique log number by eBRAP. This unique eBRAP log number will be needed during the application process on Grants.gov.

All pre-application components must be submitted by the PI through eBRAP (https://eBRAP.org/). Because the invitation to submit an application is based on the contents of the pre-application, investigators should not change the title or research objectives after the pre-application is submitted.

PIs and organizations identified in the pre-application should be the same as those intended for the subsequent application submission. If any changes are necessary after submission of the pre-application, the PI must contact the CDMRP Help Desk at help@eBRAP.org or 301-682-5507.

The pre-application consists of the following components, which are organized in eBRAP by separate tabs (refer to the General Application Instructions, Section II.B., for additional information on pre-application submission):

- **Tab 1 – Application Information**
- Select the FY16 PRMRP Topic Area addressed by the proposed research. If the proposed research project is aligned with more than one FY16 PRMRP Topic Area, select the Topic Area of highest relevance as the required first choice.

- **Tab 2 – Application Contacts**
  - ○ Enter contact information for the PI. Enter the organization's Business Official responsible for sponsored program administration (the "person to be contacted on matters involving this application" in Block 5 of the Grants.gov SF424 (R&R) Form). The Business Official must either be selected from the eBRAP list or invited in order for the pre-application to be submitted.
  - ○ Select the performing organization (site at which the PI will perform the proposed work) and the contracting organization (organization submitting on behalf of the PI, which corresponds to Block 5 on the Grants.gov SF424 (R&R) Form), and click on "*Add Organizations to this Pre-application.*" The organization(s) must either be selected from the eBRAP drop-down list or invited in order for the pre-application to be submitted.
  - ○ It is recommended that PIs identify an Alternate Submitter in the event that assistance with pre-application submission is needed.

- **Tab 3 – Collaborators and Key Personnel**
  - ○ Enter the name, organization, and role of all collaborators and key personnel associated with the application.
  - ○ FY16 PRMRP Programmatic Panel members should not be involved in any pre-application or application. For questions related to Panel members and pre-

applications or applications, refer to [Section IV.C., Withdrawal](#), or contact the CDMRP Help Desk at [help@eBRAP.org](#) or 301-682-5507.

- ○ To preserve the integrity of its peer and programmatic review processes, the CDMRP discourages inclusion of any employee of its review contractors having any role in application preparation, research, or other duties for submitted applications. For FY16, the identities of the peer review contractor and the programmatic review contractor may be found at the CDMRP website ([http://cdmrp.army.mil/about/2tierRevProcess](#)). Applications that include names of personnel from either of these companies will be administratively withdrawn unless plans to manage conflicts of interest (COIs) are provided and deemed appropriate by the Government. Refer to the General Application Instructions, Appendix 1, for detailed information.

- **Tab 4 – Conflicts of Interest**
  - ○ List all individuals other than collaborators and key personnel who may have a COI in the review of the application (including those with whom the PI has a personal or professional relationship). Refer to Appendix 1, Section C of the General Application Instructions for further information regarding COIs.

- **Tab 5 – Pre-Application Files**

  Note: Upload documents as individual PDF files unless otherwise noted. eBRAP will not allow a file to be uploaded if the number of pages exceeds the limit specified below.

  Preproposal Narrative (four-page limit): The Preproposal Narrative page limit applies to text and non-text elements (e.g., figures, tables, graphs, photographs, diagrams, chemical structures, drawings) used to describe the project. Inclusion of URLs that provide additional information to expand the Preproposal Narrative and could confer an unfair competitive advantage is prohibited and may result in administrative withdrawal of the pre-application.

  The Preproposal Narrative should include the following:

  - ○ **Topic Area:** Describe how the proposed project relates to at least one of the FY16 PRMRP Topic Areas. If applicable, describe how the proposed research project addresses an FY16 PRMRP Area of Encouragement ([Appendix 1](#)).

  - ○ **Technology/Therapeutic Development Product:** Describe the proposed product and briefly compare to existing technologies/therapeutics. Concisely state the scientific rationale, the preclinical findings that support the need for the proposed product, and a description of how proof-of-concept has been demonstrated.

  - ○ **Research Strategy:** State the hypothesis to be tested and/or the objective(s) to be reached. State the project's specific aims. Briefly describe the experimental design and methodology.

  - ○ **Personnel:** Briefly state the qualifications of the PI and key personnel to perform the described research project.

- **Impact:** Describe how the research will result in a product for clinical application, such as prevention, detection, diagnosis, treatment, or quality of life. Describe the potential short-term and long-term impact of the results of the proposed study on the research field and the patient population(s) relevant to at least one of the FY16 PRMRP Topic Areas.

- **Military Relevance:** Explain how the project is relevant to the healthcare needs of military Service members, Veterans, and/or beneficiaries.

Pre-Application Supporting Documentation: The items to be included as supporting documentation for the pre-application *must be uploaded as individual files* and are limited to:

- References Cited (one-page limit): List the references cited (including URLs if available) in the Preproposal Narrative using a standard reference format that includes the full citation (i.e., author[s], year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).

- List of Abbreviations, Acronyms, and Symbols: Provide a list of abbreviations, acronyms, and symbols used in the Preproposal Narrative.

- Key Personnel Biographical Sketches (five-page limit per individual). *All biographical sketches should be uploaded as a single combined file.* Biographical sketches should be used to demonstrate background and expertise through education, positions, publications, and previous work accomplished.

- **Tab 6 – Submit Pre-Application**
  - This tab must be completed for the pre-application to be accepted and processed.

Pre-Application Screening

- **Pre-Application Screening Criteria**

  To determine the technical merits of the pre-application and the relevance to the mission of the DHP and the PRMRP, pre-applications will be screened based on the following criteria:

  - **Technology/Therapeutic Development Product:** How well the pre-application defines a product (e.g., drug, device, clinical guidelines) that will address an unmet need. Whether the project is based on promising preclinical findings, sound scientific rationale, and demonstrated proof-of-concept.

  - **Research Strategy:** How well the specific aims and proposed methodology support the research hypothesis and/or objectives and the development of the product.

  - **Personnel:** How the personnel's background and expertise are appropriate to accomplish the proposed research.

  - **Impact:** Whether the potential immediate and long-range outcome(s)/product(s) (intellectual and/or materiel) of the proposed research, if successful, will impact a

central critical problem or question in the field of research and/or patient care in the FY16 PRMRP Topic Area(s) addressed.

- ○ **Programmatic Relevance:** Whether the proposed research idea supports the objectives of the PRMRP. How well the research will address a healthcare issue relevant to military Service members, Veterans, and/or beneficiaries.

- **Notification of Pre-Application Screening Results**

  Following the pre-application screening, PIs will be notified as to whether or not they are invited to submit applications; however, they will not receive feedback (e.g., a critique of strengths and weaknesses) on their pre-application. The estimated timeframe for notification of invitation to submit an application is indicated on the title page of this Program Announcement/Funding Opportunity. Invitations to submit a full application are based on the Pre-Application Screening Criteria as published above.

C.   Full Application Submission Content

The application process should be started early on Grants.gov to avoid missing deadlines. There are no grace periods. Verify the status of the applicant's organization's Entity registration in the SAM well in advance of the application submission deadline. Allow 3 to 4 weeks to complete the entire SAM registration process. Refer to the General Application Instructions, Section II, for additional information.

Applications will not be accepted unless the PI has received notification of invitation.

All contributors and administrators to the application must use matching compatible versions of Adobe software when editing and preparing application components. The use of different software versions will result in corruption of the submitted file. See Section II.C. of the General Application Instructions for details on compatible Adobe software.

The CDMRP cannot make allowances/exceptions to its policies for submission problems encountered by the applicant organization using system-to-system interfaces with Grants.gov.

Each application submission must include the completed Grants.gov application package for this Program Announcement/Funding Opportunity. The Grants.gov application package is submitted by the Authorized Organizational Representative through the Grants.gov portal (http://www.grants.gov/).

Note: The Project Narrative and Budget Form cannot be changed after the application submission deadline.

If either the Project Narrative or the budget fails eBRAP validation or if the Project Narrative or Budget Form needs to be modified, an updated Grants.gov application package must be submitted via Grants.gov as a "Changed/Corrected Application" with the previous Grants.gov Tracking ID *prior to the application submission deadline*.

