Program Announcement

for the

Department of Defense

Defense Health Program

Congressionally Directed Medical Research Programs

Peer Reviewed Medical Research Program

Focused Program Award

Funding Opportunity Number: W81XWH-15-PRMRP-FPA

Catalog of Federal Domestic Assistance Number: 12.420

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-Application Deadline:** 5:00 p.m. Eastern time (ET), June 18, 2015
- **Invitation to Submit an Application:** July 2015
- **Application Submission Deadline:** 11:59 p.m. ET, October 28, 2015
- **End of Application Verification Period:** 5:00 p.m. ET, November 2, 2015
- **Peer Review:** December 2015
- **Programmatic Review:** February 2016

The CDMRP eReceipt System has been replaced with the electronic Biomedical Research Application Portal (eBRAP). Principal Investigators and organizational representatives should register in eBRAP as soon as possible. All pre-applications must be submitted through eBRAP. In addition, applications submitted through Grants.gov will now be available for viewing, modification, and verification in eBRAP prior to the end of the application verification period.

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

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I. FUNDING OPPORTUNITY DESCRIPTION

A. Program Description

Applications to the Fiscal Year 2015 (FY15) Peer Reviewed Medical Research Program (PRMRP) are being solicited for the Defense Health Agency, Research, Development, and Acquisition (DHA RDA) Directorate, by the U.S. Army Medical Research Acquisition Activity (USAMRAA). As directed by the Office of the Assistant Secretary of Defense for Health Affairs, the DHA RDA Directorate manages and executes the Defense Health Program (DHP) Research, Development, Test, and Evaluation (RDT&E) appropriation. The executing agent for this Program Announcement/Funding Opportunity is the Congressionally Directed Medical Research Programs (CDMRP). The PRMRP was initiated in fiscal year 1999 (FY99) to provide support for military health-related research of exceptional scientific merit. Appropriations for the PRMRP from FY99 through FY14 totaled $844.5 million (M). The FY15 appropriation is $247.5M.

The vision of the FY15 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 FY15 Topic Areas with original ideas that foster new directions along the entire spectrum of research and clinical care. The program seeks applications in laboratory, clinical, behavioral, epidemiologic, and other areas of research to advance knowledge in disease etiology, improve prevention, detection, diagnosis, treatment, and quality of life for those affected by a relevant disease or condition, and to develop and validate clinical care or public health guidelines.

B. FY15 PRMRP Focused Program Award 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 FY15 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. ***Applications to the FY15 PRMRP Focused Program Award are restricted to the Topic Areas listed below:***

- Acupuncture
- Advanced Prosthetics
- Burn Pit Exposure
- Cardiovascular Health
- Congenital Heart Disease
- Focal Segmental Glomerulosclerosis
- Healthcare-Acquired Infection Reduction
- Hepatitis B
- Hydrocephalus
- Integrative Medicine
- Metals Toxicology
- Mitochondrial Disease
- Nanomaterials for Bone Regeneration
- Osteoarthritis
- Pathogen-Inactivated Dried Plasma
- Pulmonary Fibrosis
- Psychotropic Medications
- Respiratory Health (excludes lung cancer and mesothelioma)
- Sleep Disorders
- Vascular Malformations
- Women's Heart Disease

Focused Program Award applications addressing any of the above Topic Areas are of interest to the program. Gaps and priority research areas within each of the above FY15 PRMRP Focused Program Award Topic Areas have been identified by the Department of Defense (DoD) and the Department of Veterans Affairs (VA). Applicants are encouraged to read and consider the gaps and priority research areas found in the Appendix of this document before preparing their applications. The information provided is not exhaustive, and applicants are not restricted to submitting applications that address the identified gaps and priority research areas in this list. Any aspect of research relevant to one or more of the designated FY15 PRMRP Focused Program Award Topic Areas may be considered for funding.

Applicants seeking funding in a FY15 PRMRP Topic Area not included in the list above should apply to one of the other FY15 PRMRP Program Announcements/Funding Opportunities, which may be found at http://cdmrp.army.mil/funding/ or at www.grants.gov.

C. Award Information

The PRMRP Focused Program Award mechanism is intended to optimize research and accelerate the solution for a critical question related to a designated FY15 PRMRP Focused Program Award Topic Area through a synergistic, multidisciplinary research program.

