

I. OVERVIEW OF THE FUNDING OPPORTUNITY

Program Announcement for the Department of Defense

Defense Health Program

Congressionally Directed Medical Research Programs

Peer Reviewed Medical Research Program

Focused Program Award

Announcement Type: Initial

Funding Opportunity Number: W81XWH-17-PRMRP-FPA

**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), July 20, 2017
- **Invitation to Submit an Application:** August 2017
- **Application Submission Deadline:** 11:59 p.m. ET, October 26, 2017
- **End of Application Verification Period:** 5:00 p.m. ET, October 31, 2017
- **Peer Review:** December 2017
- **Programmatic Review:** February 2018

This Program Announcement must be read in conjunction with the General Application Instructions, version 20170516. The General Applications Instructions document is available for downloading from the Grants.gov funding opportunity announcement by selecting the “Package” tab, clicking “Preview,” and then selecting “Download Instructions.”

TABLE OF CONTENTS

I. OVERVIEW OF THE FUNDING OPPORTUNITY.....	1
II. DETAILED INFORMATION ABOUT THE FUNDING OPPORTUNITY.....	4
II.A. Program Description.....	4
II.A.1. FY17 PRMRP Topic Areas	4
II.B. Award Information	6
II.C. Eligibility Information.....	9
II.C.1. Eligible Applicants	9
II.C.2. Cost Sharing.....	10
II.C.3. Other	10
II.D. Application and Submission Information.....	10
II.D.1. Address to Request Application Package.....	11
II.D.2. Content and Form of the Application Submission	11
II.D.3. Dun and Bradstreet Universal Numbering System (DUNS) Number and System for Award Management (SAM).....	29
II.D.4. Submission Dates and Times.....	29
II.D.5. Funding Restrictions.....	30
II.D.6. Other Submission Requirements	31
II.E. Application Review Information	31
II.E.1. Criteria	31
II.E.2. Application Review and Selection Process.....	36
II.E.3. Integrity and Performance Information.....	37
II.E.4. Anticipated Announcement and Federal Award Dates.....	37
II.F. Federal Award Administration Information	37
II.F.1. Federal Award Notices.....	37
II.F.2. Administrative and National Policy Requirements.....	39
II.F.3. Reporting.....	39
II.G. Federal Awarding Agency Contacts.....	40
II.G.1. CDMRP Help Desk	40
II.G.2. Grants.gov Contact Center	40
II.H. Other Information.....	40
II.H.1. Program Announcement and General Application Instructions Versions.....	40
II.H.2. Administrative Actions.....	40
II.H.3. Application Submission Checklist	43

APPENDIX 1 ACRONYM LIST 45
APPENDIX 2 AREAS OF ENCOURAGEMENT..... 46
APPENDIX 3 DOD AND VA WEBSITES..... 65

II. DETAILED INFORMATION ABOUT THE FUNDING OPPORTUNITY

II.A. Program Description

Applications to the Fiscal Year 2017 (FY17) Peer Reviewed Medical Research Program (PRMRP) are being solicited for the Defense Health Agency (DHA) J9, Research and Development Directorate, by the U.S. Army Medical Research Acquisition Activity (USAMRAA) using delegated authority provided by United States Code, Title 10, Section 2358 (10 USC 2358). As directed by the Office of the Assistant Secretary of Defense for Health Affairs (OASD[HA]), the DHA manages the Defense Health Program (DHP) Research, Development, Test, and Evaluation (RDT&E) appropriation. The execution management agent for this Program Announcement 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 FY16 totaled \$1.371 billion. The FY17 appropriation is \$300 million (M).

The vision of the FY17 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 FY17 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.

II.A.1. FY17 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 FY17 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 FY17 PRMRP Topic Areas are listed below.

- Acute Lung Injury
- Antimicrobial Resistance
- Arthritis
- Burn Pit Exposure
- Chronic Migraine and Post-Traumatic Headache
- Congenital Heart Disease
- Constrictive Bronchiolitis
- Diabetes
- Diarrheal Diseases
- Dystonia
- Early Trauma Thermal Regulation
- Eating Disorders

- Emerging Infectious Diseases
- Epidermolysis Bullosa
- Focal Segmental Glomerulosclerosis
- Fragile X
- Guillain-Barré Syndrome
- Hepatitis B and C
- Hereditary Angioedema
- Hydrocephalus
- Immunomonitoring of Intestinal Transplants
- Inflammatory Bowel Diseases
- Influenza
- Integrative Medicine
- Interstitial Cystitis
- Malaria
- Metals Toxicology
- Mitochondrial Disease
- Musculoskeletal Disorders
- Nanomaterials for Bone Regeneration
- Non-Opioid Pain Management
- Pancreatitis
- Pathogen-Inactivated Dried Cryoprecipitate
- Polycystic Kidney Disease
- Post-Traumatic Osteoarthritis
- Pulmonary Fibrosis
- Respiratory Health
- Rett Syndrome
- Rheumatoid Arthritis
- Scleroderma
- Sleep Disorders
- Spinal Muscular Atrophy
- Sustained-Release Drug Delivery
- Tinnitus
- Tuberculosis
- Vaccine Development for Infectious Disease
- Vascular Malformations
- Women's Heart Disease

Research relevant to one or more FY17 PRMRP Topic Areas may be considered for funding. ***Applicants should select the FY17 PRMRP Program Announcement most appropriate to the stage of the proposed research.*** Areas of Encouragement related to the FY17 PRMRP Topic Areas have been identified by the Department of Defense (DoD), the Department of Veterans Affairs (VA), and other relevant stakeholders ([Appendix 2](#)). 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.***

II.B. Award Information

The PRMRP Focused Program Award mechanism is intended to optimize research and accelerate the solution for a critical question related to at least one of the Congressionally directed FY17 PRMRP Topic Areas through a synergistic, multidisciplinary research program. The anticipated total costs budgeted for the entire period of performance for an FY17 PRMRP Focused Program Award will not exceed **\$10M**. Refer to [Section II.D.5, Funding Restrictions](#), for detailed funding information.

Key aspects of this award include:

Overarching Challenge: Focused Program Award applications must describe a unifying, overarching challenge that will be addressed by a set of research projects. The overarching challenge must be relevant to a critical problem or question in the field of research and/or patient care in at least one of the FY17 PRMRP Topic Areas.

Research Projects: Applications shall include multiple, distinct research projects led by individual project leaders that address complementary aspects of the overarching challenge. Applicants are strongly encouraged to submit a minimum of four research projects; additional studies are allowed. While individual projects must be capable of standing on their own high scientific merits, they must also be interrelated and synergistic with the other proposed projects and advance a solution beyond what would be possible through individual efforts. The exploration of multiple hypotheses or viewpoints of the same line of questioning is encouraged. This award mechanism is not intended to support a series of research projects that are dependent on the success of any other project. Each project should propose a unique approach to addressing the overarching challenge and be capable of producing research findings with potential to impact the field and/or patient care. Individual research projects may range from exploratory, hypothesis-developing studies through small-scale clinical trials (i.e., up to and including Phase II or equivalent). There should be a clear intent to progress toward translational/clinical work over the course of the effort.

Implementation: The research strategy to address the overarching challenge must be supported by a detailed plan that identifies critical milestones; outlines the knowledge, resources, and technical innovations that will be utilized to achieve the milestones; and explains how the outcomes will be translated to patients. A robust statistical plan and statistical expertise should be included where applicable. A plan for assessing individual project performance and progress toward addressing the overarching challenge must be included in the implementation plan. Plans to include an External Advisory Board are encouraged; however, applicants must be careful to avoid potential conflicts of interest (COIs) during review of the application by ensuring no contact with, recruiting of, or naming of specific members in the application. For multi-institutional collaborations, plans for communication and data transfer among the collaborating institutions, as well as how data, specimens, and/or imaging products obtained during the study will be handled, must be included. An intellectual and material property plan agreed to by participating organizations is required in the application's supporting documentation.

Research Team: The overall effort will be led by a Principal Investigator (PI) with demonstrated success in leading large, focused projects. The PI is required to devote a minimum

of 20% effort to this award. The PI should create an environment that fosters and supports collaboration and innovation in a way that engages all members of the team in all aspects of the research plan. The research team assembled by the PI should be highly qualified and multidisciplinary, with identified project leaders for each of the complementary and synergistic research projects. The resources and expertise brought to the team by each project leader should combine to create a robust, synergistic collaboration. The PRMRP Science Officer assigned to a resulting award must be invited to participate in periodic research team meetings. The plan for such meetings should be noted in the application.

Milestone Meeting: The PI will be required to present an update on progress toward accomplishing the goals of the award at a Milestone Meeting to be held in the National Capital Region after the conclusion of Year 2 of the period of performance. The PI may bring up to three additional members of the research team to the meeting. The Milestone Meeting will be attended by members of the PRMRP Programmatic Panel, CDMRP staff, and the USAMRAA Grants Officer.

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 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 strongly 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 FY17 PRMRP Topic Areas can be found in [Appendix 3](#).

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.*** When possible, protocols should be written for research with human subjects and/or human anatomical substances that are specific to the DoD-supported effort outlined in the submitted application. Submission to HRPO of protocols covering more than the scope of work in the DoD-funded award will require HRPO review of the entire protocol as DoD-supported research and may include extensive modifications to meet DoD human subjects protection requirements. Refer to the General Application Instructions, Appendix 1, and the Human Subject Resource Document available on the electronic Biomedical Research Application Portal (eBRAP) “Funding Opportunities & Forms” web page (<https://ebrap.org/eBRAP/public/Program.htm>) for additional information.

A clinical trial is defined as a prospective accrual of patients (human subjects) in whom an intervention (e.g., device, drug, biologic, surgical procedure, rehabilitative modality, behavioral intervention, or other) is tested for a measurable outcome with respect to safety, effectiveness, and/or efficacy. This outcome represents a direct effect on the subject of that intervention or interaction.

Research Involving Animals: 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 http://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 the General Application Instructions, Appendix 1, for additional information.

The CDMRP intends that information, data, and research resources generated under awards funded by this Program Announcement 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 2, Section K.

Awards will be made no later than September 30, 2018. For additional information refer to [Section II.F.1, Federal Award Notices](#).

II.C. Eligibility Information

II.C.1. Eligible Applicants

II.C.1.a. Organization: All organizations, including international organizations, are eligible to apply.

Government Agencies within the United States: Local, state, and Federal Government agencies are eligible to the extent that applications do not overlap with their fully funded internal programs. Such agencies are required to explain how their applications do not overlap with their internal programs.

As applications for this Program Announcement may be submitted by extramural and intramural organizations, these terms are defined below.

Extramural Organization: An eligible non-DoD organization. Examples of extramural organizations include academia, biotechnology companies, foundations, Government, and research institutes. *Extramural Submission: Application submitted by a non-DoD organization to Grants.gov.*

Intramural DoD Organization: A DoD laboratory, DoD military treatment facility, and/or DoD activity embedded within a civilian medical center. *Intramural Submission: Application submitted by a DoD organization for an intramural investigator who is a DoD military or civilian employee working within a DoD laboratory or military treatment facility or in a DoD activity embedded within a civilian medical center.*

Note: Applications from an intramural organization or from an extramural non-DoD Federal organization may be submitted through a research foundation.

