Program Announcement

for the

Defense Health Program

Defense Medical Research and Development Program

Department of Defense

Congressionally Directed Medical Research Programs

Peer Reviewed Medical Research Program

Clinical Trial Award

Funding Opportunity Number: W81XWH-14-PRMRP-CTA

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 25, 2014
- **Invitation to Submit an Application:** August 2014
- **Application Submission Deadline:** 11:59 p.m. ET, October 17, 2014
- **End of Application Verification Period:** 5:00 p.m. ET, October 22, 2014
- **Peer Review:** December 2014
- **Programmatic Review:** March 2015

Change for Fiscal Year 2014: *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 2014 (FY14) Peer Reviewed Medical Research Program (PRMRP) are being solicited for the Assistant Secretary of Defense for Health Affairs, Defense Health Program (DHP), by the U.S. Army Medical Research Acquisitions Activity (USAMRAA). 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 FY13 totaled $644.5 million (M). The FY14 appropriation is $200M. The PRMRP is administered by the U.S. Army Medical Research and Materiel Command (USAMRMC) through the Congressionally Directed Medical Research Programs (CDMRP).

The vision of the FY14 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 FY14 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 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. FY14 PRMRP Topic Areas

All applications for PRMRP funding must specifically address at least one of the Topic Areas as directed by Congress, and must be directly relevant to the health care needs of military service members, Veterans, and/or beneficiaries. If the proposed research does not specifically address at least one of the FY14 PRMRP Topic Areas, the Government reserves the right to administratively withdraw the application. The Government also reserves the right to reassign the application's Topic Area if submitted under an inappropriate Topic Area. The FY14 PRMRP Topic Areas are listed below.

- Acupuncture
- Arthritis (other than post-traumatic osteoarthritis and rheumatoid arthritis)
- Chronic Migraine and Post-Traumatic Headaches
- Congenital Heart Disease
- DNA Vaccine Technology for Post-Exposure Prophylaxis
- Dystonia
- Epilepsy
- Food Allergies
- Fragile X Syndrome
- Hereditary Angioedema
- Illnesses Related to Radiation Exposure (excludes cancer)
- Inflammatory Bowel Disease
- Interstitial Cystitis
- Lupus
- Malaria
- Metabolic Disease
- Neuroprosthetics
- Pancreatitis

- Polycystic Kidney Disease
- Post-Traumatic Osteoarthritis
- Psychotropic Medications
- Respiratory Health (excludes lung cancer and mesothelioma)
- Rheumatoid Arthritis
- Segmental Bone Defects
- Tinnitus

Applications addressing any of the above Topic Areas are of interest to the program. Some of the Topic Areas have gaps and priority research areas that have been identified by the Department of Defense (DoD) and the Department of Veterans Affairs (VA). The list may be found in the Appendix of this document. Applicants are encouraged to read and consider these 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. Any aspect of research relevant to any FY14 PRMRP Topic Area may be considered for funding.

C. Award Information

The PRMRP Clinical Trial Award supports the rapid implementation of clinical trials with the potential to have a significant impact on a disease or condition addressed in at least one of the Congressionally directed FY14 PRMRP Topic Areas. Clinical trials may be designed to evaluate promising new products, pharmacologic agents (drugs or biologics), devices, clinical guidance, and/or emerging approaches and technologies. Proposed projects may range from small proofof-concept trials to demonstrate feasibility or inform the design of more advanced trials (e.g., pilot, first in human, Phase 0), through large-scale trials to determine efficacy in relevant patient populations. All studies must be responsive to the health care needs of the military service members, Veterans, and/or beneficiaries; however, the use of military or Veteran populations is not required.

Funding from this award mechanism must support a clinical trial. Principal Investigators (PIs) seeking funding for a preclinical research project should consider submitting an application to one of the other FY14 PRMRP Program Announcements/Funding Opportunities being offered. A clinical trial is defined as a prospective accrual of human subjects where an intervention (e.g., device, drug, biologic, surgical procedure, rehabilitative modality, behavioral intervention, or other) is tested on a human subject for a measurable outcome with respect to exploratory information, safety, effectiveness, and/or efficacy. This outcome represents a direct effect on the human subject of that intervention or interaction. The term "human subjects" is used in this Program Announcement/Funding Opportunity to refer to individuals who will be recruited for or who will participate in the proposed clinical trial. For more information, a Human Subject Resource Document is provided at https://ebrap.org/eBRAP/public/Program Studies conducted under the Animal Efficacy Rule (Code of Federal Regulations, Title 21, Part 314 [21 CFR 314]), when human efficacy studies are not ethical or feasible, also meet the definition of a clinical trial and may be submitted to the FY14 PRMRP Clinical Trial Award for consideration of funding. For the purposes of this program announcement/funding opportunity, the term "clinical trial" is used to refer to human clinical trials as well as animal efficacy trials that meet the requirements under 21 CFR 314.

If the clinical trial involves the use of a drug that has not been approved by the U.S. Food and Drug Administration (FDA) for the proposed investigational use, then an Investigational New Drug (IND) application to the FDA that meets all requirements under 21 CFR 312 may be required and must be submitted to the FDA ***prior to the application submission deadline.*** If the investigational product is a device, evidence that an Investigational Device Exemption (IDE) application that meets all requirements under 21 CFR 812 has been submitted to the FDA ***prior to the application submission deadline***, or that the device is exempt from an IDE, is required. The Government reserves the right to withdraw funding if an IND or IDE is necessary but has not been submitted to the FDA prior to the grant submission deadline, or if documented status of the IND or IDE has not been obtained within 6 months of the award date.