Grants.gov application package components: For the Technology/Therapeutic Development Award, the Grants.gov application package includes the following components (refer to the

General Application Instructions, Section II.C., for additional information on application submission):

1. **SF424 (R&R) Application for Federal Assistance Form:** Refer to the General Application Instructions, Section II.C., for detailed information.

2. **Attachments Form**

   Each attachment to the Grants.gov application forms must be uploaded as an individual PDF file in accordance with the formatting guidelines listed in Appendix 2 of the General Application Instructions. For all attachments, ensure that the file names are consistent with the guidance. Grants.gov will reject attachments with file names longer than 50 characters or incorrect file names that contain characters other than the following: A-Z, a-z, 0-9, underscore, hyphen, space, and period. In addition, Grants.gov has file size limits that may apply in some circumstances. Individual attachments may not exceed 20 MB and the file size for the entire Grants.gov application package may not exceed 200 MB.

   - **Attachment 1: Project Narrative (18-page limit): Upload as "ProjectNarrative.pdf."** The page limit of the Project Narrative applies to text and non-text elements (e.g., figures, tables, graphs, photographs, diagrams, chemical structures, drawings, etc.) used to describe the project. Inclusion of URLs that provide additional information to expand the Project Narrative and could confer an unfair competitive advantage is prohibited and may result in administrative withdrawal of the application.

     Describe the proposed project in detail using the outline below.

     ○ **Background:** Describe how the proposed research project addresses one or more of the FY16 PRMRP Topic Areas. Describe the product to be developed. Present the ideas and reasoning behind the proposed work. Cite relevant literature. Describe previous experience most pertinent to the project. Include relevant preliminary data that support proof-of-concept of the product or a prototype/preliminary version of the product; these data may be unpublished or from the published literature.

     ○ **Hypothesis/Objective:** State the hypothesis to be tested and/or the objective(s) to be reached.

     ○ **Specific Aims:** Concisely explain the project's specific aims. These aims should agree with the primary aims and associated tasks described in the Statement of Work. If the proposed work is part of a larger study, present only aims that this DoD award would fund.

     ○ **Research Strategy:** Describe the experimental design, methods, and analyses, including appropriate controls, in sufficient detail for analysis. Provide a well-developed, well-integrated research strategy that supports the translational feasibility and promise of the approach. Define the specific study outcomes and how they will be measured. Address potential problem areas and present alternative methods and approaches. Describe how data will be handled,

including rules for stopping data collection, criteria for inclusion and exclusion of data, how outliers will be defined and handled, and identification of primary endpoints. Clearly describe the statistical plan and the rationale for the statistical methodology. Provide a sample size estimate and the method by which it was derived, including power analysis calculation, if applicable. Describe how data will be reported and how it will be assured that the documentation will support a regulatory filling with the FDA, if applicable.

- If animal studies are proposed, briefly describe the key elements of the study/studies as they relate to the overall project. Explain how and why the animal species, strain, and model(s) being used can address the scientific objectives and, where appropriate, the study's relevance to human biology. Describe the randomization and blinding procedures for the study and any other measures to be taken to minimize effects of subjective bias during animal treatment and assessment of results. If randomization and/or blinding will not be utilized, provide justification.

- If human subjects or human biological samples will be used, describe the study population and include a detailed plan for the recruitment of human subjects or the acquisition of samples. Describe the availability of the proposed study population and past successes in recruiting similar populations. If active duty military, military families, and/or Veteran population(s) or datasets will be used in the proposed research project, describe the feasibility of accessing the population(s)/dataset(s). *Clinical trials are not allowed under the Technology/Therapeutic Development Award.*

- **Attachment 2: Supporting Documentation.** Start each document on a new page. **Combine and upload as a single file named "Support.pdf."** If documents are scanned to pdf, the lowest resolution (100 to 150 dpi) should be used. *There are no page limits for any of these components unless otherwise noted. Include only those components described below; inclusion of items not requested will result in the removal of those items or may result in administrative withdrawal of the application.*

  ○ References Cited: List the references cited (including URLs, if available) in the Project Narrative using a standard reference format that includes the full citation (i.e., author[s], year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).

  ○ List of Abbreviations, Acronyms, and Symbols: Provide a list of abbreviations, acronyms, and symbols.

  ○ Facilities, Existing Equipment, and Other Resources: Describe the facilities and equipment available for performance of the proposed project and any additional facilities or equipment proposed for acquisition at no cost to the award. Indicate whether or not Government-furnished facilities or equipment are proposed for use. If so, reference should be made to the original or present Government

award under which the facilities or equipment items are now accountable. There is no form for this information.

○ Publications and/or Patents: Include a list of relevant publication URLs and/or patents. If publications are not publicly available, then copies of up to five published manuscripts may be included in Attachment 2. Extra items will not be reviewed.

○ Letters of Organizational Support: Provide a letter (or letters, if applicable), signed by the Department Chair or appropriate organization official, confirming the laboratory space, equipment, and other resources available for the project. Letters of support not requested in the Program Announcement/Funding Opportunity, such as those from members of Congress, do not impact application review or funding decisions.

○ Letters of Collaboration: Provide a signed letter from each collaborating individual or organization that will demonstrate that the PI has the support or resources necessary for the proposed work.

○ Letters Confirming Access to Military or VA Patient Populations or Resources (if applicable): If the proposed research plan involves access to active duty military and/or VA patient populations or resources, include a letter of support, signed by the lowest ranking person with approval authority, confirming such access. If access cannot be confirmed at the time of application submission, the Government reserves the right to withhold or revoke funding until the PI has demonstrated support for and access to the relevant population(s) and/or resources.

○ Intellectual Property

– Intangible property acquired, created or developed under this award will be subject to all rights and responsibilities established at 2 CFR 200.315. Should the applicant intend to use, in the performance of this program, pre-existing, legally protected and perfected intangible property and for which no Federal funds had been used in the development of said property, the applicant must:

▪ Clearly identify all such property;

▪ Identify the cost to the Federal government for use or license of such property, if applicable; or

▪ Provide a statement that no property meeting this definition will be used on this project.

– Intellectual and Material Property Plan (if applicable): Provide a plan for resolving intellectual and material property issues among participating organizations.

○ Data and Research Resources Sharing Plan: Describe how data and resources generated during the performance of the project will be shared with the research community. Refer to the General Application Instructions, Appendix 4,

Section K for more information about the CDMRP expectations for making data and research resources publicly available.

- **Attachment 3: Technical Abstract (one-page limit): Upload as "TechAbs.pdf."** The technical abstract is used by all reviewers. Abstracts of all funded research projects will be posted publicly. ***Do not include proprietary or confidential information.*** Use only characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed.

  Clarity and completeness within the space limits of the technical abstract are highly important. Describe the proposed research project including the following elements:

  Background, rationale, hypothesis and/or objectives, specific aims, study design, long-term and short-term impact to the relevant research field and patient population(s), and the relevance of the project to at least one FY16 PRMRP Topic Area.

- **Attachment 4: Lay Abstract (one-page limit): Upload as "LayAbs.pdf."** The lay abstract is used by all reviewers. Abstracts of all funded research projects will be posted publicly. ***Do not include proprietary or confidential information.*** Use only characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed.

  Describe how the proposed research project addresses one or more of the FY16 PRMRP Topic Areas. Include a comprehensive overview of the proposed research project that will be ***readily understood by readers without a background in science or medicine.*** Clearly describe the central critical problem or question to be addressed and the ultimate applicability and impact of the research. ***Do not duplicate the technical abstract.***

- **Attachment 5: Statement of Work (SOW) (three-page limit): Upload as "SOW.pdf."** The suggested SOW format and examples specific to different types of research projects are available on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm). For the Technology/ Therapeutic Development Award mechanism, use the SOW format example titled "SOW (Statement of Work) Generic Format." The SOW must be in PDF format prior to attaching. Refer to the General Application Instructions, Section II.C.2., for detailed guidance on creating the SOW.

- **Attachment 6: Impact Statement (one-page limit): Upload as "Impact.pdf."**

  Explain why the proposed research project is important and relevant to developing improvements in prevention, detection, diagnosis, treatment, or quality of life in the FY16 PRMRP Topic Area(s) addressed. Describe how the study will address a central critical problem or question in the relevant Topic Area(s). If applicable, describe how the project addresses an FY16 PRMRP Area of Encouragement (Appendix 1).