The USAMRAA makes awards to eligible organizations, not to individuals.

II.C.1.b. Principal Investigator:

- The PI must be an independent investigator at or above the level of Full Professor (or equivalent).
 - Project leaders for each of the complementary and synergistic research projects must be at or above the level of Assistant Professor (or equivalent).

An eligible PI, regardless of ethnicity, nationality, or citizenship status, must be employed by, or affiliated with, an eligible organization.

The CDMRP encourages all PIs to participate in a digital identifier initiative through Open Researcher and Contributor ID, Inc. (ORCID). Registration for a unique ORCID identifier can be done online at <http://orcid.org/>.

II.C.2. Cost Sharing

Cost sharing/matching is not an eligibility requirement.

II.C.3. Other

Extramural organizations must be able to access **.gov** and **.mil** websites in order to fulfill the financial and technical deliverable requirements of the award and submit invoices for payment.

There are no limitations on the number of applications for which an investigator may be named as a PI.

For general information on required qualifications for award recipients, refer to the General Application Instructions, Appendix 3.

Refer to [Section II.H.2, Administrative Actions](#), for a list of administrative actions that may be taken if a pre-application or application does not meet the administrative, eligibility, or ethical requirements defined in this Program Announcement.

II.D. Application and 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). *As an exception, applicants may submit a research project described in their FY17 PRMRP Focused Program Award to the Discovery Award (Funding Opportunity Number: W81XWH-17-PRMRP-DA), Investigator-Initiated Research Award (Funding Opportunity Number: W81XWH-17-PRMRP-IIRA), and/or Clinical Trial Award (Funding Opportunity Number: W81XWH-17-PRMRP-CTA); however, accepting multiple awards to support the same project will not be allowed.*

Extramural Submission is defined as an application submitted by a non-DoD organization to Grants.gov.

Intramural Submission is defined as an application submission by a DoD organization for an intramural investigator, who is a DoD military or civilian employee working within a DoD laboratory or military treatment facility, or working in a DoD activity embedded within a civilian medical center.

II.D.1. Address to Request Application Package

Submitting Extramural and Intramural Organizations: Pre-application content and forms can be accessed at eBRAP (<https://eBRAP.org>).

Submitting Extramural Organizations: Full application packages can be accessed at Grants.gov.

Submitting Intramural DoD Organizations: Full application packages can be accessed at eBRAP.org.

Contact information for the CDMRP Help Desk and the Grants.gov Contact Center can be found in [Section II.G, Federal Awarding Agency Contacts](#).

II.D.2. Content and Form of the Application Submission

Submission is a two-step process requiring both ***pre-application*** and ***full application*** as indicated below. The submission process should be started early to avoid missing deadlines. There are no grace periods.

Pre-application Submission: All pre-applications for both extramural and intramural organizations must be submitted through eBRAP (<https://eBRAP.org/>).

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.

Full Application Submission: Full applications must be submitted through the online portals as described below.

Submitting Extramural Organizations: Full applications from extramural organizations must be submitted through Grants.gov. Applications submitted by extramural organizations (e.g., research foundations) on behalf of intramural DoD or other Federal organizations or investigators will be considered extramural submissions.

Submitting Intramural DoD Organizations: Intramural DoD organizations may submit full applications to either eBRAP or Grants.gov. Intramural DoD organizations that are unable to submit to Grants.gov should submit through eBRAP. Intramural DoD organizations with the capability to submit through Grants.gov may submit following the instructions for extramural submissions through Grants.gov or may submit to eBRAP. Applications from extramural organizations, including non-DoD Federal organizations, received through eBRAP will be withdrawn. See definitions in [Section II.C.1, Eligible Applicants](#).

For both Extramural and Intramural applicants: A key feature of eBRAP is the ability of an organization's representatives and PIs to view and modify the full application submissions associated with them. eBRAP will validate full application files against the specific Program Announcement 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.

The application title, eBRAP log number, and all information for the PI, Business Official(s), performing organization, and contracting organization must be consistent throughout the entire pre-application and application submission process. Inconsistencies may delay application processing and limit or negate 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.

II.D.2.a. Step 1: Pre-Application Submission Content

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 full application submission process.

To begin the pre-application process, first select whether the submitting organization is extramural or intramural, then confirm your selection or cancel. **Incorrect selection of extramural or intramural submission type may result in delays in processing.**

If an error has been made in the selection of extramural versus intramural and the pre-application submission deadline has passed, the PI or Business Official must contact the CDMRP Help Desk at help@eBRAP.org or 301-682-5507.

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 FY17 PRMRP Topic Area addressed by the proposed research. If the proposed research project is aligned with more than one FY17 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 for extramural submissions). The Business Official must be either 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 for extramural submissions), and click on “Add Organizations to this Pre-application.” The organizations must be either 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.

[FY17 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 II.H.2.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 pre-application or application preparation, research, or other duties for submitted pre-applications or applications. For FY17, 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>). Pre-applications or 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 Grants Officer. Refer to the General Application Instructions, Appendix 3, 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 the General Application Instructions, Appendix 3, Section C, 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 (five-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 program relates to at least one of the FY17 PRMRP Topic Areas. If applicable, describe how the proposed research program addresses an FY17 PRMRP Area of Encouragement ([Appendix 2](#)).
- **Overarching Challenge:** Describe the unifying challenge or question to be addressed and how it is relevant to a critical problem or question in the field of research and/or patient care in at least one of the FY17 PRMRP Topic Area(s). Clearly articulate the rationale for the overarching challenge; include relevant preliminary data and literature citations.
- **Research Strategy:** The FY17 PRMRP Focused Program Award strongly encourages a minimum of four individual but complementary research projects addressing the overarching challenge. For each proposed project, state the hypothesis to be tested, the specific aims, and the objectives to be reached. Briefly describe the experimental approach. Describe how the projects are interrelated to and synergistic with each other and align with the overarching challenge.
- **Impact:** Describe the potential short-term and long-term impact of the proposed research on at least one of the FY17 PRMRP Topic Areas and its related research field(s), and patient population(s). Explain how the effort is relevant to the healthcare needs of military Service members, Veterans, and/or beneficiaries.
- **Research Team:** Briefly describe the composition, expertise, and organization of the research team. Identify the project leaders and describe each team member's role in the projects, with additional emphasis on the leadership role of the PI. Briefly describe how these features will facilitate the success of the key aspects of the projects.
- **Clinical Trial (if applicable):** If the proposed research includes a clinical trial(s), briefly state the clinical intervention(s), subject population(s), and the type and phase of the clinical trial(s). Describe the objectives of the clinical trial(s), how it addresses the overarching challenge, and how it complements the other proposed projects. ***Only small-scale (i.e., up to and including Phase II or equivalent) clinical trials are allowed.***
- **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 the following:

- 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, reference title, and reference source, including 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:

- **Overarching Challenge:** How well the unifying challenge or question addresses a critical problem or question in the field of research and/or patient care of one or more FY17 PRMRP Topic Area(s). How well the rationale supports the overarching challenge.
- **Research Strategy:** How well a hypothesis and specific aims are defined for each proposed project and to what extent each project’s approach will address them. How well the proposed projects complement each other and synergistically address the overarching challenge to advance a solution beyond what would be possible through individual efforts.
- **Impact:** Whether the potential immediate and long-range outcome(s)/product(s) (intellectual and/or material) 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 FY17 PRMRP Topic Area(s) addressed. To what degree the project is relevant to the healthcare needs of military Service members, Veterans, and/or beneficiaries.
- **Research Team:** To what degree the background and expertise of the PI, project leaders, and key personnel are appropriate with respect to their abilities to successfully complete the projects and the extent to which the PI is well prepared and committed to lead the research team and proposed projects.

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 time frame for notification of invitation to submit an application is indicated in [Section I, Overview of the Funding Opportunity](#). Invitations to submit a full application are based on the Pre-Application Screening Criteria listed above.

II.D.2.b. Step 2: Full Application Submission Content

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. Refer to the General Application Instructions, Section III, 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 full application package for this Program Announcement. The full application package is submitted by the Authorized Organizational Representative through Grants.gov (<http://www.grants.gov/>) for extramural organizations or through eBRAP (<https://ebrap.org/>) for intramural organizations. See Table 1 below for more specific guidelines.

II.D.2.b.i. Full Application Guidelines

Extramural organizations, including non-DoD Federal agencies, must submit full applications through Grants.gov. Submissions of extramural applications through eBRAP may be withdrawn.

Table 1. Full Application Submission Guidelines

Extramural Submissions	Intramural DoD Submissions
Application Package Location	
Download application package components for W81XWH-17-PRMRP-FPA from Grants.gov (http://www.grants.gov/).	Download application package components for W81XWH-17-PRMRP-FPA from eBRAP (https://ebrap.org/).
Full Application Package Components	
SF424 (R&R) Application for Federal Assistance Form: Refer to the General Application Instructions, Section III.A.1, for detailed information.	Tab 1 – Summary: Provide a summary of the application information. Tab 2 – Application Contacts: This tab will be pre-populated by eBRAP; add Authorized Organizational Representative.

Extramural Submissions	Intramural DoD Submissions
<p>Descriptions of each required file can be found under Full Application Submission Components:</p> <ul style="list-style-type: none"> • Attachments • Research & Related Senior/Key Person Profile (Expanded) • Research & Related Budget • Project/Performance Site Location(s) Form • R&R Subaward Budget Attachment(s) Form (if applicable) 	<p>Tab 3 – Full Application Files: Upload files under each Application Component in eBRAP. Descriptions of each required file can be found under Full Application Submission Components:</p> <ul style="list-style-type: none"> • Attachments • Key Personnel • Budget • Performance Sites <p>Tab 4 – Application and Budget Data: Review and edit proposed project start date, proposed end date, and budget data pre-populated from the Budget Form.</p>
Application Package Submission	
<p>Submit package components to Grants.gov (https://www.grants.gov/). If either the Project Narrative or the budget fails eBRAP validation or if the Project Narrative or the budget need 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.</p>	<p>Submit package components to eBRAP (https://ebrap.org/). Tab 5 – Submit/Request Approval Full Application: After all components are uploaded and prior to the full application submission deadline, enter your password in the space provided “Enter Your Password Here” and press the “Submit Full Application” button. eBRAP will notify your Resource Manager/Comptroller or equivalent Business Official by email to log into eBRAP to review and to approve prior to the application submission deadline.</p>
<u>Application Verification Period</u>	
<p>The full application package submitted to Grants.gov may be viewed and modified in eBRAP until the end of the application verification period. During the application verification period, the full application package, <i>with the exception of the Project Narrative and Budget Form</i>, may be modified.</p>	<p>After eBRAP has processed the full application, the organizational Resource Manager/Comptroller or equivalent Business Official and PI(s) will receive an email notification of this status and will be able to view and modify application components in eBRAP. During the application verification period, the full application package, <i>with the exception of the Project Narrative and Budget Form</i>, may be modified.</p>
Further Information	
<p>Refer to the General Application Instructions, Section III, for further information regarding Grants.gov requirements.</p>	<p>Refer to the General Application Instructions, Section IV, for further information regarding eBRAP requirements.</p>

The organization’s Business Official or Authorized Organization Representative (or Resource Manager/Comptroller) should approve/verify the full application submission prior to the application verification deadline.