The following are important aspects of submission for the Clinical Trial Award:

- The proposed clinical trial is expected to begin no later than 12 months after the award date, or 18 months for FDA-regulated studies.
- The proposed intervention to be tested should offer significant potential impact for individuals affected by the specified disease(s)/condition(s).
- Inclusion of preliminary data relevant to the proposed research project is required.
- The proposed research project must be based on sound scientific rationale that is established through logical reasoning and critical review and analysis of the literature.
- The application should describe the planned indication for the product label, if appropriate, and include an outline of the development plan required to support that indication.
- The application should demonstrate availability of, and access to, a suitable patient population in numbers that will support a meaningful outcome for the study. The PI should discuss how accrual goals will be achieved and how standards of care may impact the study population.
- The application should demonstrate documented availability of and access to the drug/ compound, device, and/or other materials needed, including access to intellectual property rights, as appropriate. The quality of the product should be commensurate with FDA manufacturing standards applicable to the type and phase of product being developed (i.e., Quality System Regulation, Good Manufacturing Practices).
- The proposed clinical trial design should include clearly defined and appropriate endpoints, and follow Good Clinical Practice (GCP) guidelines.
- The application should include a clearly articulated statistical analysis plan, appropriate statistical expertise, and a power analysis reflecting sample size projections that will clearly answer the objectives of the study.
- The application should include a clearly articulated data management plan and use of an appropriate database to safeguard and maintain the integrity of the data.
- The application should include a clearly articulated safety management plan, outlining how safety pharmacovigilance will be conducted as applicable.

- The application should include a clearly articulated clinical monitoring plan, outlining how the study will be monitored for GCP compliance.
- The application should include a study coordinator(s) who will guide the clinical protocol through the local Institutional Review Board (IRB) of record and other regulatory approval processes, coordinate activities from all sites participating in the trial, and coordinate participant accrual.
- The application should include a Transition Plan (including potential funding and resources) showing how the product will progress to the next clinical trial phase and/or delivery to the market after the successful completion of the FY14 PRMRP Clinical Trial Award.
- The application should clearly demonstrate strong institutional support.
- The application should acknowledge the commitment to filing the study in the National Institutes of Health (NIH) clinical trials registry, www.clinicaltrials.gov.

Multi-Institutional Clinical Trials: If the proposed clinical trial is multi-institutional, plans for communication and data transfer among the collaborating institutions, as well as how specimens and/or imaging products obtained during the study will be handled, should be included in the appropriate sections of the application. A separate intellectual and material property plan agreed upon by all participating institutions is also required for multi-institutional clinical trials.

Military Relevance: Relevance to the health care 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
- 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 an exhaustive list, the following websites may be useful in identifying information about ongoing DoD and VA areas of research interest within the FY14 PRMRP 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 Medical Research and Development Program
http://dmrdp.fhpr.osd.mil/home.aspx

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

Military Infectious Disease 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.

Use of Human Subjects and Human Anatomical Substances: All DoD-funded research involving new and ongoing research with human subjects and human anatomical substances must be reviewed and approved by the USAMRMC Office of Research Protections (ORP),

Human Research Protection Office (HRPO), in addition to the local IRB of record. Local IRB approval at the time of submission is NOT required. The HRPO is mandated to comply with specific laws and directives governing all research involving human subjects that is supported by the DoD. These laws and directives will require information in addition to that supplied to the IRB. Allow a minimum of 2-3 months for regulatory review and approval processes. Refer to the General Application Instructions, Appendix 6, for more information.

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

D. Eligibility Information

- PIs at or above the level of Assistant Professor (or equivalent) are eligible to submit applications.
- Cost sharing/matching is not an eligibility requirement.
- Eligible investigators must apply through an organization. Organizations eligible to apply include national, international, for-profit, non-profit, public, and private organizations.
- Refer to the General Application Instructions, Appendix 1, for general eligibility information.

E. Funding

- The maximum period of performance is **5** years.
- Applications are not restricted to a predetermined cost limit. The requested budget must be justified and appropriate to the scope of the clinical trial proposed.
- 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 funding for a project with a period of performance less than the maximum **5** years.
- Indirect costs shall be proposed in accordance with the organization's negotiated rate agreement.

Refer to the General Application Instructions, Section II.C.4., 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.4. of the General Application Instructions***.

For this award mechanism, direct costs:

Must be requested for:

- Travel costs of up to $1,800 for the PI to disseminate project results at one DoD-sponsored meeting to be specified by the CDMRP during the award period of performance. 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
- Support for multidisciplinary collaborations
- Travel between collaborating organizations
- Travel costs of up to $1,800 per year 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 Appendix 3 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 will be executed through 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.4. Research & Related Budget, for additional information on budget considerations for applications involving federal agencies.

The CDMRP expects to allot approximately $36M of the $200M FY14 PRMRP appropriation to fund approximately six Clinical Trial 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 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/).

New for FY14: ***The CDMRP has replaced its eReceipt System with eBRAP.*** Submission remains a two-step process requiring both pre-application and application submission.

PIs must be registered in eBRAP in order to submit a pre-application and receive notification of the status of a pre-application or application. A key feature of eBRAP is that an organization's representatives and PIs are able to view and modify the Grants.gov application submissions associated with them, but only if the organization, Business Officials, and PIs are registered and affiliated to the organization in eBRAP (see *eBRAP User Guide* at *https://ebrap.org/eBRAP/public/UserGuide.pdf)*. Upon completion of an organization's registration in eBRAP and approval by the CDMRP Help Desk, the organization name will be displayed in eBRAP to assist the organization's business officials and PIs as they register.

Note: Submission of either the pre-application to eBRAP or application to Grants.gov does not require registering an organization and affiliating its Business Officials and PIs in eBRAP; however, the ability to view and modify the Grants.gov application in eBRAP is contingent upon the registration and affiliation. ***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.*** If verification is not completed by the end of the application verification period, the application will be reviewed as submitted through Grants.gov or may be subject to administrative rejection (see Section IV.A., Rejection).

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.

A. Where to Obtain the Application Package

To obtain the complete application package, including all required forms, perform a Grants.gov (http://www.grants.gov/) basic search using the Funding Opportunity Number: W81XWH-14-PRMRP-CTA.

B. Pre-Application Submission and Content Form

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

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

A change in PI or organization after submission of the pre-application will be allowed only at the discretion of the US Army Medical Research Acquisition Activity (USAMRAA) Contracting/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**
    - It is recommended that PIs identify an Alternate Submitter in the event that assistance with pre-application submission is needed.
- **Collaborators and Conflicts of Interest (COI) – Tab 3**

  FY14 PRMRP Joint Programmatic Review Panel (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.
- **Required Files – Tab 4**

  Notes: 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 (three-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 FY14 PRMRP Topic Area.
    - **Research Idea:** Describe the ideas and reasoning on which the proposed clinical trial is based; include relevant literature citations. Briefly describe the level of

scientific evidence that supports the progression of this research to a clinical trial. Clearly specify which type (e.g., drug, device, behavioral) of clinical trial is being proposed and indicate the phase of trial and/or class of device and regulatory status, as appropriate.