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 FY15 PRMRP Focused Program Award 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 shall be capable of standing on their own high scientific merits, they shall 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 one 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. Individual research projects may range from exploratory, hypothesis-developing studies through small-scale clinical trials (e.g., up to and including Phase II or equivalent). There should be an emphasis on and progression 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, though specific members should not be contacted, recruited, or named in the application to avoid potential conflicts of interest (COIs) during review of 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 Joint Programmatic Review Panel (JPRP), CDMRP staff, and the 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
- Use of military or Veteran populations or data in the proposed research
- Description of how the knowledge, information, products, or technologies gained from the proposed research could be implemented in a dual-use capacity to address a military need that also benefits the civilian population
- Collaboration with DoD or VA investigators
- 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 collaborate, integrate, and/or align their research projects with DoD and/or VA research laboratories and programs. While not a complete list, the following websites may be useful in identifying additional information about ongoing DoD and VA areas of research interest or potential opportunities for collaboration within the FY15 PRMRP Focused Program Award Topic Areas:

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

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

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

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

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

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

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

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/

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

U.S. Army Medical Research Acquisition Activity
https://www.usamraa.army.mil/

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

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

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

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

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

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

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), in addition to the local Institutional Review Board (IRB) of record. Local IRB 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. ***Allow a minimum of 2 to 3 months for HRPO regulatory review and approval processes***. Refer to the General Application Instructions, Appendix 5, and the Human Subject Resource Document available on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) for additional information.

Guidelines for Animal Research: All projects should adhere to a core set of standards for rigorous study design and reporting to maximize the reproducibility and translational potential of preclinical research. The standards are described in Landis, S. C., et al. A call for transparent reporting to optimize the predictive value of preclinical research. *Nature* 2012, 490: 187-191 (www.nature.com/nature/journal/v490/n7419/full/nature11556.html). While these standards are written for preclinical studies, the basic principles of randomization, blinding, sample-size estimation, and data handling derive from well-established best practices in clinical studies. Applicants should consult the ARRIVE (Animal Research: Reporting *In Vivo* Experiments) guidelines to ensure relevant aspects of rigorous animal research are adequately planned for and, ultimately, reported. The ARRIVE guidelines can be found at http://www.nc3rs.org.uk/page.asp?id=1357.

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. 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 3 to 4 months for regulatory review and approval processes for animal studies.*** Refer to General Application Instructions, Appendix 5, for additional information.

The CDMRP intends that information, data, and research resources generated under awards funded by this Program Announcement/Funding Opportunity be made available to the research community (which includes both scientific and consumer advocacy communities) and to the public at large. For additional guidance, refer to the General Application Instructions, Appendix 3, Section L.

D. Eligibility Information

- The PI must be an independent investigator at or above the level of Full Professor (or equivalent).
- Cost sharing/matching is not an eligibility requirement.
- Eligible investigators must apply through an organization. Organizations eligible to apply include national, international, for-profit, nonprofit, public, and private organizations. Both intramural (i.e., U.S. Federal Government agency, department, laboratory, medical treatment facility, or a U.S. Government activity embedded within a civilian medical center) and extramural investigators are encouraged to apply to this Program Announcement/Funding Opportunity.
- Refer to the General Application Instructions, Appendix 1, for general eligibility information.

E. Funding

- The maximum period of performance is **5** years.
- The anticipated total costs (direct plus indirect) budgeted for the entire period of performance will not exceed **$10M**. Associated indirect costs can 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 rate exceeding the organization's negotiated rate.
- All direct and indirect costs of any subaward (subgrant or subcontract) must be included in the total direct costs of the primary award.
- The applicant may request the entire maximum funding amount for a project that may have a period of performance less than the maximum **5** years.

Refer to the General Application Instructions, Section II.C.5., for budget regulations and instructions for the Research & Related Budget. ***For all Federal agencies or organizations collaborating with Federal agencies, budget restrictions apply as are noted in Section II.C.5. of the General Application Instructions***.

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
- Travel between collaborating organizations
- Travel costs to attend scientific/technical meetings in addition to the required meeting described above

Intramural (DoD), other Federal agency, and extramural investigators are encouraged to apply to this Program Announcement/Funding Opportunity. An intramural investigator is defined as a DoD military or civilian employee working within a DoD laboratory or medical treatment facility, or working in a DoD activity embedded within a civilian medical center. Intramural applicants and collaborators are reminded to coordinate receipt and commitment of funds through their respective resource managers. It is permissible for an intramural investigator to be named as a collaborator on an application submitted by an extramural investigator. ***In such cases, the extramural investigator must include a letter from the intramural collaborator's Commander or Commanding Officer that authorizes the involvement of the intramural collaborator.***

As required of all applicants to this Program Announcement/Funding Opportunity, if PIs from Federal agencies submit applications, they must submit through Grants.gov. Therefore, Federal applicants must be familiar with Grants.gov requirements, including the need for an active System for Award Management (SAM) registration and a Data Universal Numbering System (DUNS) number. Refer to Section II.A. of the General Application Instructions for further information regarding Grants.gov requirements.

Awards to extramural organizations will consist solely of assistance agreements (Cooperative Agreements and Grants). Awards to intramural agencies and other Federal agencies may be executed through a direct fund transfer (e.g., the Military Interdepartmental Purchase Request [MIPR] or Funding Authorization Document [FAD] process). Direct transfer of funds from the recipient to a Federal agency is not allowed except under very limited circumstances. Refer to the General Application Instructions, Section II.C.5. Research & Related Budget, for additional information on budget considerations for applications involving Federal agencies.