Application viewing, modification, and verification in eBRAP are 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.

Material submitted after the end of the application verification period, unless specifically requested by the Government, will not be forwarded for processing.

The full application package must be submitted using the unique eBRAP log number to avoid delays in application processing.

II.D.2.b.ii. Full Application Submission Components:

- **Extramural Applications Only –**

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

- **Extramural and Intramural Applications –**

Attachments:

Each attachment to the full application components must be uploaded as an individual file in the format specified and in accordance with the formatting guidelines listed in the General Application Instructions, Appendix 4.

For all attachments, ensure that the file names are consistent with the guidance. Attachments will be rejected if the file names are 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, there are file size limits that may apply in some circumstances. Individual attachments may not exceed 20 MB and the file size for the entire full application package may not exceed 200 MB.

- **Attachment 1: Project Narrative (40-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) 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.

Overall Program: Provide a description of the comprehensive effort using the following outline. Applicants are strongly encouraged to submit a minimum of four research projects; additional studies are allowed. Emphasize areas of synergy throughout the narrative.

- **Overarching Challenge:** Describe the unifying, overarching challenge or question to be addressed and how it is relevant to a critical problem or question in the field of research and/or patient care in one or more FY17 PRMRP Topic Areas. Clearly articulate the rationale for the overarching challenge; include relevant literature citations. Clearly describe how the proposed research projects are interrelated and synergistic and will advance toward a solution through a multidisciplinary research program. Describe how each project will address the overarching challenge in a unique but complementary way and how the combined efforts of the projects will address the overarching challenge more effectively than if the projects were conducted independently.
- **Leadership:** Describe how the PI's research experience, leadership skills, and commitment to making an impact in his/her field of research and/or patient care demonstrate substantial qualifications to coordinate this collaborative effort. Describe the PI's demonstrated success in leading large, focused projects and outline the PI's responsibilities during the conduct of the award. Discuss the qualifications of the research team being brought together by the PI and how the assembled expertise will create a robust, synergistic collaboration necessary to address the overarching challenge and enable the success of the proposed research.
- **Implementation Plan and Environment:** Provide an overall strategic plan for completing the proposed projects that identifies critical milestones. Outline the knowledge, expertise, and technical innovations that the investigative team will utilize to make decisions, allocate resources, and accomplish the milestones. Describe and/or provide evidence that the research can be initiated without delay once the award is made. Present an overall management plan to facilitate consistent and intensive interactions by all team members, including aspects such as adherence to regulatory requirements, administrative support, and oversight to accelerate translation of the projects' outcomes to patients and/or for clinical use. Describe the research environment(s) and how the facilities and resources will support the research requirements and the collaboration. Outline shared resources and/or cores that will be created and/or leveraged through the award. Describe plans for communication, data transfer among the collaborating institutions, and how data, specimens, and/or imaging products obtained during the study will be handled. If applicable, describe how Standard Operating Procedures will be created, reviewed, implemented, and modified during the course of the award. Describe how individual project performance will be assessed during the course of the award, including progression toward defined milestones, realization of study objectives, and addressing the overarching challenge. If an External Advisory Board (EAB) is to be utilized, describe the role of the board and the expertise to be sought in its members. To avoid potential COIs in the review of the application, potential candidates for an EAB should not be contacted, recruited, or named during the application process.

Research Plan: Provide the following details for each proposed research project, organizing each project clearly and separately. Start each project on a separate page:

- **Title:** Provide a title for each project.
- **Project Leader:** Identify the project leader and any key personnel, as appropriate, describing each person’s qualifications and specific contributions to the project.
- **Background:** Briefly describe the ideas and reasoning on which the proposed work is based. Provide sufficient preliminary data to support the feasibility of work proposed. If the project is exploratory/hypothesis-developing, preliminary data are not required. For each project, the leader must demonstrate logical reasoning and provide a sound scientific rationale for the proposed project as established through a critical review and analysis of published literature. If proposing translational or clinical research, it is important to describe the project showing proof of concept and, if applicable, efficacy in an in-vivo system(s) to support the translational feasibility and promise of the approach.
- **Hypothesis/Objective:** State the hypothesis to be tested and/or the objective(s) to be reached.
- **Specific Aims:** Concisely explain each project’s specific aims. The specific aims should align with the overall goal of the program and associated tasks described in the Statement of Work.
- **Research Strategy:** Describe the experimental design, methods, and analyses, in sufficient detail for analysis. Provide a description of how the study will be controlled and how the study variables will be measured. If the project is a clinical trial, define the primary and secondary endpoints and how they will be assessed. Explain how the research strategy will address the overarching challenge and meet appropriate milestones. Address potential problem areas and present alternative methods and approaches. Clearly describe the statistical plan and the rationale for the statistical methodology as well as an appropriate power analysis, if applicable. If animal studies are proposed, describe how they will be conducted in accordance with the ARRIVE guidelines (http://www.elsevier.com/_data/promis_misc/622936arrive_guidelines.pdf). Justify how the model system or human subjects/samples are appropriate to the proposed research project. 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 how access to the population(s)/dataset(s) will be obtained. If applicable, describe how data will be reported and how it will be assured that the documentation will support a regulatory filing with the U.S. Food and Drug Administration (FDA).

- **Statistical Plan:** Clearly describe a statistical plan appropriate to the type of study; provide the rationale for the statistical methodology. Define the number of samples and/or subjects (animal and/or human) to be used, and include a power analysis to demonstrate that the sample size is appropriate to meet the objectives of the study.
- **Impact:** Describe the anticipated outcome(s)/product(s) (intellectual and/or material) that will be directly attributed to the results of the proposed research. Explain the anticipated long-term gains from this research. Compare to the information known/products currently available, if applicable.
- **Clinical Trial (if applicable):** *Only small-scale (e.g., up to and including Phase II or equivalent) clinical trials are allowed.* Provide detailed plans for initiating and conducting the clinical trial during the course of this award. As appropriate, outline a plan for applying for and obtaining Investigational New Drug/Investigational Device Exemption (IND/IDE) status (or other FDA approvals). Describe the type of clinical trial to be performed (e.g., prospective, randomized, controlled) and indicate the phase of trial and/or class of device, as appropriate. Outline the regulatory strategy. Provide preclinical and/or clinical evidence to support the safety of the intervention.
 - Identify the intervention to be tested and describe the projected outcomes. Describe how the proposed intervention compares with currently available interventions and/or standards of care. Include a discussion of any current clinical use of the intervention under investigation, and/or details of its study in clinical trials for other indications (as appropriate).
 - Describe the methods that will be used to recruit a sample of human subjects from the accessible population (e.g., convenience, simple random, stratified random). Provide information on and justification for the inclusion and exclusion criteria.
 - Describe the process for obtaining informed consent and any screening procedures required to determine eligibility for study participation.
 - Describe the human subject-to-group assignment process (e.g., randomization, block randomization, stratified randomization, age-matched controls, alternating group, or other procedures), if applicable. Explain the specific actions to accomplish the group assignment (e.g., computer assignment, use of table of random numbers). If multiple site studies are involved, state the approximate number of subjects to be enrolled at each site.
 - Provide evidence to document the availability of and access to all critical reagents, including the intervention itself, if applicable, for the duration of the proposed trial.
 - Describe how quality control will be addressed. Describe how compliance with Good Laboratory Practices (GLP), Good Manufacturing Practices (GMP), and Good Clinical Practices (GCP) guidelines will be established, monitored, and maintained, as applicable.

- Describe the composition of the clinical trial team. Provide details on how the team (including investigator(s), study coordinator, and statistician) possesses the appropriate expertise in conducting clinical trials.
- **Attachment 2: Supporting Documentation:** Combine and upload as a single file named “Support.pdf.” Start each document on a new page. If documents are scanned to PDF, the lowest resolution (100 to 150 dpi) should be used. The Supporting Documentation attachment should not include additional information such as figures, tables, graphs, photographs, diagrams, chemical structures, or drawings. These items should be included in the Project Narrative. Any additional material viewed as an extension of the Project Narrative will be removed or may result in administrative withdrawal of the application.

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 patent abstracts. If publications are not publicly available, then copies of up to eight 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, 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. 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.
- Letters of Commitment (if applicable): If the proposed study involves use of a commercially produced investigational drug, device, or biologic, provide a letter of commitment from the commercial entity indicating availability of the product for the duration of the study, support for the proposed phase of research, and support for the indication to be tested.
 - 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: Information can be found in Code of Federal Regulations, Title 2, Part 200.315 (2 CFR 200.315), "Intangible Property."
 - 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 2, 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 effort including the following elements:

- **Overarching Challenge:** Identify the unifying, overarching challenge or question that will be addressed by the research plan and describe how it relates to a critical problem or question in one or more of the FY17 PRMRP Topic Areas.
- **Background:** Briefly articulate the rationale for the overarching challenge and the proposed research.

- **Research Plan:** Provide a brief description of the studies proposed, including hypotheses, objectives, and scientific approach.
- **Impact:** Briefly describe the potential short-term and long-term impact of the results of the proposed research on at least one of the FY17 PRMRP Topic Areas and its related research field(s) and patient population(s).
- **Military Relevance:** Explain how the effort is relevant to the healthcare needs of military Service members, Veterans, and/or beneficiaries.
- **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.

State the FY17 PRMRP Topic Area(s) addressed by the proposed research program. Include a comprehensive overview of the effort that can 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) (eight-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 Focused Program Award mechanism, use the SOW format example titled “SOW for Collaborative Projects.” The SOW must be in PDF format prior to attaching.

The SOW should include a list of major tasks that support the proposed specific aims, followed by a series of subtasks outlined related to the major tasks and milestones within the period of performance. The SOW should describe only the work for which funding is being requested by this application and, as applicable, should also:

Include the name(s) of the key personnel and contact information for each study site/subaward site.

Indicate the number (and type, if applicable) of research subjects (animal or human) and/or human anatomical samples projected or required for each task and at each site. Refer to the General Application Instructions, Appendix 1, for additional information regarding regulatory requirements.

Briefly state the methods to be used.

For studies with prospective accrual of human subjects, indicate quarterly enrollment targets.

Identify cell line(s) and commercial or organizational source(s) to be used. If human anatomical substances (including cell lines) will be used, specify whether or not identifiable information is accessible to the research team by any means.

If applicable, indicate timelines required for regulatory approvals relevant to human subjects research (e.g., IND/IDE applications) by the FDA or other Government agency.