- **Research Strategy:** Concisely state the project's objectives and specific aims. Briefly describe the patient population(s) to be recruited for the clinical trial and the experimental approach.
- **Personnel:** Briefly state the qualifications of the PI and key personnel to perform the clinical trial. Note any military- or VA-relevant collaborations.
- **Impact and Military Relevance:** Describe how the proposed work will have an impact on accelerating the movement of a promising treatment into clinical application. Explain how the project is relevant to the health care needs of military service members, Veterans, and/or beneficiaries.

Pre-Application Supporting Documentation: The items to be included as supporting documentation for the pre-application ***must be uploaded as individual 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 (four-page limit per individual).

- **Submit Pre-Application – Tab 5**

  This tab must be completed for the pre-application to be accepted and processed.

Pre-Application Screening

- **Pre-Application Screening Criteria**

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

  - **Research Idea:** The degree to which the proposed clinical trial addresses an important question in one or more of the FY14 PRMRP Topic Areas. How well the rationale is supported, and how well the background provided indicates the research is ready to move into the phase of clinical trial proposed.
  - **Research Strategy:** How well the specific aims, patient population, and proposed methodology will address the hypothesis and achieve the desired outcomes.
  - **Personnel:** How the background and experience of the PI and other key personnel are appropriate to successfully complete the clinical trial.

- **Impact and Military Relevance:** The degree to which the proposed clinical trial, if successful, will improve patient care in the FY14 PRMRP Topic Area(s) addressed. How well the research will address a health care issue relevant to military service members, Veterans, and/or beneficiaries.

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

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

C. Application Submission Content and Forms

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

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

New for FY14: ***Applications submitted through and validated by Grants.gov will be retrieved and processed by eBRAP to allow for review, modification, and verification.*** The PI and organizational representatives will receive an email request from eBRAP to review, modify, and verify the application submitted to Grants.gov. During this verification period, the PI may upload missing files (excluding those listed in Section IV.A., Rejection), replace files, and re-categorize files. These modifications must be completed by the end of the verification period.

Note: Changes to either the Project Narrative or Budget are not allowed in eBRAP; if such changes are required, the entire application package must be submitted through Grants.gov as a "Changed/Corrected Application" with the Previous Grants.gov Tracking ID ***prior to the application submission deadline (which occurs earlier than the end of the application verification period).***

Grants.gov application package components: For the Clinical Trial 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**

   The Project Narrative is NOT the formal clinical trial protocol. Instead, all essential elements of the proposed clinical trial necessary for scientific review must be included as directed in Attachment 1 (the Project Narrative) and Attachments 6-8 described below. Failure to submit these attachments as part of the application package will result in rejection of the entire application.

- **Attachment 1: Project Narrative (20-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 will result in administrative withdrawal of the application.

  Describe the proposed project in detail using the outline below.

  - **Background:** Describe in detail the rationale for the study and include a literature review, preliminary studies, and/or preclinical data that led to the development of the proposed clinical trial. Provide a summary of relevant clinical trials and distinguish how the proposed study differs from other relevant or recently completed clinical trials. Include a discussion of any current clinical use of the intervention under investigation, and/or details of its study in clinical trials for other indications (as applicable). The background section should clearly support the choice of study variables and should explain the basis for the study questions and/or study hypotheses. This section should establish the relevance of the study and explain the applicability of the proposed findings to the relevant FY14 PRMRP Topic Area(s).

    If the proposed clinical trial was initiated using other funding prior to this application, explain the history and background of the clinical trial and declare the source of prior funding. Specifically identify the portions of the study that will be supported with funds from this award.

  - **Objectives/Specific Aims/Hypotheses:** Provide a description of the purpose and objectives of the study with detailed specific aims and/or study questions/ hypotheses.

  - **Study Design:** Describe the type of study to be performed (e.g., prospective, randomized, controlled) and 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).
    - Describe the human subject-to-group assignment process (e.g., randomization, block randomization, stratified randomization, age-matched controls, alternating group, or other procedures), if applicable. Explain the specific actions to accomplish the group assignment (e.g., computer assignment, use of table of random numbers).
    - If using psychometric measures, describe their reliability and validity.

- **Statistical Plan and Data Analysis:** Describe the statistical model and data analysis plan with respect to the study objectives. Specify the approximate number of human subjects to 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. If a subpopulation of a recruited sample population will be used for analysis, complete a statistical analysis to ensure appropriate power can be achieved within the subpopulation study.

- **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 may result in the removal of those items or 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 (five-document limit): Include relevant publication URLs and/or patent abstracts. If publications are not publicly available, then a copy/copies of the published manuscript(s) must be included in Attachment 2. Extra items will not be reviewed.
  - Letters of Organizational Support: Provide a letter (or letters, if applicable), signed by the Department Chair or appropriate organization official, confirming the laboratory space, equipment, and other resources available for the project.
  - Letters of Collaboration (if applicable): Provide a signed letter from each collaborating individual or organization that will demonstrate that the PI has the support or resources necessary for the proposed work. If the proposed study involves use of a commercially produced investigational drug, device, or biologic, provide a letter of commitment from the commercial entity indicating availability of the product for the duration of the study, support for the proposed phase of research, and support for the indication to be tested.
  - Letters Confirming Access to Military or VA Patient Populations or Resources (if applicable): If the proposed research plan involves access to active duty

military and/or VA patient populations or resources, include a letter of support, signed by the lowest ranking person with approval authority, confirming such access. If access cannot be confirmed at the time of application submission, the Government reserves the right to withhold or revoke funding until the PI has demonstrated support for and access to the relevant population(s) and/or resources.

- Intellectual Property
  - Background and Proprietary Information: All software and data first produced under the award are subject to a federal purpose license in accordance with applicable DoD Grant and Agreement Regulations (DoDGAR) requirements. 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.
- Data and Research Resources Sharing Plan: Describe how data and resources generated during the performance of the project will be shared with the research community. Refer to the General Application Instructions, Appendix 4, Section L, for more information about the CDMRP expectations for making data and research resources publicly available.

- **Attachment 3: Technical Abstract (one-page limit):** Upload as "TechAbs.pdf."