Describe the short-term impact: Detail the anticipated outcome(s)/product(s) (knowledge and/or materiel) that will be directly attributed to the results of the proposed research.

Describe the long-term impact: Explain the anticipated long-term gains from this research. Compare to the information known/products currently available, if applicable. Explain the long-range vision for how the research will impact the field of study and/or clinical care.

- **Attachment 7: Military Relevance Statement (one-page limit): Upload as "MilRel.pdf."**

  Describe how the proposed study is responsive to the healthcare needs of military Service members, Veterans, and/or beneficiaries. Provide information about the incidence and/or prevalence of the disease or condition in the general population as well as in military Service members, Veterans, and/or beneficiaries.

  If active duty military, military families, and/or Veteran population(s) or datasets will be used in the proposed research project, describe the population(s)/dataset(s) and the appropriateness of the population(s)/dataset(s) for the proposed study. If a non-military population will be used for the proposed research project, explain how the population simulates the targeted population (i.e., military Service members, Veterans, and/or beneficiaries).

  If applicable, show how the proposed research project aligns with DoD and/or VA areas of research interest. Provide a description of how the knowledge, information, products, or technologies gained from the research could be implemented in a dual-use capacity to benefit the civilian population and address a military need, as appropriate.

- **Attachment 8: Transition Plan and Regulatory Strategy (three-page limit): Upload as "Transition.pdf."**

  Describe the methods and strategies proposed to move the product or knowledge outcomes to the next phase of development (e.g., clinical trials, commercialization, and/or delivery to the civilian or military market) after successful completion of the award. Outline the regulatory strategy. Applicants are encouraged to work with their organization's Technology Transfer Office (or equivalent) to develop the transition plan. PIs are encouraged to explore developing relationships with industry and/or other funding agencies to facilitate moving the product into the next phase of development. The post-award transition plan should include the components listed below.

  ○ The planned indication for the product label, if appropriate, and an outline of the development plan required to support that indication. Describe in detail the FDA regulatory strategy, to include considerations for compliance with Good Manufacturing Practice (GMP), Good Laboratory Practice (GLP), and Good Clinical Practice (GCP), if appropriate.

  ○ Details of the funding strategy to transition the product(s) to the next level of development and/or commercialization (e.g., specific potential industry

partners, specific funding opportunities to be applied for). Include a description of collaborations and other resources that will be used to provide continuity of development.

- ○ For Knowledge Products, a description of collaborations and other resources that will be used to provide continuity of development including proposed development or modification of clinical practice guidelines and recommendations, provider training materials, patient brochures, and other clinical support tools, scientific journal publications, models, simulations, and applications.

- ○ A brief schedule and milestones for transitioning the product(s) to the next phase of development (e.g., clinical trials, transition to industry, delivery to the civilian and/or military market, incorporation into clinical practice, or approval by the FDA).

- ○ Ownership rights/access to the intellectual property necessary for the development and/or commercialization of products or technologies supported with this award and the Government's ability to access such products or technologies in the future.

- ○ A risk analysis for cost, schedule, manufacturability, and sustainability.

- **Attachment 9: Collaborating DoD Military Facility Budget Form(s), if applicable: Upload as "MFBudget.pdf."**

  If a Military Facility (military health system facility, research laboratory, treatment facility, dental treatment facility, or a DoD activity embedded with a civilian medical center) will be a collaborator in performance of the project, complete the Collaborating DoD Military Facility Budget Form, available for download on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm), including a budget justification, for each Military Facility as instructed. The costs per year should be included on the Grants.gov Research and Related Budget form under subaward costs. Refer to the General Application Instructions, Section II.C.7., for detailed information**.**

3. **Research & Related Senior/Key Person Profile (Expanded):** Refer to the General Application Instructions, Section II.C.4., for detailed information.

- PI Biographical Sketch (five-page limit): Upload as "Biosketch_LastName.pdf." The suggested biographical sketch format is available on the "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) in eBRAP. The five-page National Institutes of Health Biographical Sketch may also be used. All biographical sketches should be submitted in the portable document format (pdf) that is not editable.

  Biographical Sketches should be used to demonstrate background and expertise through education, positions, publications, and previous work accomplished.

- PI Previous/Current/Pending Support (no page limit): Upload as "Support_LastName.pdf."

- Key Personnel Biographical Sketches (five-page limit each): Upload as "Biosketch_LastName.pdf."

- Key Personnel Previous/Current/Pending Support (no page limit): Upload as "Support_LastName.pdf."

4. **Research & Related Budget:** Refer to the General Application Instructions, Section II.C.4., for detailed information.

- Budget Justification (no page limit): Upload as "BudgetJustification.pdf." The budget justification for the entire period of performance must be uploaded to the Research & Related Budget after completion of the budget for Period 1.

5. **Project/Performance Site Location(s) Form:** Refer to the General Application Instructions, Section II.C.5., for detailed information.

6. **R & R Subaward Budget Attachment(s) Form (if applicable):** Refer to the General Application Instructions, Section II.C.6., for detailed information.

Collaborating DoD Military Facilities Form: A Military Facility collaborating in the performance of the project should be treated as a subaward for budget purposes. However, do not complete the Grants.Gov R & R Subaward Budget Attachment Form; instead, complete the Collaborating DoD Military Facility Budget Form (use Attachment 9, Collaborating DoD Military Facility Budget Form) to show all direct and indirect costs. The costs per year should be included on the Grants.gov Research and Related Budget form under subaward costs. Refer to the General Application Instructions, Section II.C.7., for detailed information.

D.   Applicant Verification of Grants.gov Submission in eBRAP

Prior to the end of the application verification period, PIs and organizational representatives can review and modify in eBRAP certain components of an application submitted to Grants.gov. Following retrieval and processing of the Grants.gov application, eBRAP will notify the organizational representatives and PI by email to log into eBRAP to review, modify, and verify the Grants.gov application submission. eBRAP will validate retrieved files against the specific Program Announcement/Funding Opportunity requirements and discrepancies will be noted in both the email and in the Full Application Files tab in eBRAP. eBRAP does not confirm the accuracy of file content. It is the applicant's responsibility to review all application components and ensure proper ordering as specified in the Program Announcement/Funding Opportunity. *If either the Project Narrative or the budget fails eBRAP validation or needs to be modified, an updated Grants.gov application package must be submitted via Grants.gov as a "Changed/Corrected Application" with the previous Grants.gov Tracking ID prior to the application submission deadline.* The Project Narrative and Budget Form cannot be changed after the application submission deadline.

E.   Submission Dates and Times

All submission dates and times are indicated on the title page of this Program Announcement/ Funding Opportunity. Pre-application and application submissions are required. Failure to meet either of these deadlines will result in submission rejection.

F.   Other Submission Requirements

Refer to the General Application Instructions, Appendix 2, for detailed formatting guidelines.

All extramural applications must be submitted through Grants.gov. Applicant organizations and all subrecipient organizations must have a DUNS number to submit applications to Grants.gov. The applicant organization must also be registered in the Entity Management functional area of the SAM with an "Active" status to submit applications through the Grants.gov portal. Refer to the General Application Instructions, Section II.A., for information on Grants.gov registration requirements.

III.   APPLICATION REVIEW INFORMATION

A.   Application Review and Selection Process

All applications are evaluated by scientists, clinicians, and consumers in a two-tier review process. The first tier is peer review of applications against established criteria for determining technical merit. Each application is evaluated for its own merit, independent of other applications. The second tier is a programmatic review that makes recommendations for funding to the DHA RDA Directorate and the OASD(HA), based on technical merit, the relevance to the mission of the DHP and PRMRP, the specific intent of the award mechanism, and to other specified evaluation criteria in the Program Announcement/Funding Opportunity. Programmatic review is a comparison-based process in which applications with scientific and technical merit compete in a common pool. ***The highest-scoring applications from the first tier of review are not automatically recommended for funding. Funding recommendations depend on various factors as described in Section III.B.2., Programmatic Review.*** Additional information about the two-tier process used by the CDMRP can be found at http://cdmrp.army.mil/about/fundingprocess.

