Program Announcement

Collaborative

Department of Defense
Defense Health Program

Department of Veterans Affairs
Office of Research & Development

Psychological Health and Traumatic Brain Injury Research Program (PH/TBI RP)

Consortium to Alleviate PTSD (CAP) Award

Funding Opportunity Number: W81XWH-12-PHTBI-CAP

Catalog of Federal Domestic Assistance Number: 12.420

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-Application (Preproposal) Submission Deadline:** 5:00 p.m. Eastern time (ET), October 25, 2012
- **Invitation to Submit an Application:** November 14, 2012
- **Application Submission Deadline:** 11:59 p.m. ET January 4, 2013
- **Peer Review:** February 2013
- **Programmatic Review, Stage 1:** May 2013
- **Invitation for Oral Presentation:** May 2013
- **Programmatic Review, Stage 2:** May 2013

TABLE OF CONTENTS

I. Funding Opportunity Description

A. Program Description

Applications to the Fiscal Year 2012 (FY12) Psychological Health and Traumatic Brain Injury (PH/TBI) Research Program (RP) Consortium to Alleviate PTSD (CAP) Award funding mechanism are being solicited by the Assistant Secretary of Defense for Health Affairs, Defense Health Program (DHP), in collaboration with the Department of Veterans Affairs Office of Research and Development. The Department of Defense (DoD) has dedicated approximately $20.336 million (M) of the $135.5M FY12 Peer Reviewed Traumatic Brain Injury and Psychological Health Research appropriation to support the CAP Award mechanism. Up to an additional $5M per year for 5 years (up to $25M total) will be provided by the Department of Veterans Affairs (VA), depending upon availability of funds. The total anticipated amount for the 5-year effort is thus $45.336M.

Funds added by the VA will only be utilized to support research at VA sites; such funding will be managed by the VA Office of Research and Development. ***Leveraging existing resources, including infrastructure and/or research funding, is highly encouraged.*** The Government reserves the right to increase DoD and VA funding should additional funds become available. The maximum period of performance is 5 years. A DoD/VA co-chaired Government Steering Committee (GSC) will provide Consortium oversight of research activities.

B. Award Information

There are multiple trajectories that Active Duty, National Guard, and Reserve Service Members, and Veterans (Service Members) can experience following exposure to a traumatic event that may or may not include physical injury. Research shows that the majority of Service Members who are exposed to traumatic events during the course of duty do not go on to develop clinical symptoms that impair functioning; however, an estimated 10%-18% of Service Members and Veterans develop symptoms that impair functioning and are significant enough to result in a clinical diagnosis of post-traumatic stress disorder (PTSD) (Hoge et al., 2004[1]; Vasterling et al., 2006; Hoge et al., 2007). Of these individuals, some may experience symptoms that resolve on their own, some may respond well to treatment, and some may not respond well to treatment (medication and/or psychotherapies) (Friedman, Keane, and Resick, 2007). There are also individuals who may be suffering from PTSD, but still functioning in their occupation or social/family life, albeit at an impaired level. While some of these individuals do not seek treatment, a number of them eventually will, but often only after the onset of frequently associated chronic comorbid symptoms such as depression, anger/aggression, relationship problems, and substance use/abuse. If individuals at high risk of developing chronic symptoms can be identified early on, there is an opportunity to intervene and mitigate negative outcomes.

The primary purpose of the collaborative DoD/VA Consortium will be to improve the health and well-being of Service Members (Active Duty, National Guard, and Reservist) and Veterans, with the most effective diagnostics, prognostics, novel treatments, and rehabilitative strategies to treat acute PTSD and to prevent chronic PTSD. This Consortium is responsive to the findings of the

[1] All references are listed in Section VII.

recently released DoD/VA-sponsored Institute of Medicine report focused on "Treatment for Posttraumatic Stress Disorder in Military and Veteran Populations**"** (http://www.iom.edu/Reports/2012/Treatment-for-Posttraumatic-Stress-Disorder-in-Military-and-Veteran-Populations-Initial-Assessment.aspx). Key priorities of this Consortium are elucidation of factors that influence the different trajectories (onset/progression/duration) of PTSD and associated chronic mental and physical sequelae (including depression, anger/aggression, and substance use/abuse, etc.) and identification of measures for determining who is likely to go on to develop chronic PTSD. The Consortium will therefore work to improve prognostics, advance treatments, and mitigate negative long-term consequences associated with traumatic exposure. Focused scientific efforts to understand and treat PTSD have been supported by the DoD and VA extensively. However, to date, treatments have not been fully successful in all individuals. There remains a significant number who do not respond to the currently available treatment regimens, and the question of predicting treatment response remains a priority.