- **Attachment 6: Impact Statement (two-page limit): Upload as “Impact.pdf.”**
 - Explain why the proposed program is important and relevant to understanding the cause or progression of the disease or condition, and/or to developing improvements in prevention, detection, diagnosis, treatment, or quality of life in the FY17 PRMRP Topic Area(s) addressed. Describe how the overarching challenge addresses a central critical problem or question in the relevant Topic Area(s). If applicable, describe how the project addresses an FY17 PRMRP Area of Encouragement ([Appendix 2](#)). In addition to articulating the potential impact of the overall program, address the potential impact of each individual project. Explain how the various projects’ outcomes will ultimately be translated to patients.
 - ***Describe the short-term impact:*** Detail the anticipated outcome(s)/product(s) (intellectual and/or material) 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 patient care.
- **Attachment 7: Military Relevance Statement (one-page limit): Upload as “MilRel.pdf.”**
 - Describe how the proposed effort 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 to be studied 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 dataset(s) 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 and/or patient care. 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.”**
 - Provide information on the methods and strategies proposed to move the product or knowledge outcomes of the program to the next phases of development and to eventual clinical use. Articulate this information for the overall effort as well as the individual projects. Applicants are encouraged to work with their organization’s Technology Transfer Office (or equivalent) to develop the transition plan. The transition plan should include the components listed below, as appropriate:
 - A description of the outcomes expected upon completion of the proposed research efforts. Outcomes should be specific, measurable, and should include the intended end user.
 - Details of the funding strategy that will be used to bring the outcomes to the next phase of development and/or delivery to market or incorporation into patient care (e.g., specific potential industry partners, specific funding opportunities to be applied for).
 - Details of the development plan and FDA regulatory strategy, to include considerations for compliance with GMP, GLP, and GCP guidelines (if appropriate).
 - For knowledge outcomes, a description of how the knowledge will be further developed, disseminated, and incorporated into clinical/patient care.
 - A description of collaborations and other resources that will be used to provide continuity of development.
 - A brief schedule and milestones for bringing the outcomes to the next phase of development (e.g., further research, clinical trials, transition to industry, delivery to the market, incorporation into clinical practice, approval by the FDA).
 - If applicable, ownership rights and/or 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.
- **Attachment 9: Data and Research Resource Sharing Plan (one-page limit): Upload as “Sharing.pdf.”**
 - Describe how data and resources generated during the performance of the proposed research projects will be shared with the research community. This includes cases where pre-existing data or research resources will be utilized and/or modified during the course of the proposed projects. Specifically describe a plan to make animal models, tissue samples, and other resources developed as part of the proposed research projects available to the scientific community. If there are limitations associated with a pre-existing agreement for the original data or research resources that preclude subsequent sharing, the applicant should explain this in the data- and/or

- research resource-sharing plan. Refer to the General Application Instructions, Appendix 2, Section K, for more information about the CDMRP expectations for making data and research resources publicly available.
- In preparing requested budgets, applicants may include anticipated costs associated with data- and research resource-sharing (i.e., making a large dataset available to the public or developing an important resource for the scientific community).
 - **Attachment 10: IND/IDE Documentation: *Only applicable for applications that include a clinical trial(s)*.** If submitting multiple documents, start each document on a new page. **Combine and upload as a single file named “IND-IDE.pdf.”** The IND/IDE Documentation Form located on the eBRAP website may *not* be used in place of this information:
 - State whether the trial(s) requires regulation by the FDA. If FDA regulation is required, describe the planned indication for the proposed product and whether an IND/IDE is necessary.
 - If an IND or IDE application is required, indicate when it was submitted to the FDA and provide an explanation of the status of the IND or IDE application (e.g., past the critical 30-day period, pending response to questions raised by the Agency, on clinical hold). If the IND or IDE application has not been submitted to the FDA yet, provide a detailed timeline with appropriate milestones for application preparation and submission. Identify any consultants or experts who will assist in the regulatory application, if applicable, and include a copy of any curricula vitae or biographical sketches in the Key Personnel Biographical Sketches section of the application. Provide a summary of previous meetings with the FDA on development of this product, if appropriate. A copy of the Agency meeting minutes should be included if available. Provide copies of communications from the FDA relevant to the most recent status of the IND or IDE application.
 - If an IND or IDE is not required for the proposed trial(s), or if it qualifies for an abbreviated IDE, provide evidence in the form of communication from the FDA or the IRB of record to that effect. Devices qualifying for an abbreviated IDE must comply with the abbreviated IDE requirements but do not require the submission of an IDE application to the FDA.
 - **Attachment 11: DoD Military 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 DoD Military 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 III.A.7, for detailed information.

- **Extramural and Intramural Applications –**

Research & Related Senior/Key Person Profile (Expanded): For extramural submissions (via Grants.gov), refer to the General Application Instructions, Section III.A.3, and for intramural submissions (via eBRAP), refer to the General Application Instructions, Section IV.A.2, 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 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.
- **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.”

Research & Related Budget: For extramural submissions (via Grants.gov), refer to the General Application Instructions, Section III.A.4, and for intramural submissions (via eBRAP), refer to the General Application Instructions, Section IV.A.3, 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.

Project/Performance Site Location(s) Form: For extramural submissions (via Grants.gov), refer to the General Application Instructions, Section III.A.5, and for intramural submissions (via eBRAP), refer to the General Application Instructions, Section IV.A.4, for detailed information.

- **Extramural Applications Only –**

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

- **Extramural Subaward:** Complete the Research & Related Subaward Budget Form through Grants.gov. (Refer to the General Application Instructions, Section III.A.6, for detailed information.)
- **Intramural DoD Collaborator(s):** Complete the DoD Military Budget Form and upload to Grants.gov as Attachment 11. (Refer to the General Application Instructions, Section III.A.7, for detailed information.) Intramural DoD Collaborator(s) costs per year

should be included on the Grants.gov Research and Related Budget form under subaward costs. **DoD Military Budget 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 DoD Military Budget Form (Attachment 11) to show all direct and indirect costs. The costs per year should be included on the Grants.gov Research & Related Budget Form under subaward costs. Refer to the General Application Instructions, Section III.A.7, for detailed information.

II.D.3. Dun and Bradstreet Universal Numbering System (DUNS) Number and System for Award Management (SAM)

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. Verify the status of the applicant’s organization’s Entity registration in SAM well in advance of the application submission deadline. Allow 3 to 4 weeks to complete the entire SAM registration process. If an applicant has not fully complied with the requirements by the time the Federal awarding agency is ready to make a Federal award, the Federal awarding agency may determine that the applicant is not qualified to receive a Federal award and use that determination as a basis for making a Federal award to another applicant. Refer to the General Application Instructions, Section III, for further information regarding Grants.gov requirements.

II.D.4. Submission Dates and Times

All submission dates and times are indicated in [Section I, Overview of the Funding Opportunity](#). Pre-application and application submissions are required. The pre-application and application submission process should be started early to avoid missing deadlines. There are no grace periods. Failure to meet either of these deadlines will result in submission rejection.

Applicant Verification of Full Application 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 a submitted application. Following retrieval and processing of the full application, eBRAP will notify the organizational representatives and PI by email to log into eBRAP to review, modify, and verify the full application submission. eBRAP will validate retrieved files against the specific Program Announcement 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. ***If either the Project Narrative or the budget fails eBRAP validation or needs to be modified, an updated full application package must be submitted prior to the application submission deadline.*** The Project Narrative and Budget Form cannot be changed after the application submission deadline.

II.D.5. Funding Restrictions

The maximum period of performance is **4** years.

The anticipated total costs budgeted for the entire period of performance will not exceed **\$10M**. If indirect cost rates have been negotiated, indirect costs are to be budgeted in accordance with the organization's negotiated rate. No budget will be approved by the Government exceeding **\$10M** total costs or using an indirect cost rate exceeding the organization's negotiated rate.

All direct and indirect costs of any subaward or contract 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 may have a period of performance less than the maximum **4** years.

For this award mechanism, direct costs must be requested for:

Travel costs for the PI and up to three additional members of the research team to attend a 1-day Milestone Meeting to be held in the National Capital Area during the award period of performance. This meeting will be held to provide a presentation on progress. Costs associated with travel to this meeting should be included in Year 3 of the budget. These travel costs are in addition to those allowed for annual scientific/technical meetings.

May be requested for (not all-inclusive):

- Salary
- Research supplies
- Equipment
- Research-related subject costs
- Clinical research costs
- Support for multidisciplinary collaborations, including travel
- Travel costs for up to four investigators to travel to one scientific/technical meeting per year in addition to the required meeting described above

Extramural (non-Federal) awards will consist solely of assistance agreements (Cooperative Agreements and Grants). For extramural awards with an intragovernmental component, direct transfer of funds from an extramural award recipient to a DoD or other Federal agency is not allowed except under very limited circumstances. Funding to intramural DoD and other Federal agencies will be managed through a direct fund transfer. Intragovernmental only funding to intramural DoD and other Federal agencies will be managed through a direct fund transfer. Intramural applicants are responsible for coordinating through their agency's procedures the use

of contractual or assistance funding awards or other appropriate agreements to support extramural collaborators.

Refer to the General Application Instructions, Section III.A.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 the General Application Instructions, Section III.A.4.*

The CDMRP expects to allot approximately \$60M of the \$300M FY17 appropriation to fund approximately six Focused Program Award applications, depending on the quality and number of applications received. Funding of applications received in response to this Program Announcement is contingent upon the availability of Federal funds for this program.

II.D.6. Other Submission Requirements

Refer to the General Application Instructions, Appendix 4, for detailed formatting guidelines.

II.E. Application Review Information

II.E.1. Criteria

II.E.1.a. Peer Review

To determine technical merit, all applications will be evaluated according to the following scored criteria, which are of equal importance:

Scored Review Criteria for the Overall Program:

- **Overall Impact**
 - To what extent the overarching challenge impacts a critical problem or question in the designated FY17 PRMRP Topic Area(s).
 - To what degree the proposed program could, if successful, make a significant impact on the lives of relevant patient populations in the short term or long term.
 - How well the research projects are integrated, complement each other, and provide a synergistic, multidisciplinary approach to solving a critical problem.
 - How well the research program will, if successful:
 - Make important scientific advances in the relevant field of research
 - Promote greater understanding of the causes and progression of the relevant disease(s)/condition(s), or
 - Promote the development of improvements in prevention, detection, diagnosis, treatment, or quality of life

- **Implementation Plan**

- How the proposed projects are supported by a detailed plan that identifies critical milestones and explains how these milestones will be achieved.
- How well resources and/or cores that will be created or leveraged will be utilized and shared.
- To what extent the plans to assess individual project performance during the course of the award are appropriate.
- How well the overall management plan will facilitate consistent and intensive interactions by all team members in the projects.
- How the proposed plans for communication, data and specimen collection, data transfer, and periodic meetings are appropriate and robust.
- To what extent the plans for creating, reviewing, implementing, and modifying Standard Operating Procedures are appropriate, if applicable.

- **Leadership and Environment**

- To what degree the PI is experienced in successfully leading large, focused projects and is therefore well-positioned to lead the research team in achieving the overarching goal of the proposed effort.
- How well the PI demonstrates experience, leadership skills, and commitment to making an impact in the relevant field of research and/or patient care.
- Whether the PI will devote a minimum of 20% effort to this award.
- To what degree the scientific environment(s) is appropriate for the proposed research.
- How well the research requirements are supported by the availability of and accessibility to facilities and resources (including patient populations, samples, and collaborative arrangements).
- To what degree the quality and extent of organizational support are appropriate for the proposed research.