The CDMRP expects to allot approximately $50M of the $247.5M FY15 PRMRP appropriation to fund approximately five PRMRP Focused Program Award applications, depending on the quality and number of applications received. Funding of applications received in response to this Program Announcement/Funding Opportunity is contingent upon the availability of Federal funds for this program.

II. SUBMISSION INFORMATION

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

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

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

PIs should ensure that their name and email address are the same as the name and email address that will be provided on the SF-424 Form of the Grants.gov application package submitted to Grants.gov. The organization, Business Officials, PI(s), and eBRAP log number named in the full application submitted to Grants.gov must match those named in the pre-application in eBRAP. ***Application viewing, modification, and verification in eBRAP is strongly recommended, but not required. The Project Narrative and Budget cannot be changed after the application submission deadline. Any other application component cannot be changed after the end of the application verification period.***

A. Where to Obtain the Grants.gov Application Package

To obtain the Grants.gov application package, including all required forms, perform a basic search using the Funding Opportunity Number W81XWH-15-PRMRP-FPA in Grants.gov (http://www.grants.gov/).

B. Pre-Application Submission Content

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. A change in PI or organization after submission of the pre-application may be allowed after review of a submitted written appeal (contact the CDMRP

Help Desk at help@eBRAP.org or 301-682-5507) and at the discretion of the USAMRAA Grants Officer.

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):

- **Application Information – Tab 1**
- **Application Contacts – Tab 2**
    - 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 SF-424 Form). The Business Official must either be selected from the eBRAP 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.
- **Collaborators and Key Personnel – Tab 3**
    - Enter the name, organization, and role of all collaborators and key personnel associated with the application.
    - FY15 PRMRP JPRP members should not be involved in any pre-application or application. For questions related to JPRP members and pre-applications or applications, refer to Section IV.C., Withdrawal, or contact the CDMRP Help Desk at help@eBRAP.org or 301-682-5507.
- **Conflicts of Interest (COIs) – Tab 4**
    - 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).
- **Pre-Application Files – Tab 5**

  Note: Upload document(s) 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, etc.) 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:** Indicate how the proposed project relates to at least one of the designated FY15 PRMRP Focused Program Award Topic Areas (as noted in Section I.B.).

- **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 of the designated FY15 PRMRP Focused Program Award Topic Area(s). Clearly articulate the rationale for the overarching challenge; include relevant preliminary data and literature citations.
- **Research Strategy:** The FY15 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 results of the proposed research on at least one of the FY15 PRMRP Focused Program Award 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 (e.g., 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 documents*** and are limited to:

- References Cited (one-page limit): List the references cited (including URLs if available) in the Preproposal Narrative using a standard reference format that includes the full citation (i.e., author[s], year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).
- List of Abbreviations, Acronyms, and Symbols: Provide a list of abbreviations, acronyms, and symbols used in the Preproposal Narrative.
- Key Personnel Biographical Sketches (five-page limit per individual).

- **Submit Pre-Application – Tab 6**
  - 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 FY15 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 the designated FY15 PRMRP Focused Program Award 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 address the overarching challenge and will 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 FY15 PRMRP Focused Program Award 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 work 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 timeframe for notification of invitation to submit an application is indicated on the title page of this Program Announcement/Funding Opportunity.

C. Full Application Submission Content

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

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

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

Note: The Project Narrative and Budget Form cannot be changed after the application submission deadline. If either the Project Narrative or the budget fails eBRAP validation or if the Project Narrative or Budget Form needs to be modified, an updated Grants.gov application package must be submitted via Grants.gov as a "Changed/Corrected Application" with the previous Grants.gov Tracking ID ***prior to the application submission deadline***.

Grants.gov application package components: For the Focused Program Award, the Grants.gov application package includes the following components (refer to the General Application Instructions, Section II.C., for additional information on application submission):

1. **SF-424 (R&R) Application for Federal Assistance Form:** Refer to the General Application Instructions, Section II.C., for detailed information.

2. **Attachments Form**

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

   - **Attachment 1: Project Narrative (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, etc.) used to describe the project. Inclusion of URLs that provide additional information to expand the Project Narrative and could confer an unfair competitive advantage is prohibited and may result in administrative withdrawal of the application.

     Describe the proposed program 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 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 of the designated FY15 PRMRP Focused Program Award Topic Area(s). Clearly articulate the rationale for the overarching challenge; include relevant literature citations. Clearly describe how the proposed research projects are interrelated and will accelerate toward a solution through a synergistic, 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 done 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 and realization of study objectives and the overarching challenge. If an External Advisory Board is to be utilized, describe the role of the board and the expertise to be sought in its members. Do not contact, recruit, or name potential members at this time to avoid potential COIs during review of the application.