Consortium applications should dedicate effort to the identification, collection, storage, and use of clinically relevant biomarkers to advance diagnosis, prognosis, and treatment of PTSD. Such biomarkers are defined as those that differentially diagnose or indicate changes associated with the PTSD disease or symptom remediation process to include but not limited to cognitive, imaging, and serum/cerebrospinal fluid and highly relevant physiological markers for related symptoms.

Since research efforts have been and are being supported by the DoD and VA, applications must detail a consideration of ongoing systematic collection efforts (e.g., common data elements, etc.) and propose integration with and advances to those efforts. Thus, the Consortium will coordinate clinical research studies and/or highly relevant translational preclinical studies as well as the collection, storage, use, and analyses of data and anatomical specimens. Consortium efforts will provide critical information to benefit Service Members and Veterans by positively affecting diagnosis, treatment, and rehabilitation strategies.

The CAP Award resulting from this Program Announcement/Funding Opportunity will be issued as a cooperative agreement between the recipient (Coordinating Center) and the Government (US Army Medical Research Acquisition Activity [USAMRAA]). Separate VA subawards will be funded under VA authority as detailed below. An appointed GSC will review proposed research strategies and make recommendations to the Grants Officer's Representative (GOR) and the VA. The ultimate DoD approval authority is the USAMRAA Grants Officer (GO) and the ultimate VA approval authority is the Office of Research and Development. Although the ultimate approval authority for the DoD and VA is the GO and the Office of Research and Development, respectively, no studies will be funded without the recommendation of the GSC. All DoD and VA-supported projects will be executed within the Consortium infrastructure with oversight by the GSC.

C. Consortium Objectives

a. To significantly advance treatment strategies for PTSD including interventions for early, chronic, and latent onset cases. Studies addressing prevention strategies may also be proposed to include peri- and post-traumatic interventions designed to reverse

the trajectory of initial-response stress mechanisms, obviate symptom development, and facilitate natural stress recovery processes.

b. To identify and confirm clinically relevant biomarkers as diagnostic and prognostic indicators of PTSD and co-occurring disorders. Proposed studies could address ways to effectively use specimens to develop effective diagnostics or indicators of treatment response. Studies could include focus on biomarkers as a method for guiding treatment, determining effectiveness of treatment, assessing recovery from chronic PTSD, and informing treatment response (i.e., to inform return to duty).

D. Focus Areas

Research activities must be focused on PTSD and common co-occurring psychiatric or medical conditions such as:

- Behavioral health disorders (suicide, substance abuse, risky behaviors, etc.),
- Mood and anxiety disorders,
- Sexual dysfunction,
- Neurologic disorders (including memory, autonomic system, and sleep),
- Pain (including headache),
- Cognitive deficits, and
- Neuroendocrine deficits.

Studies must focus primarily on the clinical application of biomarker-based research (diagnostic, prognostic, and treatment-focused).

E. General Consortium Requirements

The Consortium framework (Figure 1) will consist of a Coordinating Center collaborating with multiple research sites, which must include VA and military treatment facility (MTF) sites. Successful applications will demonstrate evidence of ongoing, strongly relevant collaborations between the Coordinating Center and research sites. Strong academic, industry (e.g., private clinics, rehabilitation centers), other military, and nonprofit organization collaborations are also encouraged, especially as collaborative partners with VA or DoD sites. All applications must have direct relevance to the overall objectives of the Consortium, with key expert personnel also collaborating across the multiple disciplines of interest.