- **Transition Plan and Regulatory Strategy**

- The degree to which the strategy proposed to bring the outcomes to the next level of development, including funding, milestones, and schedule, is realistic.
- Whether appropriate collaborations and other resources for providing continuity of development are established and/or well described.
- How the regulatory strategy and development plan are appropriate and well described.

- How well the application identifies intellectual property ownership, and whether there is sufficient evidence of a plan to resolve intellectual and material property issues, if applicable.
- Whether the applicant has demonstrated that they have access to all intellectual property rights necessary for development and commercialization and evidence that the Government has the ability to access such products or technologies, if applicable.
- If applicable, whether data will be appropriately reported and documented to support a regulatory filing with the FDA.

Scored Review Criteria for Individual Research Projects without a clinical trial:

- **Impact**

- To what extent the individual project impacts the overarching challenge.
- To what degree the individual project could, if successful, make a significant impact on the lives of relevant patient populations in the short term or long term.
- How well the individual project will, if successful, make important scientific advances in the relevant field of research.

- **Research Strategy and Feasibility**

- How well the scientific rationale supports the research and its feasibility, as demonstrated by a critical review and analysis of the literature, the presentation of preliminary data (where applicable), and logical reasoning.
- How well the hypothesis, objectives, and aims are developed.
- To what degree the experimental approach, methods, endpoints, and analyses support completion of the aims and are designed to achieve rigorous and reproducible results.
- How well the choice of model (animal, cell line, or other) is justified and whether it is appropriate.
- If applicable, to what degree the statistical plan and power analysis, including sample size projections, are appropriate for the proposed project.
- Whether there is sufficient evidence to support availability and accessibility of the populations, samples, or other resources required for the study, if applicable.
- How well potential problems are acknowledged and alternative approaches are addressed.

- **Personnel**

- To what degree the project team's background and expertise are appropriate with respect to its ability to perform the proposed work, including whether there is evidence of

sufficient expertise for all aspects of the work and whether there is evidence of strong commitment to the projects.

- To what degree the levels of effort are appropriate for successful conduct of the proposed work.

Scored Review Criteria for Individual Research Projects with clinical trials:

- **Impact**

- To what extent the individual project impacts the overarching challenge.
- How well the individual project will, if successful, make important scientific advances in the relevant field of research.
- How well the sample population represents the targeted patient population that might benefit from the proposed intervention.
- How the potential outcomes of the proposed clinical trial will provide/improve short-term benefits for individuals.
- How significantly the long-term benefits for implementation of the intervention may impact patient care and/or quality of life.

- **Research Strategy and Feasibility**

- How well the scientific rationale supports the research and its feasibility, as demonstrated by a critical review and analysis of the literature, the presentation of preliminary data, and logical reasoning.
- How well the hypothesis and/or objectives and specific aims are developed.
- To what degree the experimental approach, methods, endpoints, and analyses support completion of the aims and are designed to achieve rigorous and reproducible results.
- To what degree the statistical plan and power analysis, including sample size projections, are appropriate for the proposed trial and any proposed correlative studies.
- How well the application demonstrates the availability of and access to the appropriate patient population(s), as well as the ability to accrue a sufficient number of subjects.
- How well potential problems and delays (e.g., slow accrual, attrition) are acknowledged and alternative approaches are addressed.

- **Clinical Strategy**

- How the intervention compares with currently available interventions and/or standards of care.

- Whether there is evidence of support, indicating availability of the intervention from its source, for the duration of the proposed clinical trial (if applicable).
 - To what degree the PI has provided preclinical and/or clinical evidence to support the safety of the intervention.
 - How well the inclusion and exclusion criteria meet the needs of the proposed clinical trial.
 - The degree to which the informed consent, screening, and retention processes for human subjects will meet the needs of the proposed clinical trial.
 - Whether a member of the study team holds the IND/IDE for the indication proposed or whether the timeline proposed for obtaining the IND/IDE is appropriate (if applicable).
 - For investigator-sponsored INDs, whether there is evidence of appropriate institutional support, including capabilities to ensure monitoring as required by the FDA.
 - Whether plans to comply with GMP, GLP, and GCP guidelines are appropriate.
 - Whether measures are described to ensure the consistency of dosing of active ingredients for nutritional supplements (if applicable).
- **Personnel**
 - To what degree the project team's background and expertise are appropriate with respect to its ability to perform the proposed work, including whether there is evidence of sufficient expertise for all aspects of the work and whether there is evidence of strong commitment to the projects.
 - How well the project leader has assembled an appropriate and robust clinical team with the combined backgrounds and expertise needed to enable successful conduct of the clinical trial.
 - To what degree the levels of effort are appropriate for successful conduct of the proposed work.

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

- **Data and Resource Sharing**
 - To what degree the plan for sharing of project data and research resources is appropriate and reasonable to facilitate use by the wider research community.
- **Budget**
 - Whether the budget is appropriate for the proposed research and within the limitations of this Program Announcement.

- **Environment**
 - If applicable, to what degree the intellectual and material property plan is appropriate.
- **Application Presentation**
 - To what extent the writing, clarity, and presentation of the application components influence the review.

II.E.1.b. 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:

- Ratings and evaluations of the peer reviewers
- Relevance to the mission of the DHP and FY17 PRMRP, as evidenced by the following:
 - Adherence to the intent of the award mechanism
 - Military relevance
 - Program portfolio composition
 - Relative impact

II.E.2. 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 Commanding General, USAMRMC, on behalf of the DHA 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. 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 II.E.1.b, 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 18 USC 1905.

II.E.3. Integrity and Performance Information

Prior to making an assistance agreement award where the Federal share is expected to exceed the simplified acquisition threshold (currently \$150,000) over the period of performance, the Federal awarding agency is required to review and consider any information about the applicant that is available in the Federal Awardee Performance and Integrity Information System (FAPIIS).

An applicant, at its option, may review FAPIIS, accessible through SAM, and submit comments to FAPIIS on any information about itself that a Federal awarding agency previously entered and is currently available in FAPIIS.

The Federal awarding agency will consider any comments by the applicant, in addition to other information in the designated integrity and performance system, in making a judgment about the applicant's integrity, business ethics and record of performance under Federal awards when determining a recipient's qualification prior to award, according to the qualification standards of the Department of Defense Grant and Agreement Regulations (DoDGAR), Section 22.415.

II.E.4. Anticipated Announcement and Federal Award Dates

All application review dates and times are indicated in [Section I, Overview of the Funding Opportunity](#).

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.

II.F. Federal Award Administration Information

II.F.1. Federal Award Notices

Awards will be made no later than September 30, 2018. Refer to the General Application Instructions, Appendix 2, for additional award administration information.

Awards are made to organizations, not to individual PIs. The types of awards made under the Program Announcement will be assistance agreements (grants or cooperative agreements). The level of involvement on the part of DoD during project performance is the key factor in determining whether to award a grant or cooperative agreement.

Extramural Organizations: An assistance agreement (grant or cooperative agreement) is appropriate when the Federal Government transfers a "thing of value," to a "state, local

government,” or “other recipient,” to carry out a public purpose of support or stimulation authorized by a law of the United States, instead of acquiring property or service for the direct benefit and use of the U.S. Government. An assistance agreement can take the form of a grant or cooperative agreement. If “no substantial involvement” on the part of the funding agency is anticipated, a grant award will be made (31 USC 6304). Conversely, if substantial involvement on the part of the funding agency is anticipated, a cooperative agreement will be made (31 USC 6305). Substantial involvement may include collaboration, participation, or intervention in the research to be performed under the award. The award type, along with the start date, will be determined during the negotiation process.

After email notification of application review results through the eBRAP, and if selected for funding, a representative from the USAMRAA will contact the business official authorized to negotiate on behalf of the PI’s organization.

Only an appointed USAMRAA Grants Officer may obligate the Government to the expenditure of funds. No commitment on the part of the Government should be inferred from discussions with any other individual. The award document signed by the Grants Officer is the official authorizing documents.

Intramural Organizations: Awards to Federal Government organizations (to include intramural DoD organizations) will be executed through the Military Interdepartmental Purchase Request (MIPR) or Funding Authorization Document (FAD) process. Transfer of funds is contingent upon appropriate safety and administrative approvals. Intramural applicants and collaborators are reminded to coordinate receipt and commitment of funds through their respective resource managers (RM).

After email notification of application review results through the eBRAP, and if selected for funding, a representative from the CDMRP will contact the business official authorized to negotiate on behalf of the PI’s organization.

II.F.1.a. Award Transfers

Changes in PI are not allowed, except under extenuating circumstances that will be evaluated on a case-by-case basis and at the discretion of the Grants Officer. An organizational transfer of an award will not be allowed in the last year of the (original) period of performance or any extension thereof.

The organizational transfer of an award supporting a clinical trial is strongly discouraged and in most cases will not be allowed. Approval of a transfer request will be on a case-by-case basis at the discretion of the Grants Officer.

Refer to the General Application Instructions, Appendix 2, Section B, for general information on organization or PI changes.

II.F.2. Administrative and National Policy Requirements

Applicable requirements in the DoDGAR found in 32 CFR, Chapter 1, Subchapter C, and 2 CFR, Chapter XI, apply to grants and cooperative agreements resulting from this Program Announcement.

Refer to the General Application Instructions, Appendix 2, for general information regarding administrative requirements.

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

Refer to full text of the [USAMRAA General Research Terms and Conditions for Institutions of Higher Education, Hospitals, and Non-Profit Organizations](#) and the [USAMRAA General Research Terms and Conditions with For-Profit Organizations](#) for further information.

II.F.3. Reporting

Refer to the General Application Instructions, Appendix 2, Section A, for general information on reporting requirements. Annual progress reports as well as a final progress report will be required.

Quarterly technical progress reports will be required. In addition to written progress reports, in-person presentations may be requested.

Award Chart: Complete the Award Chart template, a one-page PowerPoint file that must be downloaded from the CDMRP eBRAP System at <https://ebrap.org/eBRAP/public/Program.htm>, and submit to eBRAP at the time of award.

Award Expiration Transition Plan: Complete the Transition Plan template, a one-page Word document that must be submitted with the Final Progress Report. The Transition Plan must outline if and how the research supported by this award will progress, and include source(s) of funding, either known or pending.

Awards resulting from this Program Announcement will incorporate additional reporting requirements related to recipient integrity and performance matters. Recipient organizations that have Federal contract, grant, and cooperative agreement awards with a cumulative total value greater than \$10,000,000 are required to provide information to FAPIIS about certain civil, criminal, and administrative proceedings that reached final disposition within the most recent 5-year period and that were connected with performance of a Federal award. Recipients are required to disclose semiannually information about criminal, civil, and administrative proceedings as specified in the applicable Terms and Conditions. The applicable Terms and Conditions for institutions of higher education, hospitals, and nonprofit organizations are available in OAR Article I, Section B, in [July 2016 R&D General Terms and Conditions](#). The applicable Terms and Conditions for for-profit organizations are available in Section 34 of the [February 2017 USAMRAA General Research Terms and Conditions with For-Profit Organizations](#).