  Describe the proposed research project including the following elements:

  Background, rationale, hypothesis or objective, specific aims, study design, clinical impact, military relevance, and the relevance of the project to at least one FY14 PRMRP Topic Area.

  The technical abstract is used by all reviewers; however, programmatic reviewers do not typically have access to the full application and rely on the technical abstract for appropriate description of the project's key aspects. Therefore, clarity and completeness within the space limits of the technical abstract are highly important.

- **Attachment 4: Lay Abstract (one-page limit):** Upload as "LayAbs.pdf."

  State the FY14 PRMRP Topic Area(s) addressed by the proposed research project. Include a comprehensive overview of the intervention 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. Describe the types of patients the intervention will help, and how it will help them. Do not duplicate the technical abstract.

- **Attachment 5: Statement of Work (SOW) (three-page limit):** Upload as "SOW.pdf." Refer to the General Application Instructions, Section II.C.2., for detailed guidance on creating the SOW.

  The suggested SOW format and examples specific to different types of research projects are available on the eBRAP "Program Announcement and Forms" web page (https://ebrap.org/eBRAP/public/Program.htm). For the Clinical Trial Award mechanism, use the SOW format example titled "SOW for Clinical Research (Including Trials, Special Populations)." The SOW must be in PDF format prior to attaching.

- **Attachment 6: Human Subject Recruitment and Safety Procedures (no page limit):** Upload as "HumSubProc.pdf." The Human Subject Recruitment and Safety Procedures attachment should include the components listed below.

  a. Study Population: Describe the target population (to whom the study findings will be generalized) and the nature, approximate number, and pertinent demographic characteristics of the accessible population at the study site (population from whom the sample will be recruited/drawn). Demonstrate that the research team has access to the proposed study population in the numbers necessary for a meaningful outcome. Furthermore, discuss past efforts in recruiting human subjects from the target population for previous clinical trials (if applicable). Address any potential barriers to accrual including those specific to recruitment from military and/or Veteran populations (if applicable). Provide plans for addressing unanticipated delays. Include justification of any age, race, ethnicity, or sex limitations provided.

  b. Inclusion/Exclusion Criteria: List the inclusion and exclusion criteria for the proposed clinical trial. Inclusion/exclusion criteria should take into consideration the specific risk profile of the studies to be conducted and the standard of care for that patient population. Provide detailed justification for exclusions.

  Inclusion of Women and Minorities in Study. Consistent with the Belmont Report, "Ethical Principles and Guidelines for the Protection of Human Subjects," and Congressional legislation, special attention is given to inclusion of women and/or minorities in studies funded or supported by the USAMRMC. This policy is intended to promote equity both in assuming the burdens and in receiving the benefits of human subjects research. Include an appropriate justification if women and/or minorities will be excluded from the clinical trial.

  c. Description of the Recruitment Process: Explain methods for identification of potential human subjects (e.g., medical record review, obtaining sampling lists, health care provider identification).

  - Describe the recruitment process in detail. Address who will identify potential human subjects, who will recruit them, and what methods will be used to recruit them.
  - Include a detailed description of and justification for the compensation plan if the human subjects will be compensated for participation in the study.

- Describe the recruitment and advertisement materials. The recruitment materials should not be coercive or offer undue inducements and should accurately reflect the study.

d. Description of the Informed Consent Process: Specifically describe the plan for obtaining informed consent from human subjects.

- ***For the proposed study, provide a draft, in English, of the Informed Consent Form.***
- Identify who is responsible for explaining the study, answering questions, and obtaining informed consent. Include a plan for ensuring that human subjects' questions will be addressed during the consent process and throughout the trial.
- Include information regarding the timing and location of the consent process.
- Address issues relevant to the mental capacity of the potential human subject (e.g., altered capacity due to administration of any mind-altering substances such as tranquilizers, conscious sedation or anesthesia, brain injury, stress/life situations, or human subject age), if applicable.
- Address how privacy and time for decision making will be provided and whether or not the potential human subject will be allowed to discuss the study with anyone before making a decision.
- Consider the need for obtaining ongoing consent or for re-assessing capacity over the course of a long-term study and describe any relevant procedures to assure continued consent.
- Describe the plan for the consent of the individual's Legally Authorized Representative (LAR) to be obtained prior to the human subject's participation in the study. State law defines who may act as the LAR. The local IRB of record should be consulted for guidance regarding who can serve as LAR for research at the study site. Note: The PI must describe a clear intent to benefit for human subjects who cannot give their own consent to participate in the proposed clinical trial to be in compliance with Title 10 United States Code Section 980 (10 USC 980) (http://www.gpo.gov/fdsys/pkg/USCODE-2011-title10/pdf/USCODE-2011-title10-subtitleA-partII-chap49-sec980.pdf). If applicable, please refer to the General Application Instructions, Appendix 5, for more information.
- ***Assent.*** If minors or other populations that cannot provide informed consent are included in the proposed clinical trial, a plan to obtain assent (agreement) from those with capacity to provide it, or a justification for a waiver of assent, should be provided. PIs should consult with their local IRB to identify the conditions necessary for obtaining assent.

e. Screening Procedures: List and describe any evaluations (e.g., laboratory procedures, history, or physical examination) that are required to determine eligibility/suitability for study participation and the diagnostic criteria for entry.

Please note that some screening procedures may require a separate consent or a two-stage consent process. Informed consent must be obtained prior to initiation of any procedures for the purpose of determining eligibility.

f. Risks/Benefits Assessment:

- **Foreseeable risks:** Clearly identify all study risks, including potential safety concerns and adverse events. Study risks include any risks that the human subject is subjected to as a result of participation in the clinical trial. Consider psychological, legal, social, and economic risks as well as physical risks. If the risks are unknown, this should be stated. If applicable, any potential risk to the study personnel should be identified.
- **Risk management and emergency response:**
  - Describe how safety surveillance and reporting to the IRB and FDA (if applicable) will be managed and conducted.
  - Describe all safety measures to minimize and/or eliminate risks to human subjects and study personnel or to manage unpreventable risks. Include safeguards and planned responses such as dose reduction or stopping criteria based on toxicity grading scales or other predetermined alert values.
  - Discuss the overall plan for provision of emergency care or treatment for an adverse event for study-related injuries, to include who will be responsible for the cost of such care.
  - Address any special precautions to be taken by the human subjects before, during, and after the study (e.g., medication washout periods, dietary restrictions, hydration, fasting, pregnancy prevention).
  - Describe any special care (e.g., wound dressing assistance, transportation due to side effects of study intervention impairing ability to drive) or equipment (e.g., thermometers, telemedicine equipment) needed for human subjects enrolled in the study.
- **Potential benefits:** Describe known and potential benefits of the study to the human subject, a specific community, or society.