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 may not be 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:** State the hypothesis to be tested.
- **Specific Aims:** Concisely explain each project's specific aims and describe the objectives to be reached.
- **Research Strategy:** Describe the experimental design, methods, and analyses, including appropriate controls, in sufficient detail for analysis. 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.nc3rs.org.uk/page.asp?id=1357). If human subjects will be recruited 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.
- **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 Food and Drug Administration [FDA] approvals). Describe the rationale for the trial and summarize the previous work that led to the development of the proposed clinical trial. 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 proposed methodology in sufficient detail to show a clear course of action. Describe potential challenges and alternative strategies where appropriate.
    - Identify the intervention to be tested and describe the projected outcomes.
    - Define the study variables and describe how they will be measured. Include a description of appropriate controls and the endpoints to be tested.
    - 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 the inclusion and exclusion criteria, the

availability of and access to the appropriate patient population(s), as well as the ability to accrue a sufficient number of subjects for the clinical trial.

- 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).
- Describe the statistical model and data analysis plan with respect to the study objectives. Specify the number of human subjects that will be enrolled. If multiple study sites are involved, state the approximate number to be enrolled at each site. Include a complete power analysis to demonstrate that the sample size is appropriate to meet the objectives of the study.
- Provide evidence of documented availability of and access to all critical reagents, and describe how quality control will be addressed. Include a description of how compliance with Good Laboratory Practices (GLP), Good Manufacturing Practices (GMP), and Good Clinical Practices (GCP) 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, statistician) possesses the appropriate expertise in conducting clinical trials.

- **Attachment 2: Supporting Documentation.** Start each document on a new page. Combine and upload as a single file named "Support.pdf." If documents are scanned to pdf, the lowest resolution (100 to 150 dpi) should be used. ***There are no page limits for any of these components unless otherwise noted. Include only those components described below; inclusion of items not requested will result in 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 Patent Abstracts: 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(s). Letters of support not requested in the Program Announcement/Funding Opportunity, such as those from members of Congress, do not impact application review or funding decisions.
- Letters of Collaboration: Provide a signed letter from each collaborating individual or organization that will demonstrate that the PI and project leaders have the support or resources necessary for the proposed work.
- Letters Confirming Access to Military or VA Patient Populations or Resources (if applicable): If the proposed research plan involves access to active duty military and/or VA patient populations or resources, include a letter of support, signed by the lowest ranking person with approval authority, confirming such access. If access cannot be confirmed at the time of application submission, the Government reserves the right to withhold or revoke funding until the PI has demonstrated support for and access to the relevant population(s) and/or resources.
- Intellectual Property
  - Background and Proprietary Information: All software and data first produced under the award are subject to a Federal purpose license. Provide a list of all background intellectual property to be used in the project or provide a statement that none will be used. If applicable, state and identify the proprietary information that will be provided to the Government and indicate whether the applicant will require a waiver of the Federal purpose license.
  - Intellectual and Material Property Plan (if applicable): Provide a plan for resolving intellectual and material property issues among participating organizations.

- **Attachment 3: Technical Abstract (one-page limit): Upload as "TechAbs.pdf."** Use only characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed.

  The technical abstract is used by all reviewers as a description of the proposed research program's key aspects. Therefore, 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 FY15 PRMRP Focused Program Award 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 designated FY15 PRMRP Focused Program Award 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."** 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 FY15 PRMRP Focused Program Award 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. Refer to the General Application Instructions, Section II.C.3., for detailed guidance on creating the SOW.

- **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 FY15 PRMRP Focused Program Award Topic Area(s) addressed. Describe how the overarching challenge addresses a central critical problem or question in the relevant Topic Area(s). In additional to articulating the potential impact of the overall program, address the potential impact of each individual project. Explain how the various outcomes of the projects 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 clinical 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 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), the appropriateness of the population(s)/dataset(s) for the proposed study, and the feasibility of accessing the population(s)/dataset(s). If a non-military population will be used for the proposed research project, explain how the population simulates the targeted population (i.e., military Service members, Veterans, and/or beneficiaries).

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

- **Attachment 8: Transition Plan (one-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 to develop the transition plan. The transition plan should include the components listed below, as appropriate:

  - A description of the expected outcomes that will result after completion of the proposed research efforts. Outcomes should be specific, measurable, and should include a definition of the 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, etc.).
  - For knowledge outcomes, a description of how the knowledge will be further developed, disseminated, and incorporated into clinical 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, commercialization, and/or delivery to the market.
- 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 3, Section L, 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), provide evidence in the form of communication from the FDA or the IRB of record to that effect.

- **Attachment 11: Collaborating DoD Military Facility Budget Form(s), if applicable: Upload as "MFBudget.pdf**." If a Military Facility (military health system facility, research laboratory, treatment facility, dental treatment facility, or a DoD activity embedded with a civilian medical center) will be a collaborator in performance of the project, complete the Collaborating DoD Military Facility Budget Form (available for download on the eBRAP "Funding Opportunities & Forms" web page), including a budget justification, for each Military Facility as instructed. Refer to the General Application Instructions, Section II.C.8., for detailed information.