II.G. Federal Awarding Agency Contacts

II.G.1. CDMRP Help Desk

Questions related to Program Announcement content or submission requirements as well as questions related to the pre-application or intramural application submission 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

II.G.2. Grants.gov Contact Center

Questions related to extramural 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 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.

II.H. Other Information

II.H.1. Program Announcement and General Application Instructions Versions

Questions related to this Program Announcement should refer to the Program name, the Program Announcement name, and the Program Announcement version code 20170516b. The Program Announcement numeric version code will match the General Applications Instructions version code 20170516.

II.H.2. Administrative Actions

After receipt of pre-applications or applications, the following administrative actions may occur:

II.H.2.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. Refer to [Section II.D, Application and Submission Information](#), for exceptions.

II.H.2.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.

II.H.2.c. Withdrawal

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

- An FY17 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 FY17 PRMRP Programmatic Panel members can be found at <http://cdmrp.army.mil/prmrp/panels/panels17.shtml>.*
- The application fails to conform to this Program Announcement 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 FY17, 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 Grants Officer. Refer to the General Application Instructions, Appendix 3, 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.
- Applications from extramural organizations, including non-DoD Federal agencies, received through eBRAP may be withdrawn.
- Applications submitted by an intramural DoD organization may be withdrawn if the intramural organization cannot coordinate the use of contractual, assistance, or other appropriate agreements to provide funds to extramural collaborators.
- The proposed research project does not address at least one of the Congressionally directed FY17 PRMRP Topic Areas.
- An application for which the PI does not meet the eligibility criteria will be withdrawn.

II.H.2.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.

II.H.3. Application Submission Checklist

Application Components	Action	Completed
SF424 (R&R) Application for Federal Assistance (Extramural submissions only)	Complete form as instructed.	
Summary (Tab 1) and Application Contacts (Tab 2) (Intramural submissions only)	Complete these tabs as instructed.	
Attachments	Project Narrative: Upload as Attachment 1 with file name "ProjectNarrative.pdf."	
	Supporting Documentation: Upload as Attachment 2 with file name "Support.pdf."	
	Technical Abstract: Upload as Attachment 3 with file name "TechAbs.pdf."	
	Lay Abstract: Upload as Attachment 4 with file name "LayAbs.pdf."	
	Statement of Work: Upload as Attachment 5 with file name "SOW.pdf."	
	Impact Statement: Upload as Attachment 6 with file name "Impact.pdf."	
	Military Relevance: Upload as Attachment 7 with file name "MilRel.pdf."	
	Transition Plan and Regulatory Strategy: Upload as Attachment 8 with file name "Transition.pdf."	
	Data and Research Resources Sharing Plan: Upload as Attachment 9 with file name "Sharing.pdf."	
	IND/IDE Documentation: Upload as Attachment 10 with file name "IND-IDE.pdf," if applicable.	
	DoD Military Budget Form(s): Upload as Attachment 11 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.	

Application Components	Action	Completed
Research & Related Budget (Extramural submissions only)	Complete as instructed. Attach Budget Justification (BudgetJustification.pdf) to the appropriate field.	
Budget (Intramural submissions only)	Complete the DoD Military Budget Form and justification.	
Project/Performance Site Location(s) Form	Complete form as instructed.	
R&R Subaward Budget Attachment(s) Form, if applicable	Complete form as instructed.	

**APPENDIX 1
ACRONYM LIST**

ACURO	Animal Care and Use Review Office
CDMRP	Congressionally Directed Medical Research Programs
CFR	Code of Federal Regulations
DHA	Defense Health Agency
DHP	Defense Health Program
DoD	Department of Defense
DoDGAR	Department of Defense Grant and Agreement Regulations
DUNS	Data Universal Numbering System
eBRAP	Electronic Biomedical Research Application Portal
EC	Ethics Committee
ET	Eastern Time
FAPIIS	Federal Awardee Performance and Integrity Information System
FY	Fiscal Year
GCP	Good Clinical Practices
GLP	Good Laboratory Practices
GMP	Good Manufacturing Practices
HRPO	Human Research Protection Office
IACUC	Institutional Animal Care and Use Committee
IRB	Institutional Review Board
M	Million
OASD(HA)	Office of the Assistant Secretary of Defense for Health Affairs
OMB	Office of Management and Budget
ORP	Office of Research Protections
PI	Principal Investigator
PRMRP	Peer Reviewed Medical Research Program
RDT&E	Research, Development, Test, and Evaluation
RM	Resource Manager
SAM	System for Award Management
SOW	Statement of Work
USAMRAA	U.S. Army Medical Research Acquisition Activity
USAMRMC	U.S. Army Medical Research and Materiel Command
USC	United States Code
VA	Department of Veterans Affairs

APPENDIX 2 AREAS OF ENCOURAGEMENT

Applications addressing any of the FY17 PRMRP Topic Areas are of interest to the program. ***Any aspect of research relevant to one or more FY17 PRMRP Topic Areas may be considered for funding.*** Areas of encouragement related to the FY17 PRMRP Topic Areas have been identified by the Department of Defense, Department of Veterans Affairs, 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 caused by the host's or immune system's responses to infectious disease or septic shock.
- Preventive techniques, novel and/or innovative detection technologies, and therapeutics to reduce the incidence and/or severity of acute respiratory distress syndrome and/or other lung injury secondary to trauma, transfusion, burns, hemorrhagic shock, inhalation, and/or oxygen exposure.
- Development of a clinical laboratory-based device for manufacturing/amplification of stem cells to treat acute lung injury/acute respiratory distress syndrome due to inhalation injury, trauma, or other causes.
- Clinical studies to test cellular therapies in the treatment of acute lung injury/acute respiratory distress syndrome due to inhalation injury, trauma, or other causes.
- Metrics to associate the health outcomes of acute lung injury with physiological and physical performance, as well as the psychological health of military Service members.
- Strategies to stabilize and support the safe transport of patients with lung injury in order to optimize therapeutic interventions.
- Studies to identify the prevalence and associated morbidity and mortality of blast overpressure lung injury in forward operating environments.

Antimicrobial Resistance

- Identification and evaluation of novel and/or innovative antifungals against resistant fungal infections, particularly for use as topical therapies for wounds and for surgical and post-surgical therapies.
- Identification of novel and/or innovative targets for multi-drug resistant pathogens.
- Development of novel and/or innovative interventions, diagnostics, and treatment for multi-drug-resistant pathogens.
- Development of novel and/or innovative therapies that interrupt biofilm production in wound infections and infected hardware models.
- Development and testing of treatment protocols and/or diagnostic tests to limit prescribing antibiotics for conditions that are commonly viral in nature or conditions that would resolve themselves without antibiotic treatment (e.g., sinusitis, bronchitis, viral upper respiratory infections, and acute gastroenteritis).

- Development of rapid, rugged, sensitive, and specific diagnostics for antimicrobial resistance in remote environments.
- Research to improve understanding of the impact of travelers' diarrhea, as well as antibiotic treatment for the colonization of multi-drug-resistant organisms.

Arthritis

- Studies that define the risk of contracting septic arthritis; reactive arthritis; arthritis caused by a gastrointestinal, genitourinary, or viral infection (e.g., Lyme disease, Campylobacter, chikungunya); and other arthritis types in active duty military personnel.
- Research toward the development of clinical practice guidelines to prevent, identify, and treat arthritis, particularly that resulting from traumatic injury, surgery, and/or infectious diseases.
- Research to establish activity recommendations for maximal joint life following joint repair, particularly in young patient populations.
- Strategies for repairing focal cartilage defects using cell-based therapies.
- Research quantifying the impacts of obesity, weight loss, physical fitness (all components—cardiovascular, strength, flexibility, balance), and dietary factors on the development of or prevention/risk reduction of arthritis.
- Identification and/or validation of biomarkers for early psoriatic arthritis.
- Basic and translational research to identify treatments to mitigate and/or reverse osteoarthritis, particularly in the knee, hip, ankle, and shoulder.
- Studies to examine using existing regenerative medicine techniques and therapies to treat osteoarthritis, including dose response information and the frequency and timing of application.
- Development of novel and/or innovative treatments or combination therapies for psoriatic arthritis.

Burn Pit Exposure

- Research on the etiology and treatment of adverse health events related to military deployment to Iraq and Afghanistan that are associated with exposure to airborne hazards and open pit burning of solid waste and other materials.
- Toxicological studies to ascertain the toxicity of natural dust, burn pit combustion products and interactions between pollutants, as well as their mechanisms of action.
- Characterization of emissions from open air burns, burn boxes, and incinerators.
- Development and validation of instruments for assessing levels of exposure to airborne hazards for use in research and for occupational and environmental exposure monitoring.

Chronic Migraine and Post-Traumatic Headache

- Research to investigate, develop, and validate biomarkers that are 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 the 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 for 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 responses to treatment.
- Evaluation of the differences in etiology, diagnosis, treatment plan, and prevention of migraine headaches between men and women.

Congenital Heart Disease

- Population-based and outcomes-based research projects to assess the health outcomes of individuals with congenital heart disease across their life spans.
- 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 understanding of the causes of congenital heart defects, including genomic, proteomic, and metabolomic profiling.
- Research on transition of the care of congenital heart disease patients from pediatric to adult providers.
- Research both on the risk of neurologic injury and on enhanced neuroprotection before, during, and after surgery for congenital heart disease.
- Research to design and implement disease-in-a-dish and/or microfluidic models with an established phenotype to increase the efficacy of finding novel and/or innovative drug targets, screen existing drugs, perform cardiotoxicity testing, and/or uncover pathogenesis.

Constrictive Bronchiolitis

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

- Development and testing of less invasive and non-invasive approaches for diagnosing constrictive bronchiolitis.
- Research to develop novel and/or innovative therapeutics to slow or reverse the progression of constrictive bronchiolitis.
- Development and/or validation of animal models for 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.
- Research on interventions to prevent diabetes complications, 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, including current good manufacturing practices for cell line development.
- Identification and/or evaluation of interventions to reduce the development of diabetes among individuals meeting the clinical criteria for pre-diabetes.
- 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 health care, and promote a seamless transition of care between inpatient and outpatient arenas.
- Research to design and implement disease-in-a-dish and/or microfluidic models to model pancreatic islets to uncover pathogenesis and improve the efficiency of drug discovery.

Diarrheal Diseases

- Development and testing of vaccines, including multi-pathogen combination approaches, against the most common causes of bacterial and viral travelers' diarrhea, including *Campylobacter jejuni*, *Shigella*, and Enterotoxigenic *E. coli*.
- Development and evaluation of antibiotic and non-antibiotic therapies to treat all-cause travelers' diarrhea to improve the time to clinical cure, minimize resistance acquisition, and mitigate the chronic health consequences of these infections.
- Research to improve understanding of host responses and develop therapies to treat acute bacterial and viral infections that are associated with travel and may lead to chronic functional bowel and rheumatologic disorders.
- Development of evidence necessary to demonstrate the need, impact, and potential market value of a therapeutic for post-infectious functional bowel disorders to include preventive, treatment, or vaccine technology strategies.
- Development and evaluation of point-of-care diagnostics for acute diarrheal illness that distinguishes between bacterial, viral, protozoal, and toxin-mediated etiologies and leads to actionable public health or individual management interventions.