- **Attachment 7: Intervention (no page limit):** Upload as "Intervention.pdf." The Intervention attachment should include the components listed below.

a. Description of the Intervention: As applicable, the description of the intervention should include the following components: complete name and composition, storage and handling information, source, dose, schedule, administration route, washout period, duration of the intervention, and concomitant medications allowed. Description of devices should include detailed operational instructions, any potential risks to users, and intended benefits. Other types of interventions should be fully described. Indicate who holds the intellectual property rights to the intervention, if applicable, and how the PI has obtained access to those rights for conduct of the clinical trial.

Summarize key preclinical pharmacological findings, dosage studies, and other clinical studies (if applicable) that examine the safety of the intervention.

b. Study Procedures: Describe the interaction with the human subject to include the study intervention that he/she will experience. Provide sufficient detail in chronological order for a person uninvolved in the study to understand what the human subject will experience. Provide a schedule (e.g., flowchart or diagram) of study evaluations and follow-up procedures. Discuss how compliance with Good Laboratory Practices (GLP), Good Manufacturing Practices (GMP), and other regulatory considerations will be established, monitored, and maintained, as applicable.

c. Clinical Monitoring Plan: Describe how the study will be conducted by and monitored for ICH E6 (International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use) GCP compliance, by an independent clinical trial monitor (or clinical research associate). The monitoring plan should describe the types of monitoring visits to be conducted, the intervals (based on level of risk), how corrective actions will be reported to the Sponsor and PI, and how they will be corrected and prevented by the clinical trial site/PI.

- **Attachment 8: Data Management (no page limit):** Upload as "Data_Manage.pdf." The Data Management attachment should include the components listed below.

a. Data Management: Describe all methods used for data collection to include the following:

- **Identifiers:** Describe the unique identifiers or specific code system to be used to identify human subjects, if applicable.
- **Confidentiality:**
  - Explain measures taken to protect the privacy of study human subjects and maintain confidentiality of study data. Strategies to protect the privacy and confidentiality of study records, particularly those containing identifying information, should be addressed.
  - Address who will have access to study records, data, and specimens, including an acknowledgment that representatives of USAMRMC are eligible to review study records.
  - Address requirements for reporting sensitive information to state or local authorities.
- **Data capture, verification, and disposition:** Describe how data will be captured and verified. Describe where data (both electronic and hard copy) will be stored, who will keep the data, how the data will be stored, the process for locking the database at study completion, and the length of time data will be stored. Describe the proposed database, how it will be developed and validated, and its capability to safeguard and maintain the

integrity of the data. For FDA-regulated studies, compliance with 21 CFR 11 is required.

- **Sharing study results:** In cases where the human subject could possibly benefit medically or otherwise from the information, explain whether or not the results of screening and/or study participation will be shared with human subjects or their primary care provider, to include results from any screening or diagnostic tests performed as part of the study.

b. Laboratory Evaluations:

- **Specimens to be collected, schedule, and amount:** All specimens that will be collected for study purposes must be clearly stated. The collection schedule and amount of material collected must also be clearly described.
- **Evaluations to be made:** Describe all evaluations that will be made for study purposes. Explain how the results of laboratory evaluations will be used to meet the objectives of the study (or to monitor safety of human subjects).
- **Storage:** Describe specimen storage, to include location of storage, how long specimens will be stored, any special conditions required, labeling, and disposition. Outline the plan to store specimens for future use to include considerations for informed consent and providing human subjects with an opportunity to decline participation in the study.
- **Labs performing evaluations and special precautions:** Identify the laboratory performing each evaluation, as well as any special precautions that should be taken in handling the samples. Special precautions that should be taken by the human subject before, during, or after the laboratory procedure should be clearly defined. If transport of samples is required, describe provisions for ensuring proper storage during transport.

- **Attachment 9: Study Personnel and Organization (no page limit):** Start each document on a new page. Combine into one document and upload as "Personnel.pdf." The Study Personnel and Organization attachment should include the components listed below.

a. Organizational Chart: Provide an organizational chart identifying key members of the study team including institution/center/department and name each person's position on the project. A medical monitor (external to the study and not reimbursed by the study) and study coordinator(s) should be included. If applicable, include any external consultants or other experts who will assist with FDA applications. While there is no specified format for this information, a table(s) or diagram is recommended. Note: This item may be made available for programmatic review.

b. Study Personnel Description: Briefly describe the roles of the individuals listed in the organizational chart on the project. Describe relevant experience and qualifications that demonstrate appropriate expertise for the given role.

c. Study Management Plan: Provide a plan for ensuring the standardization of procedures among staff and across sites (if applicable). If the proposed clinical trial is multi-institutional, plans for communication and data transfer between the collaborating institutions, as well as how data, specimens, and/or imaging products obtained during the study will be handled, should be included. Provide a plan for real-time communication among collaborating institutions (if applicable).

- **Attachment 10: Surveys, Questionnaires, and Other Data Collection Instruments, if applicable (no page limit):** Upload as "Surveys.pdf." The Surveys, Questionnaires, and Other Data Collection Instruments attachment should include a copy of the most recent version of surveys, questionnaires, data collection forms, rating scales, interview guides, or other instruments. For each instrument, describe how the information collected is related to the objectives of the study.
- **Attachment 11: Impact Statement (one-page limit).** Upload as "Impact.pdf."
    - Identify the volunteer population(s) that will participate in the proposed intervention, and describe the potential impact of the proposed clinical trial on the outcomes of individuals within the targeted population. Describe how the study will address a critical problem or question in the relevant FY14 PRMRP Topic Area(s).
    - ***Describe the short-term impact:*** Detail the anticipated outcomes that will be directly attributed to the results of the proposed clinical trial.
    - ***Describe the long-term impact:*** Explain the long-range vision for implementation of the intervention in the clinic or field, and describe the anticipated long-term benefits for the targeted population.
    - Describe any relevant controversies or treatment issues that will be addressed by the proposed clinical trial.
    - Describe any potential issues that might limit the impact of the proposed clinical trial.
    - Compare the proposed intervention to pharmacologic agents, devices, and/or clinical guidance currently available, if applicable.
- **Attachment 12: Transition Plan (one-page limit).** Upload as "Transition.pdf." Provide information on the methods and strategies proposed to move the product or knowledge outcomes to the next phase of clinical trials, commercialization, and/or delivery to the civilian or military market after successful completion of the award. The transition plan should include the components listed below.
    - The planned indication for the product label, if appropriate, and an outline of the development plan required to support that indication.
    - A description of relevant product patents and intellectual property ownership, and their potential impact on product development.