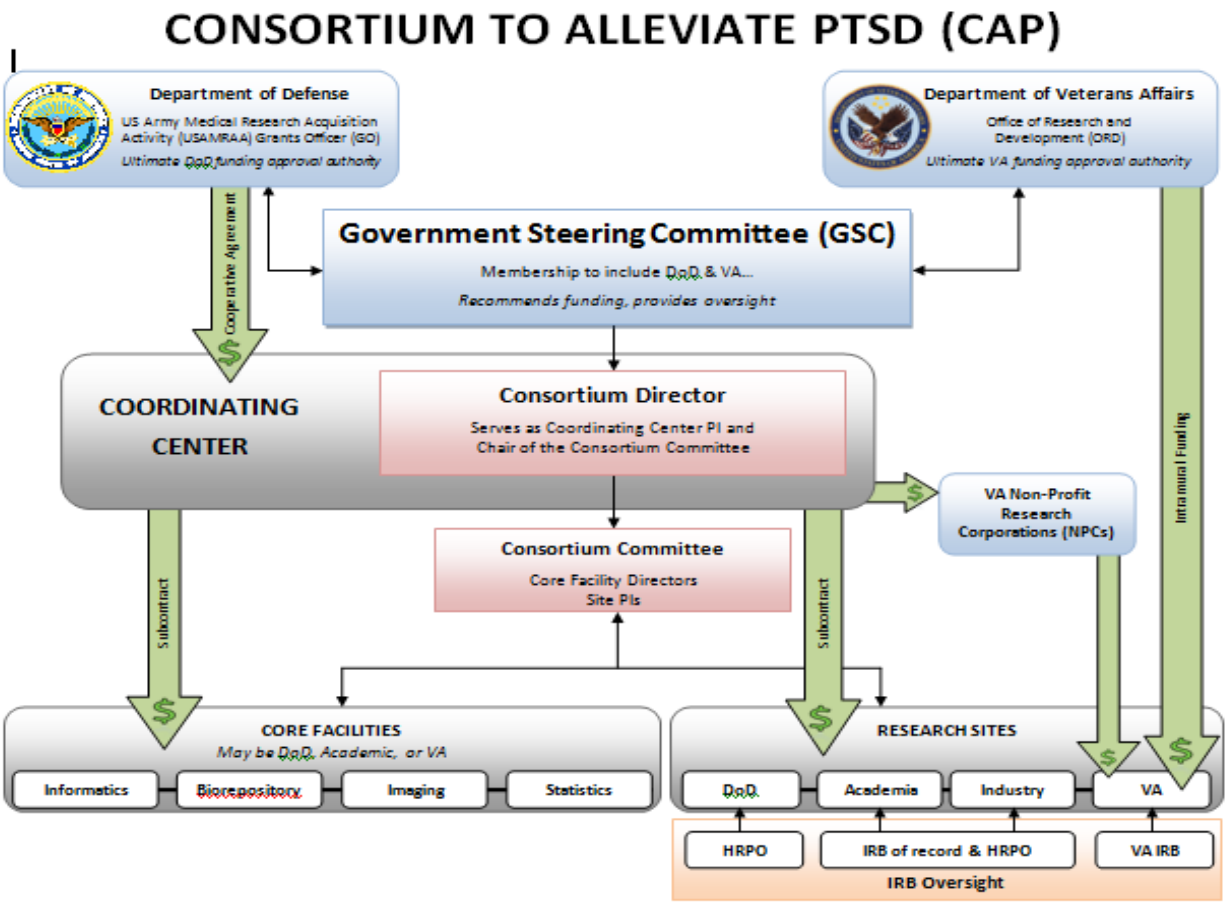

Figure 1

The initial application should include the overarching research strategy to adequately address all of the objectives of the Consortium. The application should also describe the Coordinating Center and infrastructure, core laboratory facilities, and any proposed Study Sites. Award funds will be used to support the Coordinating Center's efforts as well as the Consortium-associated studies at the Study Sites. The Coordinating Center will provide management and funding through the appropriate instruments for the non-MTF sites funded through the DoD. Additionally, the VA Office of Research and Development may also directly fund research studies conducted at VA sites approved in coordination with the GSC. VA support will be detailed as subawards in the initial application (see Section I.J., Funding).