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

   - PI Biographical Sketch (five-page limit): Upload as "Biosketch_LastName.pdf." The suggested biographical sketch format is available on the "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) in eBRAP. The five-page National Institutes of Health Biographical Sketch may also be used.
   - PI Previous/Current/Pending Support (no page limit): Upload as "Support_LastName.pdf."
   - Key Personnel Biographical Sketches (five-page limit each): Upload as "Biosketch_LastName.pdf."
   - Key Personnel Previous/Current/Pending Support (no page limit): Upload as "Support_LastName.pdf."

4. **Research & Related Budget:** Refer to the General Application Instructions, Section II.C.5., for detailed information.

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

5. **Project/Performance Site Location(s) Form:** Refer to the General Application Instructions, Section II.C.6., for detailed information.

6. **R & R Subaward Budget Attachment(s) Form (if applicable):** Refer to the General Application Instructions, Section II.C.7., for detailed information.

D. Applicant Verification of Grants.gov Submission in eBRAP

Prior to the end of the application verification period, PIs and organizational representatives can review and modify in eBRAP certain components of an application submitted to Grants.gov. Following retrieval and processing of the Grants.gov application, eBRAP will notify the organizational representatives and PI by email to log into eBRAP to review, modify, and verify

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

E. Submission Dates and Times

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

F. Other Submission Requirements

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

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

III. APPLICATION REVIEW INFORMATION

A. Application Review and Selection Process

All applicants are evaluated by scientists, clinicians, and consumer advocates using a two-tier review process. The first tier is peer review of applications against established criteria for determining technical merit. The second tier is a programmatic review that makes recommendations for funding to the DHA RDA Directorate and the Office of the Assistant Secretary of Defense for Health Affairs, based on (a) technical merit and (b) the relevance to the mission of the DHP and PRMRP, and to the specific intent of the award mechanism. The highest-scoring applications from the first tier of review are not automatically recommended for funding. 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 nondisclosure statement that application and evaluation information will not be disclosed outside the panel. Violations of confidentiality can result in the dissolving of a panel(s) and other corrective actions. In addition, personnel at the applicant or collaborating organizations are prohibited from contacting persons involved in the review process to gain protected evaluation information or to influence the evaluation process.

Violations of these prohibitions will result in the administrative withdrawal of the organization's application. Violations by panel members or applicants that compromise the confidentiality of the review process may also result in suspension or debarment from Federal awards. Furthermore, the unauthorized disclosure of confidential information of one party to another third party is a crime in accordance with Title 18 United States Code 1905.

B. Application Review Process

1. **Peer Review:** To determine technical merit, all applications will be evaluated according to the following scored criteria, which are 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 FY15 PRMRP Focused Program Award 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**
    - The degree to which the strategy proposed to bring the outcomes to the next level of development, including funding, milestones, and schedule, is appropriate.
    - Whether appropriate collaborations and other resources for providing continuity of development are established and/or 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.

Scored Review Criteria for Individual Research Projects:

- **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,
        - 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.

- **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, aims, experimental design, methods, endpoints, and analyses are developed and integrated into the projects.
  - How well potential problems are acknowledged and alternative approaches are addressed.
  - If animal studies are included, how well they are designed to achieve reproducible and rigorous results.
  - If applicable, to what degree the statistical plan and power analysis 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.
- **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.
  - If a clinical trial is proposed, 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.

Projects with a clinical trial will also be evaluated on the following criterion:

- **Clinical Strategy**
  - To what extent the type of clinical trial (e.g., prospective, randomized, controlled) proposed is appropriate to meet the project's objectives.
  - How well the clinical trial is designed with appropriate study variables, controls, and endpoints.
  - 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.
  - Whether the clinical trial design, methods, and analysis plan meet the requirements for applying for and obtaining IND/IDE status (or other FDA approvals), if appropriate.

- Whether there is documented availability of, access to, and quality control for all critical reagents.
- Whether there are resources available for the development of sufficient quantities of critical reagents under GMP or GLP, if applicable.
- To what degree the data analysis plan is suitable for the planned study.
- To what extent the statistical plan, including sample size projections and power analysis, is adequate for the study and all proposed correlative studies (if applicable).

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/Funding Opportunity.
- **Application Presentation**
  - To what extent the writing, clarity, and presentation of the application components influence the review.

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

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

   b. **Relevance to the mission of the DHP and FY15 PRMRP, as evidenced by the following:**
      - Adherence to the intent of the award mechanism
      - Military relevance
      - Program portfolio composition
      - Relative impact
      - Relevance to program objectives

C. Recipient Qualification

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

D. Application Review Dates

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

E. Notification of Application Review Results

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

IV. ADMINISTRATIVE ACTIONS

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

A. Rejection

The following will result in administrative rejection of the pre-application:

- Preproposal Narrative exceeds page limit.
- Preproposal Narrative is missing.