All CDMRP review processes are conducted confidentially to maintain the integrity of the merit-based selection process. Panel members sign a statement that application and evaluation information will not be disclosed outside the panel. Violations of confidentiality can result in the dissolving of a panel(s) and other corrective actions. In addition, personnel at the applicant or collaborating organizations are prohibited from contacting persons involved in the review process to gain protected evaluation information or to influence the evaluation process. Violations of these prohibitions will result in the administrative withdrawal of the organization's application. Violations by panel members or applicants that compromise the confidentiality of the review process may also result in suspension or debarment from Federal awards. Furthermore, the unauthorized disclosure of confidential information of one party to another third party is a crime in accordance with Title 18 United States Code 1905.

B. Application Review Process

1. Peer Review: To determine technical merit, all applications will be evaluated according to the following scored criteria, which are listed in decreasing order of importance:

- **Research Strategy and Feasibility**
  - How well the scientific rationale supports the project and its feasibility, as demonstrated by a critical review and analysis of the literature, supporting data, and logical reasoning.
  - To what extent the outcomes will support the translation of promising preclinical findings into a product for clinical application.
  - How well the hypothesis or objective(s) and specific aims are developed.
  - How well the experimental design, methods, data collection procedures, and analyses are developed and support completion of the aims.
  - The degree to which the expected outcomes are specific and measurable.
  - If applicable, to what degree the statistical plan and power analysis are appropriate for the proposed project.
  - How well the application acknowledges potential problems and addresses alternative approaches.
  - If applicable, the degree to which the plan to study patient populations is appropriate and feasible and whether the application provides evidence of availability of and access to the necessary study populations and/or resources.
  - Whether the research can be completed within the proposed period of performance.
  - How well the study (or studies) is designed to achieve the objectives, including the choice of model, if applicable, and the endpoints/outcome measures to be used.
  - How well the study (or studies) is designed to achieve reproducible and rigorous results, including controls, sample size estimation, blinding, randomization, and data handling.

- **Impact**
  - To what extent the project impacts a central critical problem or question in at least one FY16 PRMRP Topic Area.
  - If applicable, how well the proposed research project addresses one or more FY16 PRMRP Areas of Encouragement.
  - How the proposed research project, if successful, will make important scientific advances in the relevant field of research.

- To what degree the proposed project could, if successful, make a significant impact on the lives of relevant patient populations in the short term and/or long term.

- **Transition Plan and Regulatory Strategy**

  - Whether the identified next level of development and/or commercialization is realistic.

  - Whether the funding strategy described to bring the product(s) to the next level of development (e.g., specific potential industry partners, specific funding opportunities to be applied for) is reasonable and realistic.

  - How the regulatory strategy and the development plan to support the proposed product label, if applicable, are appropriate and well described.

  - If applicable, whether the proposed collaborations and other resources for providing continuity of development, including proposed development or modification of clinical practice guidelines and recommendations, provider training materials, patient brochures, and other clinical support tools, scientific journal publications, models, simulations, and applications are established and/or achievable.

  - Whether the schedule and milestones for bringing the anticipated product(s) to the next level of development (clinical trials, transition to industry, delivery to the military or civilian market, incorporation into clinical practice, or approval by the FDA) are achievable. Whether the potential risk analysis for cost, schedule, manufacturability, and sustainability is realistic and reasonable.

- **Personnel**

  - How the background and expertise of the PI and other key personnel demonstrate their ability to perform the proposed work.

  - How the levels of effort by the PI and other key personnel are appropriate to ensure the successful conduct of the project.

  - How the PI's record of accomplishment demonstrates his/her ability to accomplish the proposed work.

In addition, the following unscored criteria will also contribute to the overall evaluation of the application:

- **Environment**

  - How the scientific environment is appropriate for the proposed research.

  - How the research requirements are supported by the availability of and accessibility to facilities and resources (including collaborative arrangements).

  - How the quality and extent of organizational support are appropriate for the proposed research.

- **Budget**
  - Whether the budget is appropriate for the proposed research and within the limitations of this Program Announcement/Funding Opportunity.
- **Application Presentation**
  - To what extent the writing, clarity, and presentation of the application components influence the review.

2. **Programmatic Review:** To make funding recommendations and select the application(s) that, individually or collectively, will best achieve the program objectives, the following criteria are used by programmatic reviewers:

   a. **Ratings and evaluations of the peer reviewers**

   b. **Relevance to the mission of the DHP and FY16 PRMRP, as evidenced by the following:**
      - Adherence to the intent of the award mechanism
      - Military relevance
      - Program portfolio composition
      - Relative impact

C.   Recipient Qualification

For general information on required qualifications for award recipients, refer to the General Application Instructions, Appendix 1.

D.   Application Review Dates

All application review dates and times are indicated on the title page of this Program Announcement/Funding Opportunity.

E.   Notification of Application Review Results

Each PI and organization will receive email notification of posting of the funding recommendation in eBRAP. Each PI will receive a peer review summary statement on the strengths and weaknesses of the application.

IV. ADMINISTRATIVE ACTIONS

After receipt of pre-applications from eBRAP or applications from Grants.gov, the following administrative actions may occur:

A.   Rejection

The following will result in administrative rejection of the pre-application:
- Preproposal Narrative is missing.

The following will result in administrative rejection of the application:

- Submission of an application for which a letter of invitation was not received.
- Project Narrative exceeds page limit.
- Project Narrative is missing.
- Budget is missing.
- Submission of the same research project to different Funding Opportunities within the same program and fiscal year.

B.   Modification

- Pages exceeding the specific limits will be removed prior to review for all documents other than the Project Narrative.
- Documents not requested will be removed.

C.   Withdrawal

The following may result in administrative withdrawal of the pre-application or application:

- An FY16 PRMRP Programmatic Panel member is named as being involved in the research proposed or is found to have assisted in the pre-application or application processes including, but not limited to, concept design, application development, budget preparation, and the development of any supporting documentation. *A list of the FY16 PRMRP Programmatic Panel members can be found at http://cdmrp.army.mil/prmrp/panels/panels16.*
- The application fails to conform to this Program Announcement/Funding Opportunity description to the extent that appropriate review cannot be conducted.
- Inclusion of URLs, with the exception of links in References Cited and Publication and/or Patent Abstract sections.
- Page size is larger than 8.5 inches x 11.0 inches (approximately 21.59 cm x 27.94 cm).
- To preserve the integrity of its peer and programmatic review processes, the CDMRP discourages inclusion of any employee of its review contractors having any role in the preparation, research or other duties for submitted applications. For FY16, the identities of the peer review contractor and the programmatic review contractor may be found at the CDMRP website (http://cdmrp.army.mil/about/2tierRevProcess). Applications that include names of personnel from either of these companies will be administratively withdrawn unless plans to manage COIs are provided and deemed appropriate by the Government. Refer to the General Application Instructions, Appendix 1, for detailed information.
- Personnel from applicant or collaborating organizations are found to have contacted persons involved in the review process to gain protected evaluation information or to influence the evaluation process.

- The proposed research project is not relevant to any of the Congressionally directed FY16 PRMRP Topic Areas.

- If a clinical trial is proposed, the application will be withdrawn.

- An application submitted by a PI who does not meet the eligibility criteria will be withdrawn.

D. Withhold

Applications that appear to involve research misconduct will be administratively withheld from further consideration pending organizational investigation. The organization will be required to provide the findings of the investigation to the USAMRAA Grants Officer for a determination of the final disposition of the application.

V. AWARD ADMINISTRATION INFORMATION

A. Award Notice

Awards will be made no later than September 30, 2017. Refer to the General Application Instructions, Appendix 4, for additional award administration information.

Any assistance instrument awarded under this Program Announcement/Funding Opportunity will be governed by the award terms and conditions, which conform to DoD's implementation of the Office of Management and Budget (OMB) circulars applicable to financial assistance. Terms and conditions of new awards made after December 26, 2014 may include revisions to reflect DoD implementation of new OMB guidance in the Code of Federal Regulations, Title 2, Part 200, "Uniform Administrative Requirements, Cost Principles, and Audit Requirements for Federal Awards" (2 CFR part 200).