CAP Award applications should name and describe individual core facilities that will serve as official Consortium research core facilities that may include informatics, biorepository, imaging, and statistical support. Establishment of Consortium-wide core facilities will enable more consistent, high-quality, standardized data to be collected across sites for Consortium-supported studies, as well as biologic specimens for planned and future analyses. Proposed studies could address ways to effectively use specimens to develop effective diagnostics or indicators of treatment response.

In addition to the proposed structure and core laboratory organization, CAP Award applications must include an initial set of proposed studies (minimum of four) reflective of the two overall goals of the Consortium (as noted above in the Consortium Objectives, Section I.C.) for consideration during the review and selection process. Some or all of the initial studies proposed may be carried out if recommended for funding by the GSC and approved for funding by the USAMRAA GO or the VA. Proposed initial studies should include a range of scope, size, and type designed to meet the overall goals of the Consortium. Studies submitted for VA research support should be clearly identified, and the VA Principal Investigator (PI) must be eligible to submit for VA funding.

Funding selection will depend upon evaluation of the proposed strategic research plan design and methodology, Coordinating Center structure, core laboratories, scientific studies, record of productivity, evidence of VA and/or DoD collaboration, available capabilities, and feasibility of the entire group to accomplish the overall award objectives.

During the performance period of the award, the Coordinating Center and all Study Sites, including the DoD and VA sites, will be responsible for working collaboratively to identify new studies for implementation by the Consortium. Additional applications from new Study Sites may be considered by the GSC. All proposed studies utilizing funds from this award will be subject to GSC review and GO approval prior to selection and implementation. Projects from new sites after the initial award has been made may be solicited and funded as appropriate. Such projects will be incorporated into the CAP management structure.

It is anticipated that the Consortium budget will support the Coordinating Center, core laboratory facilities, and selected research studies. The Coordinating Center will be required to submit quarterly written reports that outline overall progress toward performance measures.

Typically, it is expected that proposed studies would include VA and DoD sites that may incorporate collaboration with academic, industry, other military, and nonprofit organizations. Priority will be given to sites that represent ongoing strong collaborations between DoD or VA sites and academic, industry, other military, and nonprofit organizations, with established ties to the proposed Coordinating Center. Of note, in some cases, civilian sites/populations may be justified. Recruitment of civilian populations must be justified with respect to the overall relevance to supporting research on Service Members and Veterans.

The Coordinating Center will also facilitate the rapid selection, design, and execution of studies within the Consortium and will provide the administrative protocol development, regulatory, statistical resources, and data management/storage functions necessary to facilitate Consortium studies. The Coordinating Center shall be focused on the overall coordination of data collection, organization, and use, as well as specimen collection, storage, and use. The Coordinating Center will coordinate clinical research studies and highly relevant translational preclinical studies as well as the collection, storage, use, and analyses of data and anatomical specimens. Consortium efforts will therefore provide critical information to benefit Service Members and Veterans by positively affecting diagnosis, treatment, and rehabilitation strategies. The PI of the Coordinating Center shall provide evidence of prior experience with the design and administration of multi-institutional research studies.

CAP Award applications should include a description of plans to coordinate with the Study Sites to propose, design, independently scientifically review, and prioritize the most relevant initial studies for review and selection by the GSC. Additional studies will be presented to the GSC at twice-yearly meetings for review and approval of recommendations prior to implementation. While the Consortium and initially proposed sites may be approved to conduct specific studies, additional Study Site applications may be considered and approved should funding be available, thus allowing additional participation from investigators after the initial award. Additionally, VA applicants may also apply for new studies in the Consortium out-years via standing VA mechanisms, provided GSC approval is obtained in advance. See Section I.K.a. for further information regarding the GSC.