- Details of the funding strategy that will be used to bring the outcomes to the next level of development and/or commercialization (e.g., specific potential industry partners, specific funding opportunities to be applied for).
- For knowledge products, 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 outcome(s) to the next phase of clinical trials, commercialization, and/or delivery to the military or civilian market, including when it can be anticipated to be transitioned to an industry partner or approved by the FDA, if applicable.
- A risk analysis for cost, schedule, manufacturability, and sustainability.
- A description of relevant product patents and intellectual property ownership, and their potential impact on product development and the Government's ability to access any products or technology supported with this award.

- **Attachment 13: IND/IDE Documentation:** If submitting multiple documents, start each document on a new page. Combine and upload as a single file named "IND-IDE.pdf."
  - State whether the trial 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 is required, it must be submitted to the FDA ***prior to the application submission deadline.***
  - 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). 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 study, provide evidence in the form of communication from the FDA or the IRB of record to that effect.
- **Attachment 14: Military Relevance Statement (one-page limit):** Upload as "MilRel.pdf."

  Describe how the proposed study is responsive to the health care 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) will be used in the proposed research project, describe the population(s), the appropriateness of the population(s) for the proposed study, and the feasibility of accessing the

population. 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 interests.

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

   - PI Biographical Sketch (four-page limit): Upload as "Biosketch_LastName.pdf."
   - PI Previous/Current/Pending Support (no page limit): Upload as "Support_LastName.pdf."
   - Key Personnel Biographical Sketches (four-page limit each): Upload as "Biosketch_LastName.pdf."
   - Key Personnel Previous/Current/Pending Support (no page limit): Upload as "Support_LastName.pdf."

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

   - Budget Justification (no page limit): Upload as "BudgetJustification.pdf."

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

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

D. Verification of Grants.gov Application in eBRAP

For FY14, a new process has been initiated whereby organizational representatives and PIs can view their applications as submitted through Grants.gov and prior to peer review of the application. This will enable applicants to make modifications prior to scientific and programmatic evaluation of applications, provided the modifications are made by either the end of the application verification period or, for changes to the Project Narrative or Budget, by the application submission deadline.

After application submission to Grants.gov, eBRAP will retrieve and validate the application submission. eBRAP will notify the organizational representatives and PI via email and instruct them to log into eBRAP to review, modify, and verify the application. Files that fail eBRAP validation will be noted in both the email and in the Full Application Files tab. eBRAP does not validate the accuracy or completeness of content in the files. PIs are strongly encouraged to review all application components. If either the Project Narrative or the Budget fail eBRAP validation, an updated Grants.gov application package must be submitted via Grants.gov prior to the application submission deadline, which occurs earlier than the end of the application verification period. ***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.

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, Appendix 3, for information on Grants.gov 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 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 non-disclosure statement that application and evaluation information will not be disclosed outside the panel. Violations of confidentiality can result in the dissolving of a panel(s) and other corrective actions. In addition, personnel at the applicant or collaborating organizations are prohibited from contacting persons involved in the review process to gain protected evaluation information or to influence the evaluation process. Violations of these prohibitions will result in the administrative withdrawal of the organization's application. Violations by panel members or applicants that compromise the confidentiality of the review process may also result in suspension or debarment from federal awards. Furthermore, the unauthorized disclosure of confidential information of one party to another third party is a crime in accordance with 18 USC 1905.

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:

   - **Clinical Impact**
     - How relevant the anticipated outcomes of the proposed clinical trial are to individuals affected by the specified disease/condition.
     - How well the sample population represents the targeted patient population that might benefit from the proposed intervention.
     - The degree to which the potential outcomes of the proposed clinical trial will provide/improve short-term benefits for individuals.
     - How significantly the long-term benefits for implementation of the intervention may impact patient care and/or quality of life.
     - The degree to which the results of the proposed clinical trial will affect the patterns of clinical practice for the specified disease/condition.
   - **Intervention**
     - Whether there is evidence of support, indicating availability of the intervention from its source, for the duration of the proposed clinical trial (if applicable).
     - To what degree the intervention addresses the clinical need(s) described.
     - To what degree the PI has provided preclinical and/or clinical evidence to support the safety of the intervention.
     - How the intervention compares with currently available interventions and/or standards of care.
     - To what degree the data collection instruments (e.g., surveys, questionnaires), if applicable, are appropriate to the proposed study.
     - Whether a member of the study team holds the IND/IDE for the indication proposed, or whether the timeline proposed for obtaining the IND/IDE is appropriate (if applicable).
     - For investigator-sponsored INDs, whether there is evidence of appropriate institutional support, including capabilities to ensure monitoring as required by the FDA.
     - Whether plans to comply with GMP, GLP, and GCP guidelines are appropriate.
     - Whether measures are described to ensure the consistency of dosing of active ingredients for nutritional supplements (if applicable).
   - **Research Strategy**
     - How well the scientific rationale for testing the intervention is supported by the preliminary data, critical review and analysis of the literature, and/or laboratory/ preclinical evidence.

- How well the study aims, hypotheses or objectives, experimental design, methods, data collection procedures, and analyses are designed to answer clearly the clinical objective.
- How well the inclusion and randomization criteria meet the needs of the proposed clinical trial, as applicable.
- How well the exclusion criteria are justified.
- How well plans to collect specimens and conduct laboratory evaluations are addressed, if applicable.