B. Administrative Requirements

Refer to the General Application Instructions, Appendix 4, for general information regarding administrative requirements.

C. National Policy Requirements

Refer to the General Application Instructions, Appendix 5, for general information regarding national policy requirements.

D. Reporting

Refer to the General Application Instructions, Appendix 4, Section H, for general information on reporting requirements.

Quarterly technical progress reports and quad charts may be required.

E. Award Transfers

An organizational transfer of an award will not be allowed in the last year of the (original) period of performance or any extension thereof.

Refer to the General Application Instructions, Appendix 4, Section L, for general information on organization or PI changes.

VI. VERSION CODES AND AGENCY CONTACTS

A. Program Announcement/Funding Opportunity and General Application Instructions Version

Questions related to this Program Announcement/Funding Opportunity should refer to the Program name, the Program Announcement/Funding Opportunity name, and the Program Announcement/Funding Opportunity version code [20160210i]. The Program Announcement/Funding Opportunity numeric version code will match the General Applications Instructions version code [20160210].

B. CDMRP Help Desk

Questions related to Program Announcement/Funding Opportunity content or submission requirements as well as questions related to the submission of the pre-application through eBRAP should be directed to the CDMRP Help Desk, which is available Monday through Friday from 8:00 a.m. to 5:00 p.m. ET. Response times may vary depending upon the volume of inquiries.

Phone: 301-682-5507

Email: help@eBRAP.org

C. Grants.gov Contact Center

Questions related to application submission through Grants.gov portal should be directed to the Grants.gov Contact Center, which is available 24 hours a day, 7 days a week (closed on U.S. Federal holidays). Note that the CDMRP Help Desk is unable to provide technical assistance with Grants.gov submission.

Phone: 800-518-4726; International 1-606-545-5035

Email: support@grants.gov

Sign up on Grants.gov for "send me change notification emails" by following the link on the Synopsis page for the Program Announcement/Funding Opportunity or by responding to the prompt provided by Grants.gov when first downloading the Grants.gov application package. If the Grants.gov application package is updated or changed, the original version of the application package may not be accepted by Grants.gov.

VII. APPLICATION SUBMISSION CHECKLIST

Grants.gov Application Components	Upload Order	Action	Completed
SF424 (R&R) Application for Federal Assistance		Complete form as instructed.	
Attachments Form	1	Project Narrative: Upload as Attachment 1 with file name "ProjectNarrative.pdf."	
	2	Supporting Documentation: Upload as Attachment 2 with file name "Support.pdf."	
	3	Technical Abstract: Upload as Attachment 3 with file name "TechAbs.pdf."	
	4	Lay Abstract: Upload as Attachment 4 with file name "LayAbs.pdf."	
	5	Statement of Work: Upload as Attachment 5 with file name "SOW.pdf."	
	6	Impact Statement: Upload as Attachment 6 with file name "Impact.pdf."	
	7	Military Relevance Statement: Upload as Attachment 7 with file name "MilRel.pdf."	
	8	Transition Plan: Upload as Attachment 8 with file name "Transition.pdf."	
	9	Collaborating DoD Military Facility Budget Form(s): Upload as Attachment 9 with file name "MFBudget.pdf," if applicable.	
Research & Related Senior/Key Person Profile (Expanded)		Attach PI Biographical Sketch (Biosketch_LastName.pdf) to the appropriate field.	
		Attach PI Previous/Current/Pending Support (Support_LastName.pdf) to the appropriate field.	
		Attach Biographical Sketch (Biosketch_LastName.pdf) for each senior/key person to the appropriate field.	
		Attach Previous/Current/Pending (Support_LastName.pdf) for each senior/key person to the appropriate field.	
Research & Related Budget		Complete as instructed. Attach Budget Justification (BudgetJustification.pdf) to the appropriate field.	
Project/Performance Site Location(s) Form		Complete form as instructed.	
R & R Subaward Budget Attachment(s) Form		Complete form as instructed.	

APPENDIX 1
AREAS OF ENCOURAGEMENT

Applications addressing any of the FY16 PRMRP Topic Areas are of interest to the program. *Any aspect of research relevant to one or more FY16 PRMRP Topic Areas may be considered for funding.* Areas of encouragement related to the FY16 PRMRP Topic Areas have been identified by the DoD, VA, and other relevant stakeholders. Applicants are urged to read and consider these areas of encouragement before preparing their applications. *The information provided is not exhaustive, and applicants are not restricted to submitting applications that address an area of encouragement in this list.*

Acute Lung Injury

- Research on the etiology and prevention of acute respiratory distress syndrome (ARDS) caused by the immune system's responses to infectious disease.

- Preventive techniques, novel detection technologies, and therapeutics to reduce the incidence and/or severity of ARDS and/or other lung injury secondary to trauma, transfusion, burns, hemorrhagic shock, and/or oxygen exposure.

- Development of clinical laboratory-based device for manufacturing/amplification of stem cells to treat acute lung injury/ARDS due to inhalation injury or due to single or polytrauma.

- Clinical studies to test cellular therapies in the treatment of acute lung injury/ARDS due to inhalation injury or due to single or polytrauma.

- Metrics to associate health outcomes of acute lung injury with physiological and physical performance of military Service members.

- Strategies to support the safe transport of patients with lung injury in order to optimize therapeutic interventions.

Antimicrobial Resistance

- Identification and evaluation of novel antifungals against resistant fungal infections, particularly topical therapies for wounds, surgical, and post-surgical therapies.

- Identification of novel targets for development of antibacterials for resistant strains.

- Development and testing of an aqueous-based multi-spectral antibiotic for immediate flushing of wounds on the battlefield.

- Research on the use of bacteriophages to treat antibiotic-resistant bacteria.

- Development and testing of novel interventions to directly engage patients and families in reducing inappropriate antibiotic use.

- Research on utilizing treatment protocols or diagnostic tests to limit the prescription of antibiotics for conditions that are commonly viral in nature or resolve without antibiotic treatment, such as sinusitis, bronchitis, and viral upper respiratory infections.

Chronic Migraine and Post-Traumatic Headache

- Research to investigate, develop, and validate biomarkers useful in diagnosing and monitoring traumatic brain injury patients with chronic migraine or post-traumatic headache.

- Epidemiological/natural history studies to characterize specific types of post-traumatic headache, the pathobiology of these headaches (such as the role of cortical spreading depression acutely after injury as a risk factor for chronic headaches of a migrainous type), and risk factors that might predispose people to certain types of post-traumatic headache.

- Double-blind, placebo-controlled trials in the post-traumatic headache population in order to determine whether similar phenotypes in primary headache disorders and post-traumatic headache will respond similarly to treatment.

- Research on the optimal approaches to effective management of co-occurring psychological health disorders and acute and chronic pain management for chronic migraine and post-traumatic headache, with a focus on assessing and eliminating adverse outcomes and decreasing polypharmacy.

- Research on the utility of the Patient-Centered Medical Home model of care of patients with chronic migraine or post-traumatic headache.

- Research on the treatment and prevention of acute flares of chronic migraine and post-traumatic headaches with an emphasis on non-opioid medications.

- Evaluation of the use of mechanical stimulation and/or other non-pharmaceutical treatments to reduce acute and chronic migraines and headaches.

- Precision medicine research to investigate, develop, and validate biomarkers that are not only useful in diagnosing and monitoring traumatic brain injury patients with chronic migraine or post-traumatic headache, but can also identify individual response to treatment.

Congenital Heart Disease

- Population-based and outcomes-based research projects to assess health outcomes of individuals with congenital heart disease across the lifespan.

- Research on tissue engineering approaches to patches, grafts, and transplantation that provide structural support, restore native activity, allow for tissue growth, and prevent the need for reoperation.

- Research to improve the understanding of the causes of congenital heart defects.

- Research on the transition of care of congenital heart disease patients from pediatric to adult providers.

- Research on the risk of neurologic injury and enhanced neuroprotection before, during, and after surgery for congenital heart disease.

- Research on the ability of patients with congenital heart disease to join or remain on active duty.

Constrictive Bronchiolitis

- Clinical assessments to determine the prevalence and severity of constrictive bronchiolitis and related respiratory diseases in previously deployed military Service members.

- Development and testing of less invasive and non-invasive approaches for diagnosing constrictive bronchiolitis.