- Investigations into the relationship between existing gastrointestinal flora (microbiome) and the susceptibility, duration, and severity of diarrheal disease, as well as the impacts of dietary modification and/or probiotic use.
- Research to identify, reduce, or eliminate sources of infection causing diarrheal diseases.

Dystonia

- Research on the risk, incidence, and etiology of generalized dystonia, focal dystonia, multifocal dystonia, segmental dystonia, and/or hemidystonia.
- Research on interventions to prevent, slow the progression of, or treat dystonia.
- Research to improve identification of delayed onset dystonia following traumatic brain injury.

Early Trauma Thermal Regulation

- Research into regional cooling for different environments, including prolonged care, as a therapeutic for secondary ischemic injury (e.g., head with traumatic brain injury, limb with tourniquet).
- Development of a tunable support mechanism for thermal homeostasis for use in prolonged field care, extended evacuation, or unmanned evacuation.
- Development and evaluation of a novel and/or innovative technology and techniques to reduce the impact of hypothermia.
- Research to determine the benefits of invasive warming/cooling during patient movement.
- Research to validate the attenuating effects of (early) external head cooling on concussive brain injuries.
- Research into therapeutic cooling or targeted temperature management as a neuroprotective treatment for traumatic brain injury.

Eating Disorders

- Investigations into the prevalence, diagnosis, and treatment patterns of eating disorders in Service members and their families, including potential relationships with military-unique behaviors or conditions.
- Assessment of patterns of comorbidity between eating disorders and other mental health conditions, including an examination of whether eating disorders are more likely to precede or follow the development of other mental health conditions.
- Studies to identify the most effective treatments (and order of treatment) for patients with an eating disorder and a comorbid disorder.
- Research to advance the understanding of the biological, genetic, and environmental factors that influence eating disorders.
- Studies to elucidate risk factors for the onset or recurrence of eating disorders.
- Research to develop screening tools and valid biomarkers that accurately identify individuals with binge eating disorder versus healthy controls in order to monitor at-risk populations and tailor treatments for disordered eating.

- Research to better understand subclinical disordered eating and other specified feeding and eating disorders and the potential for these to develop into full-blown eating disorders.

Emerging Infectious Diseases

- Methods to minimize risk from arboviruses among military Service members and their families deployed to/living in high-risk areas, including personal protective equipment and environmental controls.
- Investigation of revaccination strategies and identification of correlates of protection for currently available vaccines (especially mumps).
- Targeted vector management of *Aedes aegypti*, *Anopheles sp.* and related mosquito species, including focus areas on novel and/or innovative 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.
- Characterization of health emergency relevant infectious disease threats in West Africa.
- Development of biomarker-guided clinical management strategies for severe infectious disease in the austere African setting.
- Validation of airborne and droplet precaution recommendations in the medical transport environment.
- Development of new testing methods for emerging pathogens and pathogen reduction technologies for blood-borne pathogens, including Zika, malaria, dengue, and others, in blood products.
- Modeling of epidemics and development of strategies to counter risks in emerging infectious diseases.
- Rapid, rugged, sensitive, and specific screening and diagnostics, including biomarkers for infectious threats such as Zika and other clinically relevant bacterial, viral, or protozoal pathogens in clinical samples or blood products that can be transmitted sexually or by blood transmission.
- Development of broad-acting detection systems to identify emerging members of a known viral family (for example, a broad Coronavirus panel that can detect Middle Eastern Respiratory Syndrome).
- Determination of the human health effects, host preference, vector competence, and co-infection status of the dengue, chikungunya, Zika, and Mayaro viruses in *Aedes aegypti* and related mosquito species.

Epidermolysis Bullosa

- Research to provide further insight into those cellular pathways that might be corrected or bypassed that otherwise promote the development of squamous cell carcinomas in recessive dystrophic and junctional epidermolysis bullosa.

- Research, including randomized controlled clinical trials, focused on systemic drugs that prevent, delay the onset, or modify the aggressiveness of squamous cell carcinoma in patients with recessive and junctional epidermolysis bullosa.
- Research, including clinical trials, focused on medications (topical or systemic) or dressings that might enhance wound healing in inherited epidermolysis bullosa.

Focal Segmental Glomerulosclerosis

- Development of a curative therapy or treatments to delay or halt the progression of focal segmental glomerulosclerosis and/or prevent post-transplantation recurrence.
- Research to determine the efficacy of medications used off-label (outside the FDA-approved indication) to treat focal segmental glomerulosclerosis.
- Research to improve understanding of the causes of primary and secondary focal segmental glomerulosclerosis, especially genetic mutations.
- Development of non-invasive methods to diagnose focal segmental glomerulosclerosis and its variants.
- Research on the impact of dietary modifications on the progression of renal disease.

Fragile X

- 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 life span.
- Identification and testing of novel and/or innovative targets for fragile X syndrome therapeutics.
- Development and evaluation of novel, innovative, or existing therapeutics for the treatment of fragile X syndrome.

Guillain-Barré Syndrome

- Research to elucidate the characteristics of various exposures (e.g., viruses, bacteria, vaccinations, surgery) associated with Guillain-Barré syndrome and their effects on the immune system.
- Research on the immune system cell types and molecular mechanisms responsible for the disease pathology of Guillain-Barré syndrome.
- Research to prevent or reduce the effects of residual weakness, relapse of muscle weakness, and other neurological symptoms of Guillain-Barré syndrome to improve patients' quality of life and increase their independence.
- Development of new treatments and refinement of existing treatments for Guillain-Barré syndrome.

Hepatitis B and C

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

- Development of strategies for reliable, non-invasive, early detection of hepatitis-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 hepatitis infection to symptomatic disease and parameters for the initiation and duration of disease treatment.
- Clinical studies to evaluate combination or curative therapies for treatment of hepatitis infection.
- Identification and reduction of hepatitis in blood products for transfusion.
- Research on strategies to reduce vertical (mother-to-child) transmission of hepatitis B virus and hepatitis C virus.
- Development of a vaccine against hepatitis C.
- Development of treatment protocols for patients with hepatitis B and C co-infections.

Hereditary Angioedema

- Research to improve early diagnosis of hereditary angioedema.
- Evaluation of existing, innovative, or novel therapeutics in pediatric hereditary angioedema patients.
- Research toward development of a cure for hereditary angioedema.
- Development and/or validation of novel and/or innovative therapeutic strategies for the treatment and/or prevention of hereditary angioedema attacks.

Hydrocephalus

- Research on the etiology, prevention, diagnosis, and treatment of post-traumatic hydrocephalus.
- Discovery or validation of novel and/or innovative 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 of 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.

Immunomonitoring of Intestinal Transplants

- Studies to elucidate the role of the mucosal immune system, other host-derived factors, or gut microbiota-derived factors in maintaining intestinal transplant viability.

- Development and evaluation of intestinal implant strategies that circumvent the induction of immunity against the transplant through the use of autologous stem cells or organoids derived from intestinal stem cells.
- Development and evaluation of evidence-based approaches that focus on dampening the regional immune response against intestinal transplants without inducing global immune suppression.
- Development and evaluation of implant-associated materials (e.g., scaffolds) with anti-inflammatory properties that protect the intestinal transplant from immune attack.
- Development and evaluation of strategies for inducing and maintaining populations of anti-inflammatory regulatory immune cell populations at the transplant site.
- Studies to improve immunomonitoring of recipient immune responses after intestinal transplantation, with a focus on prospective leukocyte profiling, to aid in diagnosis and treatment of immunological and immunosuppression-related complications.
- Development and/or validation of precise, real-time implanted monitoring devices to improve individualized patient outcomes after intestinal transplantation.

Inflammatory Bowel Diseases

- 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, including systems biology approaches.
- Mechanistic studies in animal models designed to understand how enteric infection may trigger inflammatory bowel disease, including genomic, microbiomic, and immune mechanisms.
- Epidemiological studies of post-infectious acute and sub-acute inflammatory bowel diseases that define risk and provide estimates of illness-associated disability, health care costs, and symptom duration from a military health system and societal perspective.
- Studies to understand the interaction between acute/chronic stress and infection and the development of inflammatory bowel disease.
- 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 inflammatory bowel disease.
- Research on the role of diet in the development and progression of inflammatory bowel disease.
- Research on the influence of the microbiome on inflammatory bowel disease.
- Research on hyperbaric oxygen treatment of inflammatory bowel disease.
- Research on treatment strategies for patients whose inflammatory bowel disease is refractory to standard care medications or who positively respond to standard care medications, but become nonresponsive over time.

Influenza

- Development of a diagnostic test for influenza drug resistance.
- Development and testing of a universal influenza vaccine.
- Development and evaluation of novel, innovative, and/or combination influenza therapies.
- Research to improve the understanding of host responses to influenza infection and the mechanisms of drug resistance.
- Research on the factors that contribute to and/or reduce the risk 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, and/or herbal medicine/nutritional supplementation, to improve the 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 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 and small-deck ships; or in combat-fatigued military health care providers.

Interstitial Cystitis

- Studies that define the risk, prevalence, and operational impact of interstitial cystitis among active duty personnel.
- Identification of biological markers for making a definitive diagnosis of interstitial cystitis.
- Evaluation and assessment of novel and/or innovative treatment options for interstitial cystitis patients, including intravesical therapy.
- Research on the etiology of interstitial cystitis to inform targeted therapy development.

Malaria

- Investigation of mechanisms of drug resistance in malaria, to include host and pathogen, against drugs used for treatment and prophylaxis.
- Development of a vaccine that induces high levels of long-lived, broadly protective immunity against *Plasmodium falciparum* and/or *P. vivax*.
- Operational research to optimize application of existing malaria drugs to reduce impact of artemisinin resistant *P. falciparum* in military forces.

- Operational research to optimize deployment of pharmacovigilance systems to ensure capture of adverse events related to malaria chemoprophylaxis and treatment.
- Operational research to assess efficacy and spread of artemisinin combination therapies across the Greater Mekong Subregion's military forces.
- Development of malaria prophylactic regimens that encourage higher compliance and methods to monitor compliance in deployed Service members.
- Identification of novel and/or innovative malaria drug targets for blood and liver stage malaria parasites.
- Development of new, or improvement of existing, strategies for culturing relapsing malaria parasites, with emphasis on *Plasmodium vivax*, *P. ovale*, and *P. cynomolgi* in vitro.
- Development, testing, and evaluation of spatial repellents to provide protection against Anopheline vectors.
- Identification of a correlate of immunity against malaria and development of a surrogate test of protection.
- Structurally optimize validated malaria antigens by engineering protective epitopes to elicit specific and enhanced immune responses.