Summary of Responsibilities:

a. All Consortium Participants: Procedures for the Consortium, while proposed by the Coordinating Center, will be fully developed and agreed upon by all participants working collaboratively via a process to be detailed in the CAP Award application. The process shall be codified in a Standard Operating Procedure (SOP), for review by the GSC within 90 calendar days of the award date. A preliminary draft of the Consortium execution SOP is required at the time of application submission.

b. Consortium Coordinating Center Director: The Coordinating Center PI will serve as the Director of the Consortium, Chair of the Consortium Committee, and the primary liaison with the GOR; and

- Participate in a DoD/VA hosted pre-award planning meeting;
- Ensure that a minimum number of studies, as agreed upon by the GSC, Consortium Committee, and the DoD and VA during the pre-award planning meeting, are initiated by 6 months after award. Justification must be provided to the GSC in the event of a delay in initiating any of the agreed upon studies;
- Ensure that the Consortium adheres to the planned timeline and milestones for overall study execution;
- Develop and maintain the Consortium organizational structure;
- Manage Consortium-developed procedures for external scientific review, prioritization, and implementation of studies proposed by or through Consortium members;
- Facilitate a mechanism to provide MTF and VA sites with resources necessary for participation in the Consortium;
- Establish and manage procedures to ensure that all sites that receive DoD funding maintain compliance with local Institutional Review Boards (IRBs) and the Army Surgeon General's Human Research Protection Office (HRPO) for the proper conduct of clinical studies and the protection of human subjects (as appropriate) along with any other applicable DoD policies. All VA-funded studies at VAs involving human subjects and human biological/anatomical substances must be reviewed by a VA IRB and must adhere to all applicable VA policies;

- Establish and manage procedures for ensuring compliance with US Food and Drug Administration (FDA) requirements for investigational agents, devices, and procedures;
- During the performance period of the award, identify potential studies and develop projects in accordance with the Consortium SOP for presentation to the GSC;
- Establish and manage a communications plan and a real-time communications system among the Coordinating Center, core laboratory facilities, and Study Sites, including the purchase of multi-site licenses, if necessary;
- Ensure the standardized collection, storage and use of specimens, imaging products, and other data by core laboratory facilities;
- Manage Consortium-developed quality assurance and quality control mechanisms for study monitoring appropriate to the proposed work (as applicable):
    - Registration, tracking, and reporting of participant accrual,
    - Timely medical review, rapid reporting, communication of adverse events, and data management/coordination among all sites, and
    - Interim evaluation and consideration of measures of outcome;
- Manage Consortium-developed comprehensive data collection and data management systems that address the needs of all Study Sites in terms of access to data, data security, and data integrity measures;
- Implement statistical execution plans/support for all Consortium studies;
- Manage costs to support the Study Sites, including provision of personnel, equipment, and materials required to conduct approved studies (as applicable);
- Manage Consortium-developed intellectual and material property issues among organizations participating in the Consortium with respective VA and DoD Technology Transfer departments;
- Manage Consortium-developed procedures for the timely publication of major findings and other public dissemination of data;
- Coordinate the preparation of written and oral quarterly briefings to the GSC and US Army Medical Research and Materiel Command (USAMRMC) and VA staff at 1-2 day meetings to be held in a centralized location to be determined by the USAMRMC and VA; activity to be included in Coordinating Center Budget; and
- Develop, organize, and submit quarterly written progress reports, annual reports, and a final written comprehensive report to the USAMRMC and VA.

c. Study Site PIs

- Participate fully in the Consortium Committee;
- Participate in a DoD/VA hosted pre-award planning meeting;
- During the period of performance of the award, identify potential studies to develop projects in accordance with the Consortium SOP for presentation to the GSC;

- Integrate with studies at other Study Sites as appropriate;
- A Consortium Data Management Committee will monitor each Study Site for minimal recruitment rate on an ongoing basis;
- As applicable, provide a Clinical Research Coordinator who will interact with the Clinical Research Coordinators of other Clinical Study Sites and the Consortium Clinical Research Manager at the Coordinating Center to expedite and guide clinical protocols through regulatory approval processes and to coordinate patient accrual and study activities across sites;
- Implement the Consortium's core data collection methodology and strategies;
- Comply with Consortium-developed quality assurance and quality control procedures, as appropriate, including:
    - Participate in an onsite monitoring program to be managed by the Coordinating Center;
    - Implement the Consortium-developed management plan for acquisition and aggregation of protocol-specified specimens, images, and data to the appropriate laboratories for testing or storage necessary for the conduct and analyses of clinical studies during the performance of the award;
    - Submit appropriate data and materials to allow for verification and review of protocol-related procedures (e.g., pathology, imaging techniques, surgical methods, therapeutic use, etc.)
- Implement procedures established by the Coordinating Center for ensuring compliance with FDA requirements for investigational agents, as applicable;
- Implement procedures established by the Coordinating Center to meet the local IRB and the Army Surgeon General's HRPO requirements for the conduct of clinical studies and the protection of human subjects as applicable. All VA-funded and non-VA funded studies at VAs involving human subjects and human biological/anatomical substances must be reviewed by a local VA IRB, or if it is multi-site, the VA Central IRB;
- Serve as a resource or core for the conduct of protocol-specified laboratory projects (including correlative studies), as applicable;
- Participate in Consortium-developed procedures for the timely publication of major findings as applicable;
- Participate in Consortium-developed procedures for resolving intellectual and material property issues among organizations participating in the Consortium;
- Participate in the preparation of written and oral twice-yearly briefings to the GSC and USAMRMC and VA staff at 1-2 day meetings to be determined by USAMRMC and the VA;
- Assist with the preparation of quarterly written progress reports and a final written comprehensive report;