- Research to develop novel therapeutics to slow or reverse progression of constrictive bronchiolitis.

- Development and/or validation of animal models of constrictive bronchiolitis, particularly models that reflect inhalation exposure-related constrictive bronchiolitis.

- Research to understand the role of environmental exposures, including mineralized dust and other particulates, in the etiology of constrictive bronchiolitis.

Diabetes

- Development of biomarkers to identify and monitor at-risk individuals and assess treatment response.

- Development and standardization of an electronic medical record (EMR) system for diabetes care to include components such as a comprehensive automated data flow chart, automated health reminders to meet standard of care metrics per the Healthcare Effectiveness Data and Information Set (HEDIS) and National Committee for Quality Assurance (NCQA), automated order entry with decision support algorithms, glycemic management tools to track and monitor glycemic variables, electronic order sets to track, monitor, and adjust insulin usage.

- Development and evaluation of an inpatient glycemic management program with strategies to improve in-hospital dysglycemia, improve short-term and long-term morbidity/mortality, reduce the cost of healthcare, and promote a seamless transition of care between inpatient and outpatient arenas.

- Research on the effectiveness, tolerability, safety, and accessibility of FDA-approved pharmacology for the treatment of obesity and prevention/improvement of obesity-related comorbid diseases in military healthcare beneficiaries, including the active duty population.

- Research on interventions to prevent complications of diabetes including diabetic retinopathy and diabetic neuropathy.

- Research to better understand the heterogeneity of diabetes.

- Research on the transplantation of allogenic or autologous pancreatic islet cells for long term natural insulin production.

Dystonia

- Research on the risk, incidence, etiology, prevention, and/or treatment of generalized dystonia, focal dystonia (including embouchure dystonia), multifocal dystonia, segmental dystonia, and/or hemidystonia.

- Research to improve identification of delayed onset dystonia following traumatic brain injury.

Emerging Infectious Diseases

- Methods to minimize risk from arboviruses among military Service members and families deployed to/living in high-risk areas, including personal protective equipment and environmental controls.

- Development and testing of practical and rapid diagnostics for clinically relevant bacterial pathogens, including biomarkers.

- Targeted vector management of Aedes aegypti, including focus areas on novel adult surveillance devices, pathogen identification, spatial repellents, and barrier treatments.

- Research toward understanding the potential influence of dietary intake as a potential repellent to mosquito vectors and vector behavior.

- Evaluation of non-vaccine prophylactics or therapeutics to prevent/treat dengue or Zika virus disease.

- Validation of airborne and droplet precaution recommendations in the medical transport environment.

- Methods for screening and diagnostic detection of emerging bloodborne pathogens, including Zika and others, in blood products.

- Methods for pathogen reduction of emerging bloodborne pathogens, including Zika and others, in blood products.

- Development of rapid diagnostic testing methods for emerging bloodborne pathogens, including Zika virus and others that can be transmitted sexually or by blood transfusion.

Focal Segmental Glomerulosclerosis

- Development of a curative therapy or treatments to delay or halt the progression of focal segmental glomerulosclerosis (FSGS) and/or prevent post-transplantation recurrence.

- Appropriate testing of medications on the market that are being used to treat FSGS without clear evidence of benefit.

- Research to improve understanding of the causes of primary and secondary FSGS, especially genetic mutations.

- Development of non-invasive methods to diagnose FSGS and its variants.

Fragile X Syndrome

- Research to advance the understanding of the pathophysiology of fragile X syndrome.

- Identification and validation of functional measures of the manifestations of fragile X syndrome across the lifespan.

- Identification and testing of novel targets for fragile X syndrome therapeutics.

- Development and evaluation of novel or existing therapeutics for the treatment of fragile X syndrome.

Hepatitis B

- Research on vaccination options for those persons unable to mount immunity to hepatitis B virus (HBV).

- Development of strategies for reliable, non-invasive, early detection of HBV-related liver disease and hepatocellular carcinoma.

- Research on strategies to promote reversal of liver fibrosis and/or assess the associated clinical and pathological outcomes.

- Natural history or other studies to establish risk indicators of progression from asymptomatic or inactive chronic HBV infection to symptomatic disease and parameters for initiation and duration of disease treatment.

- Development and evaluation of strategies to promote vaccination for HBV.

- Research to support development of a curative therapy for HBV infection.

- Clinical studies to evaluate combination therapies for treatment of HBV infection.

- Identification and reduction of HBV in blood products for transfusion.

- Research on strategies to reduce vertical (mother-to-child) transmission of HBV.

Hereditary Angioedema

- Research to improve early diagnosis of hereditary angioedema (HAE).

- Evaluation of existing or novel therapeutics in pediatric HAE patients.

- Research toward the development of a cure for HAE.

- Development and/or validation of novel therapeutic strategies for the treatment and/or prevention of HAE attacks.

Hydrocephalus

- Research on the etiology, prevention, diagnosis, and treatment of post-traumatic hydrocephalus.

- Discovery or validation of novel therapies and therapeutic targets for the treatment of hydrocephalus and its sequelae, including therapies directed at myelin regeneration and repair.

- Research on approaches to lessening the impact of brain damage caused by hydrocephalus.

- Development or validation of biomarkers and imaging techniques, particularly multimodal approaches, to aid in diagnosis, prognosis, and monitoring therapeutic efficacy.

- Research on the prevention of shunt failure.

- Studies to better understand the causes and/or pathogenesis of hydrocephalus.

- Development or validation of improved hydrocephalus model systems.

Inflammatory Bowel Disease

- Clinical studies in human subjects directed toward understanding how acute enteric infections may trigger chronic bowel diseases with acute and sub-acute inflammatory bowel disease (IBD), including systems biology approaches.

- Mechanistic studies in animal models designed to understand how enteric infection may trigger IBD, including genomic, microbiomic, and immune mechanisms.

- Epidemiological studies of post-infectious acute and sub-acute IBD that define risk and provide estimates of illness-associated disability, healthcare costs, and symptom duration from a military health system and societal perspective.

- Studies (epidemiological, clinical, animal model) directed toward understanding the interaction between acute/chronic stress and infection and development of IBD.

- Research to explore whether the travel patterns of active duty personnel increase the risk of developing inflammatory bowel disease by means of exposure to changes in intestinal microflora.

- Research to better characterize the association between the use of drugs, such as isotretinoin and long-term doxycycline, and the development of IBD.

- Research on the role of diet in the development and progression of IBD.

- Research on the influence of the microbiome on IBD.

Influenza

- Research investigating acute and timely diagnostic testing of influenza patients.

- Development and testing of a universal influenza vaccine.

- Development and evaluation of novel and/or combination influenza therapies.

- Research on the underlying mechanisms of influenza drug resistance.

- Research to improve understanding of host responses to influenza infection.

- Research on the factors that contribute to, and/or the risk reduction of, the emergence of zoonotic and pandemic influenza viruses.

Integrative Medicine

- Research on the use of integrative medicine strategies, such as meditation, tai chi, acupuncture, herbal medicine, to improve psychological health and quality of life in cancer patients and survivors.

- Research on the use of integrative medicine in treatment and management of chronic pain disorders, including comparative efficacy studies relative to standard of care.

- Rigorous longitudinal studies of integrative medicine approaches for enhancing resilience and for treating psychological health issues and co-occurring disorders.

- Precision medicine research to investigate, develop, and validate biomarkers that can help determine an individual's response to integrative medicine treatments for pain.

- Development of outcomes tools and measures to evaluate the effectiveness of integrative medicine pain management approaches.

- Definitive studies to determine the effectiveness of self-care meditation-based treatments, courses and training programs in improving resiliency to stress in a military environment, in austere operational platforms such as submarines, small-deck ships, or in combat-fatigued military healthcare providers.

Interstitial Cystitis

- Studies that define the risk and prevalence and assess the impact of interstitial cystitis among active duty personnel.

- Identification biological markers that could be used to make a definitive diagnosis of interstitial cystitis.

- Evaluation and assessment of novel treatment options for interstitial cystitis patients, including intravesical therapy.

Lupus

- Development of early diagnosis technologies and strategies to detect lupus that can be implemented within the Military Health System.