- **Statistical Plan**
  - To what degree the statistical model and data analysis plan are suitable for the planned study.
  - How the statistical plan, including sample size projections and power analysis, is adequate for the study and all proposed correlative studies.
  - Whether the statistical plan compensates for the use of a subpopulation of a recruited sample population to ensure appropriate power can be achieved within the subpopulation study.
- **Recruitment, Accrual, and Feasibility**
  - How well the PI addresses the availability of human subjects for the clinical trial and the prospect of their participation.
  - Whether the PI has demonstrated access to the proposed human subjects population.
  - The degree to which the recruitment, informed consent, screening, and retention processes for human subjects will meet the needs of the proposed clinical trial.
  - How well the application identifies possible delays (e.g., slow accrual, attrition) and presents adequate contingency plans to resolve them.
  - To what extent the proposed clinical trial might affect the daily lives of the individual human subjects participating in the study (e.g., Will human subjects still be able to take their regular medications while participating in the clinical trial? Are human subjects required to stay overnight in a hospital?).
- **Ethical Considerations**
  - How the level of risk to human subjects is minimized and how the safety monitoring and reporting plan is appropriate for the level of risk.
  - How well the evidence shows that the procedures are consistent with sound research design and, when appropriate, that these procedures are already in use for diagnostic or treatment purposes.
  - To what degree privacy issues are appropriately considered.
  - To what degree the process for seeking informed consent is appropriate and whether safeguards are in place for vulnerable populations.

- **Transition Plan**
    - Whether the funding strategy described to bring the outcome(s) to the next level of development (e.g., higher phase clinical trial, transition to industry, delivery to the market, incorporation into standard practice) is appropriate.
    - How the development plan to support a product label change, if applicable, is appropriate and well described.
    - Whether appropriate collaborations and other resources for providing continuity of development are established and/or well described.
    - How the schedule and milestones for bringing the outcome(s) to the next level of development (e.g., higher phase clinical trial, transition to industry, delivery to the market, incorporation into standard practice) are appropriate.
    - How well the potential risk analysis for cost, schedule, manufacturability, and sustainability is developed.
    - How well the application identifies intellectual property ownership, describes any appropriate intellectual and material property plan among participating organizations (if applicable), and addresses any impact of intellectual property issues on product development and subsequent Government access to products supported by this Program Announcement/Funding Opportunity.
- **Personnel and Communication**
    - Whether the composition of the study team (e.g., study coordinator, statistician) is appropriate.
    - To what degree the study team's background and expertise are appropriate to accomplish the proposed work (e.g., statistical expertise, expertise in the disease, and clinical studies).
    - How the levels of effort of the study team members are appropriate for successful conduct of the proposed trial.
    - How well the logistical aspects of the proposed clinical trial (e.g., communication plan, data transfer and management, standardization of procedures) meet the needs of the proposed clinical trial.

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

- **Environment**
    - To what degree the scientific environment, clinical setting, and the accessibility of institutional resources support the clinical trial at each participating center or institution (including collaborative arrangements).
    - Whether there is evidence for appropriate institutional commitment from each participating institution.

- **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, 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 FY14 PRMRP, as evidenced by the following:

   - Adherence to the intent of the award mechanism
   - Military relevance
   - Program portfolio composition
   - Regulatory and development risk
   - Relative impact
   - Relevance to the 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.
- Human Subject Recruitment and Safety Procedures (Attachment 6) is missing.
- Intervention (Attachment 7) is missing.
- Data Management (Attachment 8) is missing.

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.
- Following application submission to Grants.gov, the PI will receive an email request from eBRAP to review, modify, and verify the application submitted to Grants.gov. During this verification period, the PI may upload missing documents (excluding those listed in Section IV.A., Rejection), replace files, and re-categorize files. These modifications must be completed by the end of the application verification period; otherwise, the application will be reviewed as submitted.

C. Withdrawal

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

- A FY14 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 FY14 PRMRP JPRP members can be found at http://cdmrp.army.mil/prmrp/panels/panel14.

- 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 is not a clinical trial.
- IND/IDE application has not been submitted to the FDA, if applicable.
- The PI does not meet the eligibility criteria.
- The proposed research is not relevant to any of the Congressionally directed FY14 PRMRP Topic Areas.

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, 2015. Refer to the General Application Instructions, Appendix 4, for additional award administration information.

B. Administrative Requirements

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

C. National Policy Requirements

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

D. Reporting

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

Quarterly technical progress reports and quad charts will be required.

E. Award Transfers

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 4, 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 application package. If the 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	Action	Completed
SF-424 (R&R) Application for Federal Assistance	Complete form as instructed.	
Attachments Form	Project Narrative: Upload as Attachment 1 with file name "ProjectNarrative.pdf."	
	Supporting Documentation: Upload as Attachment 2 with file name "Support.pdf."	
	Technical Abstract: Upload as Attachment 3 with file name "TechAbs.pdf."	
	Lay Abstract: Upload as Attachment 4 with file name "LayAbs.pdf."	
	Statement of Work: Upload as Attachment 5 with file name "SOW.pdf."	
	Human Subject Recruitment and Safety Procedures: Upload as Attachment 6 with file name "HumSubProc.pdf."	
	Intervention: Upload as Attachment 7 with file name "Intervention.pdf."	
	Data Management: Upload as Attachment 8 with file name "Data_Manage.pdf."	
	Study Personnel and Organization: Upload as Attachment 9 with file name "Personnel.pdf."	
	Surveys, Questionnaires, and Other Data Collection Instructions: Upload as Attachment 10 with file name "Surveys.pdf," if applicable.	
	Impact Statement: Upload as Attachment 11 with file name "Impact.pdf."	
	Transition Plan: Upload as Attachment 12 with file name "Transition.pdf."	
	IND/IDE Documentation: Upload as Attachment 13 with file name "IND-IDE.pdf."	
	Military Relevance Statement: Upload as Attachment 14 with file name "MilRel.pdf."	
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

IDENTIFIED GAPS AND RESEARCH PRIORITIES

Applications addressing any of the FY14 PRMRP Topic Areas are of interest to the program. Some of the Topic Areas have gaps and priority research areas that have been identified by the DoD and the VA and are listed below. Applicants are encouraged to read and consider these 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. Any aspect of research relevant to any FY14 PRMRP Topic Area may be considered for funding.

Acupuncture:

- Definitive studies to determine the effectiveness of acupuncture for pain associated with traumatic neuromusculoskeletal injuries.
- 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, substance abuse, agitation, anxiety, and other co-morbid disorders.