Metals Toxicology

- Identification and validation of biomarkers to evaluate military Service members' acute exposure to toxic metals in an operational environment and predict potential consequent health risks and associated health outcomes.
- Retrospective studies to evaluate risk and exposure among workers at 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).
- Research on underlying diet quality and micronutrient sufficiency and the risk for metals toxicity.
- Research on the toxicity of metal-based engineered nanomaterials.

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.
- Research on novel and/or innovative treatments to alleviate symptoms or slow down the progression of mitochondrial diseases.

Musculoskeletal Disorders

- Research to increase understanding, diagnosis, prevention, and/or treatments of chronic overuse musculoskeletal disorders.
- Research on measures (e.g., clinical biomarkers, novel/innovative interventions, therapeutics) to diagnose, predict, reduce the incidence of, or optimize health outcomes in military training- and Service-related musculoskeletal disorders.
- Research on the validation and/or optimization of rehabilitation strategies for Service-related musculoskeletal disorders.
- Research to prevent, control, and/or optimize musculoskeletal health outcomes for work-related musculoskeletal disorders.
- Research on lower back pain strategies to prevent surgery and recurrence of symptoms, identify factors that predict optimal treatment response for different patients, and encourage self-management as a treatment.
- Research to determine whether tailored psychosocial education interventions are effective in improving psychological resilience to musculoskeletal pain.
- Research on standardized approaches for early identification and prevention of chronic musculoskeletal pain.

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.
- Development of technologies that repair the soft tissue envelope to enhance bone regeneration.

Non-Opioid Pain Management

- Research on pain management strategies for patients with limited access to skilled providers and resources, including battlefield, prolonged field, transport, and other resource-limited environments.
- Development of population-based outcomes, tools, and measures to evaluate the effectiveness of pain management approaches across time and environments.
- 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 which pain management strategies work for whom and under what conditions.
- Research to identify and address biopsychosocial aspects of pain to reduce or eliminate the 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.
- Development of non-opioid pain medicine that can be given via inhalation or intramuscularly, submucosally, or intravenously on the battlefield to provide adequate relief of pain without affecting the cardiorespiratory systems.
- Research on case management strategies designed to optimize the effectiveness of pain clinics, support use of non-opioid pain therapies, and reduce dependence on opioid therapies.
- Research that will directly obtain an FDA analgesic indication for oral transmucosal or intramuscular ketamine.

Pancreatitis

- Retrospective studies to determine the risk and incidence of pancreatitis among former and current active duty personnel.
- Development and testing of novel and/or innovative 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 Cryoprecipitate

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

Polycystic Kidney Disease

- Development of improved treatment strategies for polycystic kidney disease, 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 polycystic kidney disease, including studies of genetic factors, cyst formation and growth, the role of cilia, and factors that modify disease progression and/or severity.
- Research on the lifestyle factors that may modify the progression of polycystic kidney disease.

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

- Development or validation of novel and/or innovative 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 the development of post-traumatic osteoarthritis, including cell death, inflammation, matrix changes, and changes in catabolic and anabolic responses.
- Development and/or validation of predictive models for early onset post-traumatic osteoarthritis in extremity-injured patients for the purpose of tailoring rehabilitation programs toward prevention, delay, or mitigation of onset.

Pulmonary Fibrosis

- Retrospective studies to determine the risk and incidence of pulmonary fibrosis among military Service members, including Veterans.
- Identification of biomarkers of pulmonary injury or early predictors of interstitial lung disease.
- Research into the pathobiology and molecular mechanisms underlying the development of pulmonary fibrosis.
- Development and/or testing of novel and/or innovative 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 causes, treatment, and prevention of chronic obstructive pulmonary disease (COPD), including identification and validation of biomarkers and disease phenotypes, as well as employing personalized medicine in clinical research and disease management.
- Research investigating the treatment of patients with chronic mild hypoxia.
- Research on the cause, treatment, and prevention of respiratory symptoms and ailments possibly associated with deployed and redeployed 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 and Veterans.
- Development and/or validation of methods to detect volatile organic hydrocarbons from the breath of individuals exposed to toxic chemicals or other agents that can cause lung injury, which can be utilized for diagnosis and prognosis of lung injury or disease.
- Identification of biochemical, physiological, or combined biomarkers for evaluating risk or extent of injury from either acute or long-term toxic occupational or environmental exposures.

- Research investigating exposure rates, detection, and treatment of diseases related to inhalation of mold and fungi, such as coccidioidomycosis.

Rett Syndrome

- Identification and/or validation of novel and/or innovative 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 on 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 and/or innovative therapies and identification of novel and/or innovative 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, including biologics and small molecule inhibitors, in the treatment of morphea and scleroderma (systemic sclerosis).
- Research on the efficacy of UVA1 for topical treatment in localized scleroderma and systemic sclerosis.

Sleep Disorders

- Research on how the disruption of normal sleep and circadian biological rhythms adversely affects the physical and psychological 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, traumatic brain injury, depression, and/or anxiety and suicidal behaviors.
- 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.
- Research focused on investigating how psychiatric disorders (post-traumatic stress disorder in particular), combined with the disruption/degradation of sleep quality, impact long-term physical health through changes in hormonal physiology.
- Development and/or testing of non-pharmacological treatments for sleep disorders.
- Research on the impact of sleep deprivation on the efficacy of psychological treatments for post-traumatic stress disorder, depression, and other mood disorders.
- 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.
- Development of tools and technologies that allow rapid and objective measurement of Service member performance in the face of fragmented sleep and/or sleep maintenance difficulty.
- Research examining the broader effects of Warfighters' sleep disorders on the sleep, behavioral health, and productivity of their family members, as well as the readiness of their military unit.

Spinal Muscular Atrophy

- Research into phenotyping the spinal muscular atrophy disease state.
- Research into which molecular deficiency imposed by a deficiency of SMN, a motor neuron protein, causes motor neuron deficits.
- Exploration of the form and function of SMN-depleted neuromuscular junctions at ultrastructural (e.g., dysregulation of endocytosis), transcriptomic, and proteomic levels, particularly the mildest SMN reduction that leads to consistent quantifiable motor neuron loss.
- Research to find non-SMN-altering spinal muscular atrophy modifying genes in cellular, small animal, and human models that may lead to identification of novel and/or innovative therapeutic targets.
- Research to further understand SMN gene regulation and post-transcriptional mechanisms leading to synergistic SMN-repleting approaches, as well as to determine whether boosting SMN induction maximizes efficacy.
- Research to determine whether SMN can be repleted to physiologic levels in all cells in the spinal muscular atrophy model immediately post-natally and whether there is a limit to the therapeutic response.
- Clinical research to determine what clinical findings persist even with treatment; whether these findings are related to drug timing, dosage, biodistribution, or a combination of factors; and whether these factors are modifiable.

- Research involving dietary/nutritional studies in spinal muscular atrophy to identify the optimal anabolic diet.
- Research to determine mitochondrial involvement and astrocytic and other non-neuronal contributions to motor neuron vulnerability.

Sustained-Release Drug Delivery

- Development of technology that can provide a sustained-release delivery of drugs for a minimum of 1 week or more. Potential applications of this technology could include long-acting therapies for post-traumatic stress, opiate dependence, low-dose pain control, allergies, attention deficit/hyperactivity disorder, chemoprophylaxis, and other conditions.
- Research into the use of printable, sustained-release scaffolds for predictable delivery of prescription and non-prescription medications.
- Research into novel and/or innovative approaches to developing bioavailable and sustained-release oral formulations of intravenous broad-spectrum fungicidal and anti-microbial medications.

Tinnitus

- Research to understand the mechanisms of tinnitus, its relationship to noise-induced hearing loss, and progression to chronic tinnitus, with the focus on developing interventions for tinnitus.
- Research to increase knowledge of the prevalence, incidence, natural history, and occupational and sex-related differences of tinnitus and its possible relation to individual blast/noise exposures.
- Research to understand the operational readiness impacts of tinnitus on the military.
- Development and validation of objective tools/methods 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 and/or innovative therapies for interventions to prevent, manage, and treat tinnitus, including behavioral approaches, new uses for existing drugs, nutritional and pharmaceutical 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.
- Development of novel and/or innovative tuberculosis vaccines or optimization of current tuberculosis vaccines.
- Identification and/or validation of biomarkers that can be used to assess vaccine efficacy and protection against tuberculosis disease.
- Research to understand, diagnose, or treat multi-drug-resistant tuberculosis or extensively drug-resistant tuberculosis.
- Research to determine the appropriate precautions to use for transport of active tuberculosis patients.

- A sustained release formulation of anti-tuberculosis drugs that would facilitate long-term treatment and reduce the emergence of resistance due to poor compliance.

Vaccine Development for Infectious Disease

- Development of a therapeutic vaccine and/or other strategies to achieve HIV remission.
- Evaluation of passive immunization strategies to use in conjunction with dengue and Zika vaccinations.
- Research leading to a better understanding of the immune mechanisms involved in clearance of the dengue and Zika viruses and the 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 compared to natural infection.
- Development of a safe, effective dengue human challenge model for clinical trials.
- Development of a non-human primate model to study Zika virus-induced microcephaly/fetal neuropathology as a tool to measure the safety and efficacy of vaccines and antivirals.
- Development and fielding of vaccines to prevent U.S. Service members from becoming ill from endemic disease exposure during operational deployments. This includes, but is not limited to, arthropod-borne diseases (Zika virus, dengue, chikungunya, hantavirus hemorrhagic fever with renal/pulmonary syndrome, rickettsioses, and trypanosomiasis), leptospirosis, HIV, norovirus, Middle East Respiratory Syndrome coronavirus, schistosomiasis, leishmaniasis, Nipah virus, Lassa fever, and West Nile fever.

Vascular Malformations

- Studies into the natural history, genetics, and pathogenesis of vascular malformations.
- Research to discover or develop novel and/or innovative 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.
- Studies to elucidate the progression of vascular malformations in disease-in-a-dish/microfluidic models for the purpose of identifying novel and/or innovative drug targets, screening existing drugs, and/or elucidating the pathogenesis of the disease.

Women's Heart Disease

- Retrospective studies to determine the risk and incidence of heart disease among former and current female active duty personnel, including Reservists and National Guard members.
- Research focused on elucidating the potential relationship between post-traumatic stress disorder and women's heart disease.
- Identification of sex-specific approaches to increase the effectiveness of diagnosis, treatment, and/or cardiac rehabilitation programs.
- Research on factors to predict and prevent the long-term impacts of gestational diabetes, gestational hypertension, and preeclampsia on the cardiovascular health of women.
- Research on trauma-induced cardiac arrest secondary to hemorrhage and polytrauma in the female population.

APPENDIX 3 DOD AND VA WEBSITES

PIs are encouraged to integrate and/or align their research projects with Department of Defense (DoD) and/or Department of Veterans Affairs (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 FY17 PRMRP Topic Areas.

Air Force Office of Scientific Research

<http://www.wpafb.af.mil/afri/afosr/>

Air Force Research Laboratory

<http://www.wpafb.af.mil/afri>

Armed Forces Radiobiology Research
Institute

<http://www.usuhs.edu/afri/>

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

<http://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://www.wrair.army.mil/>