- Studies to elucidate the etiology of lupus and its heterogeneity, with emphasis on gene-environment interactions.

- Studies that seek to identify molecular factors that contribute to the increased incidence and severity of lupus in non-European ancestry populations, such as African-Americans and Hispanic-Americans.

- Research the utility of newer immunosuppressive agents in the treatment of both cutaneous and systemic lupus.

- Research to explore novel sunblocking materials or methods that provide lupus patients, including active duty personnel, more effective and sustained protection from sunlight.

- Epidemiological studies to better elucidate the risk of developing systemic lupus in patients with discoid lupus.

Malaria

- Identification and/or development of novel circulating biomarkers that indicate presence of hepatic hypnozoites in relapsing malarias.

- Identification of novel malaria drug targets for blood and liver stage parasites.

- Development of new, or improvement of existing, strategies for culturing relapsing parasites such as Plasmodium vivax, P. ovale, and P. cynomolgi in vitro.

- Development of rodent models of human/rhesus relapsing malarias.

- Development of methods to induce high levels of long-lived, broadly protective (against multiple strains) immunity against pre-erythrocytic stages of P. falciparum.

- Development, testing, and evaluation of spatial repellents to provide protection against Anopheline vectors.
- Development and/or testing of new technologies or methods to reduce transfusion-transmitted malaria.

Metals Toxicology

- Identification and development of biomarkers as an assessment tool to evaluate military Service members' acute exposure to toxic metals in an operational environment, and association of health outcomes.
- Retrospective studies to evaluate risk and exposure among workers at DoD industrial facilities.
- Research on the toxicity of metal combinations and the interaction between different metal components.
- Research on the additive effects of multiple exposures to metal(s).

Mitochondrial Disease

- Research on the basic biology and physiology of mitochondria to better understand the pathology of primary mitochondrial diseases.
- Development of improved tools and animal models to study primary mitochondrial disease and evaluate therapeutics.
- Identification and testing of non-invasive techniques and biomarkers to monitor mitochondrial function, aid in diagnosis, and/or evaluate therapeutic efficacy.

Nanomaterials for Bone Regeneration

- Research on nanomaterials-based methods to facilitate recruitment of endogenous cell populations for enhanced bone regeneration and osseointegration.
- Technologies addressing segmental/large bone defects in craniomaxillofacial and/or load-bearing regions.
- Development of controlled release/extended release of growth factors for bone regeneration.
- Technologies that repair the soft tissue envelope to enhance bone regeneration.
- Development and testing of laboratory grown hydroxyapatite crystals for bone regeneration.

Non-Opioid Pain Management

- Research on pain management strategies for patients with limited access to skilled providers and resources, including battlefield and resource-limited environments.
- Development of population-based outcomes tools and measures to evaluate the effectiveness of pain management approaches across time and environment.
- Research on treatments for chronic pain management particularly in complex patients (i.e., chronic, high-utilization polypharmacy patients).

- Research to increase understanding of and preventative treatments for conversion of acute to chronic pain.

- Research that provides evidence of what pain management strategies work for whom and under what conditions.

- Research to identify and address biopsychosocial aspects of pain to reduce or eliminate use of opioid pain medication(s).

- Comparative studies evaluating the efficacy of different pain management strategies, including complementary and alternative medicine approaches.

- Identification and development of non-opioid pain management techniques that promote positive psychological health-related outcomes.

- Research on non-opioid pain management practices appropriate for use in the transport environment (helicopter, aircraft, ambulance, etc.) or in a prolonged field care setting (up to 72 hours).

- Development of non-opioid pain medicine that can be given intramuscularly, inhaled, submucosally, or intravenously on the battlefield to provide adequate relief of pain without affecting the cardiorespiratory systems.

- Research on case management strategies that optimize the effectiveness of pain clinics and use of non-opioid pain therapies.

- Research on standardized approaches for early identification and prevention of chronic musculoskeletal pain.

- Research on the effects of early use of case management to reduce dependence on opioid therapies for pain management.

- Research investigating the use of ketamine for acute flares of chronic, non-cancer painful conditions.

Pancreatitis

- Retrospective studies to determine risk and incidence of pancreatitis among former and current active duty personnel.

- Development and testing of novel therapeutics for acute and/or chronic pancreatitis.

- Research on the basic biology and physiology of the pancreas to better understand the etiology and pathology of pancreatitis.

Pathogen-Inactivated Dried Plasma

- Development of technology to produce pathogen-reduced dried plasma in military/civilian donor centers that is acceptable for FDA licensure in support of contingency/combat operations.

- Development and/or validation of methods for pathogen reduction of emerging bloodborne pathogens, including malaria, Babesi, Ebola, West Nile Virus, dengue, Chikungunya, Zika virus and other pathogens found in blood products.

- Development of a next-generation pathogen reduction device with increased throughput for donor center production of whole blood, platelets and plasma in support of contingency/combat operations.

- Development and/or validation of next generation technologies for the production of pathogen-reduced dried plasma (including emerging pathogens) derived from whole blood that has been pathogen-reduced. Technology should be suitable for military blood bank use in deployed scenarios.

Polycystic Kidney Disease

- Development of improved treatment strategies for polycystic kidney disease (PKD), including approaches to identify and monitor patients at higher risk for progressing to end stage renal disease.

- Research on the underlying pathobiology and molecular mechanisms of PKD, including genetic studies, cyst formation and growth, the role of cilia, and factors that modify disease progression and/or severity.

- Research on the lifestyle factors which may modify the progression of PKD.

Post-Traumatic Osteoarthritis

- Research to establish activity recommendations for maximal joint life following joint repair, particularly in young patient populations.

- Research into cell-based approaches for long-term steroid release.

- Studies to evaluate and develop best practices for multidisciplinary team approaches and treatment algorithms for post-traumatic osteoarthritis.

- Development or validation of novel approaches to restoring joint stability after injury.

- Sustained release, intra-articular injectable steroidal, non-steroidal, or disease-modifying therapies that offer two or more months of symptomatic relief of pain and/or inflammation in a single injection.

- Research on therapies that target multiple phases of the cellular response pathways that are implicated in development of post-traumatic osteoarthritis, including cell death, inflammation, matrix changes, and changes in catabolic and anabolic responses.

Psychotropic Medications

- Research on the use of ketamine in patients presenting with suicidal ideations or intent.

- Research on the use of psychotropic medications to increase resilience in military units.

- Identification and/or development of therapies that can completely or selectively reverse the effects of psychotropic medications.

- Research into the use and repurposing of psychotropic medications for the treatment of psychiatric disorders including post-traumatic stress, suicidal ideation, substance abuse, and other comorbidities.

- Research to evaluate the use of psychotropic medications for mental health issues specific to women in the military.

- Research toward increasing the accuracy and effectiveness of prescription practices for mental health medications, including but not limited to development of biomarkers to match patients to medications and measure treatment responsiveness, development of better outcome measures, and/or methods to improve collection of patient data in real time.

Pulmonary Fibrosis

- Retrospective studies to determine risk and incidence of pulmonary fibrosis among current and former military Service members.

- Identification of biomarkers of pulmonary injury or early predictors of lung disease.

- Research into the pathobiology and molecular mechanisms underlying the development of pulmonary fibrosis.

- Development and/or testing of novel treatments to delay or modify the progression of pulmonary fibrosis.

- Development and/or validation of improved tools and animal models to study pulmonary fibrosis and evaluate therapeutics.

Respiratory Health (excludes lung cancer and mesothelioma)

- Research on the cause, treatment, and prevention of respiratory symptoms and ailments possibly associated with deployed and re-deployed military personnel, including acute eosinophilic pneumonia, asthma, allergies, and other chronic lung diseases and breathing problems.

- Research to evaluate the impact of deployment on the prevalence and severity of respiratory disease in military Service members.

- Studies to determine the natural history of deployment-related respiratory disease and to identify factors associated with respiratory disease.

- Identification and development of biomarkers of exposure to military-relevant hazards such as airborne nanomaterials, diesel exhaust, and other combustion products and fuels.

- Development and/or validation of methods to detect volatile organic hydrocarbons from the breath of individuals exposed to toxic chemicals.

- Identification of biochemical, physiological, or combined biomarkers of effect or exposure for evaluating injury from acutely toxic occupational or environmental exposures in military operational environments.