The following will result in administrative rejection of the application:

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

B. Modification

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

C. Withdrawal

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

- A FY15 PRMRP JPRP 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 FY15 PRMRP JPRP members can be found at http://cdmrp.army.mil/prmrp/panels/panel15.

- The application fails to conform to this Program Announcement/Funding Opportunity description to the extent that appropriate review cannot be conducted.
- Inclusion of URLs, with the exception of links in References Cited and Publication and/or Patent Abstract sections.
- Page size is larger than 8.5 inches x 11.0 inches (approximately 21.59 cm x 27.94 cm).
- Inclusion of any employee of CDMRP review contractors in applications for funding without adequate plans to mitigate conflicts of interest. Refer to the General Application Instructions, Section II.B., for detailed information.
- Personnel from applicant or collaborating organizations are found to have contacted persons involved in the review process to gain protected evaluation information or to influence the evaluation process.
- The proposed research project is not relevant to any of the designated FY15 PRMRP Focused Program Award Topic Areas.
- An application submitted by a PI who does not meet the eligibility criteria will be withdrawn.

D. Withhold

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

V. AWARD ADMINISTRATION INFORMATION

A. Award Notice

Awards will be made no later than September 30, 2016. Refer to the General Application Instructions, Appendix 3, for additional award administration information.

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

B. Administrative Requirements

Refer to the General Application Instructions, Appendix 3 for general information regarding administrative requirements.

C. National Policy Requirements

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

D. Reporting

Refer to the General Application Instructions, Appendix 3, Section I, for general information on reporting requirements.

Quarterly technical progress reports and quad charts will be required.

In addition to written progress reports, oral presentations may be requested.

E. 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.

The institution 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 3, Section M, for general information on organization or PI changes.

VI. AGENCY CONTACTS

A. CDMRP Help Desk

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

Phone: 301-682-5507

Email: help@eBRAP.org

B. Grants.gov Contact Center

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

Phone: 800-518-4726

Email: support@grants.gov

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

VII. APPLICATION SUBMISSION CHECKLIST

Grants.gov Application Components	Upload Order	Action	Completed
SF-424 (R&R) Application for Federal Assistance		Complete form as instructed.	
Attachments Form	1	Project Narrative: Upload as Attachment 1 with file name "ProjectNarrative.pdf."	
	2	Supporting Documentation: Upload as Attachment 2 with file name "Support.pdf."	
	3	Technical Abstract: Upload as Attachment 3 with file name "TechAbs.pdf."	
	4	Lay Abstract: Upload as Attachment 4 with file name "LayAbs.pdf."	
	5	Statement of Work: Upload as Attachment 5 with file name "SOW.pdf."	
	6	Impact Statement: Upload as Attachment 6 with file name "Impact.pdf."	
	7	Military Relevance: Upload as Attachment 7 with file name "MilRel.pdf."	
	8	Transition Plan: Upload as Attachment 8 with file name "Transition.pdf."	
	9	Data and Research Resources Sharing Plan: Upload as Attachment 9 with file name "Sharing.pdf."	
	10	IND/IDE Documentation: Upload as Attachment 10 with file name "IND-IDE.pdf," if applicable.	
	11	Collaborating DoD Military Facility Budget Form(s): Upload 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.	
Research & Related Budget		Complete as instructed. Attach Budget Justification (BudgetJustification.pdf) to the appropriate field.	
Project/Performance Site Location(s) Form		Complete form as instructed.	
R & R Subaward Budget Attachment(s) Form		Complete form as instructed.	

APPENDIX
FOCUSED PROGRAM AWARD GAPS AND PRIORITY RESEARCH AREAS

Applications addressing any of the Fiscal Year 2015 (FY15) Peer Reviewed Medical Research Programs (PRMRP) Topic Areas are of interest to the program. Gaps and priority research areas related to the FY15 PRMRP Topic Areas have been identified by the Department of Defense (DoD) and the Department of Veterans Affairs and are listed below. Applicants are encouraged to read and consider these gaps and priority research areas before preparing their applications. The information provided is not exhaustive, and applicants are not restricted to submitting applications that address the identified gaps and priority research areas in this list. Any aspect of research relevant to one or more FY15 PRMRP Topic Area may be considered for funding.

Acupuncture

- Definitive studies to determine the effectiveness of acupuncture for acute and chronic pain associated with traumatic neuromusculoskeletal injuries, including the role of acupuncture in reducing pain medication use.
- Research on the role of acupuncture in pain management following traumatic brain injury, spinal cord injury, and/or peripheral nerve injury.
- Research on the use of acupuncture as prevention of or treatment for mental health disorders such as post-traumatic stress, depression, suicide and suicidal ideation, substance abuse, agitation, anxiety, and other co-morbid disorders.
- Research to contribute to clinical guidelines on use of acupuncture, including dose response, degree of rigor, how long it should be continued for specific conditions, and how to incorporate it into standard care.
- Research on the use of acupuncture in patient transport to manage pain.