Chronic Migraine and Post-Traumatic Headache:

- Epidemiological/natural history studies of post-trauma headache to determine specific types of headache encountered, the pathobiology behind these headaches (such as the role of cortical spreading depression acutely after injury as a risk factor for chronic headaches of a migrainous type) as well as risk factors that might predispose people to certain types of post-traumatic headache.
- Double-blind placebo-controlled trials in the post-traumatic headache population in order to determine whether similar phenotypes in primary headache disorders and post-traumatic headache will respond similarly to treatment.
- Research on the optimal approaches to acute and chronic pain management for chronic migraine and post-traumatic headache, with a focus on assessing and eliminating adverse outcomes.
- Research on the utility of the Patient Centered Medical Home model in care of patients with chronic migraine or post-traumatic headache.
- Research to investigate, develop, and validate biomarkers useful in diagnosing and monitoring traumatic brain injury patients with chronic migraine or post-traumatic headache.

DNA Vaccine Technology for Post-Exposure Prophylaxis:

- The design and manufacture of a cost-efficient DNA vaccine that is simple to manufacture, stable without the need for refrigeration or freezing, can be used in both immune-competent and immune-compromised individuals, and expresses a highly conserved, chimeric protein antigen displaying multiple antigenic domains of key virulence factors of enteric pathogens.

- Development of innovative approaches to cure HIV (human immunodeficiency virus) using multiple therapeutic modalities in acute HIV infection. Additionally, there is a need to optimize antibody responses using novel adjuvants for HIV vaccine.
- Development of mechanisms or devices for mucosal delivery of a DNA vaccine for enteric pathogens. This includes research to understand and improve the mechanisms to stimulate immune responses with a cost-efficient DNA vaccine for enteric pathogens that is simple to manufacture and stable without the need for refrigeration or freezing.
- Research leading to a better understanding of the immune mechanisms involved in the clearance of enteric pathogens that would most likely be stimulated by a DNA vaccine. There is a need to evaluate humoral immune responses after DNA vaccination and to determine immunological correlates of protection, including both antibodies and cellular immune mechanisms in reproducible small animal models.

Epilepsy:

- Epidemiological and pathobiological studies that will inform early diagnosis, monitoring, and evidence-based treatment guidelines for seizure disorders.
- Pharmacologic and non-pharmacologic interventions demonstrating objective improvement in measureable outcomes of decreased seizure frequency.
- Development of technologies that can identify prodromal markers of epileptiform activity so that the patient can medicate and/or find a safe place to rest before the seizure occurs.

Illnesses Related to Radiation Exposure:

- Research addressing acute radiation syndrome (ARS).
- Research addressing the delayed effects of acute radiation exposure (DEARE).
- Research related to qualification of drug development tools (biomarkers, clinical outcome assessments, or animal models).
- Research on prototype countermeasures with the intent to develop data to support FDA approval.

Inflammatory Bowel Disease:

- Studies on the long-term health consequences of acute enteric infection as they relate to inflammatory bowel disease (IBD) in the areas of epidemiology, animal model development, understanding disease pathogenesis, and development of effective preventive and clinical management modalities.
- Studies designed specifically to examine disease markers (genetic, microbiomic, immunologic) of severity or risk of IBD after acute enteric infections.
- Mechanistic studies in relevant post-infectious inflammatory disease animal models to elucidate the interactions among genomics, microbiome, and immune mechanisms behind infection and chronic health consequences.
- Studies of well-defined post-infectious IBD patients are needed to provide estimates of illness-associated disability, health care costs, and symptom duration from a military health system and societal perspective.

Malaria:

- Development and optimization of multi-platform based (i.e., protein, DNA, viral vector, or live-attenuated) pre-erythrocytic based malaria vaccines to increase efficacy and enable identification of correlates of protection in preclinical studies and clinical trials.
- Identification of novel pre-erythrocytic stage *Plasmodium vivax* antigens and assessment of potential predictors of candidate vaccine efficacy in preclinical studies and clinical trials.
- Development of orally administered, bioavailable, novel chemical entities or alternative formulations of known anti-malarial drugs suitable for weekly prophylaxis, radical cure, treatment of severe/complicated disease indications, and to replace artemisinin class drugs in targeting immature blood stage parasites.
- Identification of modes of action of new generation anti-malarial drugs, optimization of drug partnering strategies for new malaria therapeutics and prophylaxis indications, and characterization of interactions between 8-aminoquinoline class anti-malarial drugs and cytochrome p450 2D6 enzyme to optimize development of next generation anti-malarial drugs.

Neuroprosthetics:

- 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 gait.
- Development of device afferent communication, science of proprioception and pressure sensing and 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.

Post-Traumatic Osteoarthritis:

- Development of best practices to maximize function and evaluation of multidisciplinary team (orthopaedics, pain, rehabilitation, etc.) approaches evaluating the success of treatment algorithms.
- Technologies that restore joint stability after injury (e.g., connective tissues such as ligament/tendon/meniscus structures).
- Sustained release, intra-articular injectable steroidal, non-steroidal, or disease-modifying therapies that offer two or more months of symptomatic relief of pain and/or inflammation in a single injection.
- Development of preventive therapies and/or techniques to minimize the progression of post-traumatic osteoarthritis after traumatic injury to the joint.

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, suicide, 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.

Respiratory Health:

- 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 develop new agents with which to treat them as it relates to respiratory disease.
- Technology- and/or therapeutic-based treatments for acute lung injury due to an inhalational injury
- Preventive techniques and therapeutics to reduce the incidence of acute respiratory syndrome after acute lung injury in trauma patients.
- Research on the prevalence, 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.

Segmental Bone Defects:

- 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.

Tinnitus:

- Research to understand the mechanisms of tinnitus, its relationship to noise-induced hearing loss, and progression to chronic tinnitus.
- Identification of effective non-invasive interventions to include neuromodulation and tinnitus retraining therapy for tinnitus treatment.
- Identification of novel therapies for early interventions to prevent tinnitus, including new uses for existing drugs, nutritional and pharmaceutical based strategies, and acoustic, electrical, and other stimulation technologies.
- Improvement of objective tools to diagnose and characterize tinnitus (e.g., imaging techniques to identify functional and structural changes in the brain).