- Identification of biochemical, physiological, or combined biomarkers of effect or exposure for the early assessment of long-term health consequences of military-relevant occupational or environmental toxicant exposures.

- Research investigating the treatment of patients with chronic mild hypoxia.

Rett Syndrome

- Identification and/or validation of novel biological targets for the treatment of Rett syndrome.

- Development and testing of interventions to improve the neurological symptoms of Rett syndrome.

- Research to understand the relationship between genetic mutations, physical traits, and symptoms in individuals with Rett syndrome.

- Research on the pathobiology of the MeCP2 gene and protein.

- Research to understand Rett syndrome's commonalities with and differences from classic autism and regressive autism.

Rheumatoid Arthritis

- Research to better understand the relationship between genetic risk and environmental triggers, such as infection or smoking, in developing rheumatoid arthritis.

- Studies that identify or validate biomarkers or personalized medicine strategies that allow for individualized medication choice based upon the patient's underlying biology or disease state.

- Research on the long-term use of immunosuppressants in patients with rheumatoid arthritis and the likelihood of developing infections.

- Research to establish activity recommendations following joint replacement for maximal joint life.

Scleroderma

- Research on the molecular mechanisms and pathogenesis of scleroderma.

- Development and/or testing of novel therapies and identification of novel therapeutic targets in scleroderma.

- Research on biomarkers and other approaches to diagnose scleroderma, monitor disease progression, and/or assess response to treatment.

- Epidemiologic studies investigating the impact of localized scleroderma (morphea) on duty performance, use of personal protective equipment, and deployability.

- Research on the efficacy of newer immunosuppressive agents in the treatment of morphea and scleroderma.

Sleep Disorders

- Research on how the disruption of normal sleep and circadian biological rhythms adversely affects health, safety, performance, and productivity of military and civilian populations.

- Studies to assess sleep disturbance and clinical sleep disorders in female military personnel.

- Research on the association between sleep disorders and post-traumatic stress disorder (PTSD), traumatic brain injury, depression, and/or anxiety.

- Research to assess clinical algorithms that improve adherence to Continuous Positive Airway Pressure (CPAP).

- Investigations into non-CPAP-based treatment regimens that enhance readiness and deployability in active duty military personnel.

- Studies to determine the efficacy of cognitive behavioral therapy for insomnia (CBTI) in active duty military personnel with insomnia.

- Research focused on investigating how psychiatric disorders (PTSD in particular), combined with the disruption/degradation of sleep quality, impact long-term physical health through changes in glucocorticoid regulation.

- Development and/or testing of non-pharmacological treatments for sleep disorders.

- Research on the impact of sleep deprivation on the efficacy of psychological treatments.

- Research on the prevention and/or mitigation of sleep disorders that are associated with long aeromedical evacuation flights for both clinical team members and patients.

Tinnitus

- Research to understand the mechanisms of tinnitus, its relationship to noise-induced hearing loss, and progression to chronic tinnitus.

- Research to increase the knowledge of the prevalence, incidence, natural history, occupational, and sex-related differences of tinnitus and its possible relation to individual blast/noise exposures.

- Improvement of objective tools to diagnose and characterize tinnitus (e.g., imaging techniques to identify functional and structural changes in the brain, biomarkers of resiliency, and susceptibility to tinnitus).

- Identification of novel therapies for early interventions to prevent and treat tinnitus, including new uses for existing drugs, nutritional and pharmaceutical based strategies, and acoustic, electrical, and other stimulation technologies.

Tuberculosis

- Development of a diagnostic assay that can be used at the point of care to rapidly and accurately diagnose tuberculosis (TB).

- Development of novel TB vaccines, or optimization of current TB vaccines.

- Identification and/or validation of biomarkers that can be used to assess vaccine efficacy and protection against TB disease.

- Research to understand, diagnose, or treat multi-drug resistant TB or extensively drug-resistant TB.

- Research to determine the appropriate precautions to use for the transport of active TB patients.

Vaccine Development for Infectious Disease

- Development of vaccines for Chikungunya virus, dengue virus, and Zika virus.

- Evaluation of passive immunization strategies to use in conjunction with dengue vaccination and Zika vaccination.

- Research leading to a better understanding of the immune mechanisms involved in the clearance of dengue virus and Zika virus and mechanisms of immune enhancement that lead to more severe clinical disease.

- Development of flexible vaccine technologies that can be used to rapidly respond to emerging and re-emerging infectious diseases threats.

- Evaluation of humoral and cellular immune responses after vaccination and natural infection.

- Development of a safe, effective dengue human challenge model for clinical trials.

Vascular Malformations

- Studies into the natural history, genetics, and pathogenesis of vascular malformations.

- Research to discover or develop novel therapeutic targets and treatments to regress or prevent vascular malformations.

- Research to improve methods to diagnose and manage vascular malformations.

- Development of non-invasive or minimally invasive technologies or approaches for the control of internal bleeding associated with vascular malformations.

- Studies to identify risk and/or establish standard practices for the treatment of hemorrhage from brain arteriovenous malformations.

- Research on the prevention or treatment of complications associated with vascular malformations such as pain, infection, seizures, tissue breakdown, tissue overgrowth, or airway obstruction.

Women's Heart Disease

- Retrospective studies to determine risk and incidence of heart disease among former and current female active duty personnel.

- Research focused on elucidating the potential relationship between PTSD and women's heart disease.

- Identification of sex-specific approaches to increase the effectiveness of cardiac rehabilitation programs.

- Research on factors to predict and prevent gestational diabetes, hypertension, preeclampsia, and placental insufficiency.

- Research on trauma-induced cardiac arrest secondary to hemorrhage and polytrauma in the female population.

APPENDIX 2
DOD AND VA WEBSITES

PIs are encouraged to integrate and/or align their research projects with DoD and/or VA research laboratories and programs. Collaboration with DoD or VA investigators is also encouraged. Below is a list of websites that may be useful in identifying additional information about DoD and VA areas of research interest, ongoing research or potential opportunities for collaboration within the FY16 PRMRP Topic Areas.

Air Force Office of Scientific Research
http://www.wpafb.af.mil/afrl/afosr/

Air Force Research Laboratory
http://www.wpafb.af.mil/afrl

Armed Forces Radiobiology Research Institute
http://www.usuhs.edu/afrri/

Clinical and Rehabilitative Medicine Research Program
https://crmrp.amedd.army.mil

Combat Casualty Care Research Program
https://ccc.amedd.army.mil

Congressionally Directed Medical Research Programs
http://cdmrp.army.mil

Defense Advanced Research Projects Agency
http://www.darpa.mil/

Defense Technical Information Center
http://www.dtic.mil

Defense Threat Reduction Agency
http://www.dtra.mil/

Military Health System Research Symposium
https://mhsrs.amedd.army.mil/SitePages/Home.aspx

Military Infectious Diseases Research Program
https://midrp.amedd.army.mil

Military Operational Medicine Research Program
https://momrp.amedd.army.mil

Naval Health Research Center
http://www.med.navy.mil/sites/nhrc

Navy and Marine Corps Public Health Center
http://www.nmcphc.med.navy.mil/

Office of Naval Research
http://www.med.navy.mil/

Office of the Under Secretary of Defense for Acquisition, Technology and Logistics
http://www.acq.osd.mil/

Telemedicine and Advanced Technology Research Center
http://www.tatrc.org/

Uniformed Services University of the Health Sciences
http://www.usuhs.edu/research

U.S. Army Institute of Surgical Research
http://www.usaisr.amedd.army.mil/

U.S. Army Research Institute of Environmental Medicine
http://www.usariem.army.mil/

U.S. Army Medical Research Institute of Infectious Diseases
http://www.usamriid.army.mil/

U.S. Army Medical Research and Materiel Command
https://mrmc.amedd.army.mil/

U.S. Army Research Laboratory
http://www.arl.army.mil

U.S. Department of Defense Blast Injury Research Program
https://blastinjuryresearch.amedd.army.mil/

U.S. Department of Veterans Affairs, Office of Research and Development
http://www.research.va.gov

U.S. Naval Research Laboratory
http://www.nrl.navy.mil

Walter Reed Army Institute of Research
http://wrair-www.army.mil