Advanced Prosthetics

- Advancement of efferent control, i.e., control of multi-degree-of-freedom prostheses. This could include an upper extremity with fine motor movements, or a lower extremity to provide a biologically accurate gate.
- Development of device afferent communication, science of proprioception, and pressure sensing, and determining how to communicate this information to the user. The end goal of this research would be for the user to obtain natural feedback from a terminal device.
- Research on the development and use of prosthetics for urogenital injury.

Burn Pit Exposure

- Research on the etiology and treatment of adverse health events related to military deployment to Iraq and Afghanistan associated with exposure to airborne hazards and open pit burning of solid waste and other materials.
- Toxicological studies to ascertain toxicity of natural dust, burn pit combustion products, interactions between pollutants, and mechanisms of action.

- Characterization of emissions from open air burns, burn boxes, and incinerators. This includes determining relative contributions of background anthropogenic and geogenic sources.
- Development and validation of exposure assessment instruments for use in research and clinical validation.

Cardiovascular Health

- Risk assessment, prevention, and treatment of trauma-induced cardiac arrest secondary to hemorrhage and polytrauma.
- Research to better understand the hypermetabolic state of combat casualties while at Level 5 military medical treatment facilities and beyond, including etiology, outcomes (e.g., left ventricular hypertrophy), and treatment.
- Research to understand the relationship between physical (e.g., traumatic brain injury) and psychological (e.g., post-traumatic stress disorder, depression, anxiety) disorders and cardiovascular disease.
- Research toward development of guidelines for the management of active duty patients with non-operative disease of the aortic valve and/or ascending aorta. With increased availability and use of CT (computed tomography) scans and echocardiography, the known incidence of aortic aneurysm and aortic valve disease in the active duty population is increasing, but current management is variable, non-standardized, and inconsistent.
- Research to assess the impact of the DoD Physical Fitness Tests in influencing reduction of cardiovascular risk from atherosclerosis.

Congenital Heart Disease

- Research on the transition of care of congenital heart disease patients from pediatric to adult providers in the Military Health System.
- Research on the ability of patients with congenital heart disease to join or remain on active duty.

Focal Segmental Glomerulosclerosis

- Development of non-invasive methods to diagnosis focal segmental glomerulosclerosis and its variants.
- Research on the long-term use of immunosuppressants in patients with focal segmental glomerulosclerosis and the likelihood of developing infections.
- Research to improve understanding of the causes of primary and secondary focal segmental glomerulosclerosis.
- Development of a curative therapy or treatments to better halt the progression of the disease and/or prevent post-transplantation recurrence.

Healthcare-Acquired Infection Reduction

- Development of a multi-center infection control consortium in military hospitals to assess ways to reduce transmission of nosocomial pathogens.
- Research to improve understanding of bacterial mechanisms of resistance and ways to counter them.
- Development of new modalities to identify, prevent, and treat patients with *Clostridium difficile* infection.
- Development of new antimicrobials for the treatment of emerging resistant healthcare-associated infections.
- Establishment of a pilot program to determine whether restricting antibiotic use in military or civilian hospitals leads to reduction in multidrug-resistant pathogens.
- Assessment of proper implementation of existing healthcare-associated infection reduction techniques and technologies in military and civilian healthcare settings and identification of best practices for prevention.
- Utilization of a systems engineering approach to develop automated systems to remove human introduction of infection in high-risk processes.
- Research to identify minimum necessary infection control practices in the transport environment (e.g., fixed-wing aircraft, helicopter, ships, ambulance) to safely conduct clinical procedures, including dressing changes, central line placement, and surgery.
- Research to identify minimum necessary infection control practices in the forward surgical setting (e.g., tents and other temporary shelters, buildings of opportunity, and other non-clean environments) to safely conduct clinical procedures, including standard nursing care and operative procedures.

Hepatitis B

- Identification and reduction of hepatitis B virus in blood products for transfusion.

Hydrocephalus

- Research on the etiology, prevention, diagnosis, and treatment of delayed-onset hydrocephalus following traumatic brain injury.
- Research on how to manage hydrocephalus and resulting intracranial pressure in Service members who have sustained severe and/or penetrating head injury from point of injury through acute hospitalization.

Integrative Medicine

- Research on the use of integrative medicine in treatment and management of chronic pain disorders, including comparative efficacy studies relative to standard of care.
- Research on the use of integrative medicine in strategic aeromedical evacuation (i.e., non-pharmacy options that would improve transport experience for patients through the continuum of care).

- Rigorous longitudinal studies of integrative medicine approaches for enhancing resilience and for treating psychological health issues and co-occurring disorders.
- Development of outcomes tools and measures to evaluate the effectiveness of integrative medicine.

Metals Toxicology

- Identification and development of biomarkers as a tool to evaluate exposure to toxic metals in an operational environment.
- Retrospective studies to evaluate risk and exposure among workers at DoD industrial facilities.
- Assessment of the health effects of embedded metal fragments and development of treatment strategies to enhance elimination of metals from the body.

Mitochondrial Disease

- Research to determine the frequency of genetic testing for mitochondrial diseases in military children with global developmental delay, intellectual disability, or autism.

Nanomaterials for Bone Regeneration

- Technologies addressing segmental/large bone defects in the craniomaxillofacial body region.
- Controlled release/extended release of growth factors for bone regeneration.
- Technologies that enable enhanced recruitment of endogenous cell populations for bone regeneration.
- Technologies that repair the soft tissue envelope to enhance bone regeneration.

Osteoarthritis

- Basic and translational research to identify treatments to reverse osteoarthritis.
- Studies to examine use of existing regenerative medicine techniques and therapies, including dose response information and frequency and timing of application.
- Research to establish activity recommendations for maximal joint life following joint repair, particularly in young patient populations.
- Repair of focal cartilage defects using cell-based therapies.
- Basic and translational research to describe the acute inflammatory response to neuromusculoskeletal combat injury as it relates to osteoarthritis.

Pathogen-Inactivated Dried Plasma

- Identify the clinical impact of administering dried plasma in the en route care system, before and during transport.

Psychotropic Medications

- Identification and/or development of therapies that can completely or selectively reverse the effects of psychotropic medications.
- Research into the use of psychotropic medications for the treatment of mental health disorders including post-traumatic stress, suicidal ideation, substance abuse, and other co-morbid disorders.
- Research to determine and test psychological interventions related to mental health issues specific to women in the military.
- Research toward increasing the accuracy and effectiveness of prescription practices for mental health medications, including but not limited to development of biomarkers to match patients to medications and follow treatment response, better measures of outcomes, and better collection of patient data in real time.
- Research on use of psychotropic medications in strategic aeromedical evacuation.

Pulmonary Fibrosis

- Research to enhance biomarker discovery work to identify indicators of pulmonary injury.
- Retrospective studies to determine risk and incidence of pulmonary fibrosis among former and current active duty personnel.

Respiratory Health (excluding lung cancer and mesothelioma)

- Development of an innovative, next-generation adenovirus vaccine, ideally one that may be modified for different adenovirus serotypes, for the prevention of acute respiratory illness caused by adenovirus.
- Research into opportunistic infections that will assist in understanding their basic metabolism, create ex vivo growth systems or small animal models where there are none available, and/or development of new agents with which to treat them as it relates to respiratory disease.
- Research on the cause, treatment, and prevention of respiratory symptoms and ailments possibly associated with deployed and re-deployed military personnel, including acute eosinophilic pneumonia, constrictive bronchiolitis, asthma, allergies, and other chronic lung diseases and breathing problems.
- Clinical assessments to determine the prevalence and severity of respiratory disease in returned Service members, including pre- and post-deployment and retrospective medical record studies.
- Studies to determine the natural history of deployment-related respiratory disease and to identify factors associated with respiratory disease.
- Identification and development of biomarkers of exposure for a set of military-relevant hazards selected from airborne nanomaterials, diesel exhaust, and other combustion products and fuels.
- Assessment of the impact of aeromedical evacuation on respiratory health, including ventilator settings, oxygen use, etc.

- Development of improved therapeutics for influenza.
- Research to improve the identification of pathogens in lower respiratory tract infections.

Sleep Disorders

- Research on how the disruption of normal sleep and circadian biological rhythms adversely affects health, safety, performance, and productivity of military and civilian populations.
- How to prevent/reduce sleep disorders that are associated with long aeromedical evacuation flights for both clinical team members and patients (sleep/rest cycles, in-flight entertainment, etc.).
- Research to assess the validity of improving adherence to nightly CPAP (continuous positive airway pressure) in children with neurodevelopmental disorders and obstructive or mixed sleep apnea through habituation with behavioral techniques and pharmacological management.
- Research to identify the most effective treatment protocols for sleep disorders in DoD beneficiaries.
- Investigation of how mental disorders, and post-traumatic stress disorder in particular, combined with the disruption/degradation of sleep quality, impact long-term physical health through changes in glucocorticoid regulation.
- Research on non-pharmacological treatments for sleep disorders.

Vascular Malformations

- Development of improved screening mechanisms to find vascular malformations and determination of whether such individuals should be allowed to serve in the military.
- Development of improved methods to diagnose and manage vascular disruptions with or without hemorrhagic shock.
- Development of improved methods to manage circulation and control junctional and truncal hemorrhaging in the pre-hospital environment.

Women's Heart Disease

- Retrospective studies to determine risk and incidence of heart disease among former and current female active duty personnel.
- Research on trauma-induced cardiac arrest secondary to hemorrhage and polytrauma in the female population.