- Participate in site visit audits. Frequency and details of process for execution of site visit audits will be defined at the pre-award meeting.

F. Data Sharing

In order for a VA investigator to disclose individual identifiers, including protected health information (PHI), to a non-VA entity, the investigator must obtain a VA IRB approved research informed consent and a valid VA IRB approved Health Information Portability and Accountability Act (HIPAA) authorization signed by the research subject or the research subject's personal representative. In addition, all Privacy Act requirements must be met. The research informed consent and the HIPAA authorization must contain sufficient information so that the research subject will understand that his/her information will be sent out of the VA to the non-VA entity. The HIPAA authorization would need to meet all requirements as found in Title 45 of the Code of Federal Regulations Part 164.508(c). Data shared with a non-VA entity will remain under VA authority unless specific prior agreements have been approved by the Chief Research and Development Officer of the Veterans Health Administration Office of Research and Development.

The DoD/VA intends that data and research resources generated via this award mechanism be made available to the research community (which includes both scientific and consumer advocacy communities) and to the public at large. Specific reporting requirements will be detailed during the June 2013 pre-award meeting.

G. Eligibility Information

This funding opportunity allows DoD, VA, and other investigators to apply. Refer to the General Application Instructions, Appendix 1, for general eligibility information for DoD funding. Individuals selected for VA intramural funding must identify their VA eligibility (VA appointment) at the pre-application step. To be eligible for VA funding (salary, equipment, site support, core laboratory support, project support), an individual must have a VA-paid appointment of at least five-eighths at the time of pre-application submission, unless a previous eligibility waiver has been granted. Questions regarding VA eligibility should be directed to rd-era@va.gov.

H. Award Type

This award will be a cooperative agreement between the recipient and the Government (namely, the USAMRAA). Additionally, VA funding will support both subawards submitted under the Cooperative Agreement and/or studies supported by the Consortium in out-years submitted directly to the VA for review. Studies selected for VA funding will be supported as Service Directed Research programs under VA Biomedical, Clinical, Rehabilitation or Health Services Research and Development Service.

I. Performance Metrics

Applicants should lay out a plan for the number and types of studies the Consortium expects to execute over the course of the award. While no set number of studies has been determined, it is

expected that each of the objectives will be covered/addressed in the application. ***Within 6 months of award***, a minimum number of studies, as agreed upon by the Consortium Committee, the GSC, the VA, and USAMRMC, shall be approved for initiation. A timeline outlining the overall plan for study approval, initiation, performance, and analyses shall be developed, with clear milestones to which the Consortium will be held accountable. A similar timeline and performance measures should describe the start-up and implementation of core laboratory facilities. The Consortium SOP should contain an overall strategy for managing oversight of performance metrics and a plan to address underperforming sites. It is expected that the Consortium will submit to other agencies for additional funding in order to increase the breadth of research and create a self-sustaining entity that may continue functioning beyond the 5-year performance period of the award.

J. Funding

- The maximum period of performance is 5 years.
- The maximum allowable total costs for the entire period of performance are $20.336M via the DoD.
- All DoD direct and indirect costs of any subaward (subgrant or subcontract) must be included in the total direct costs of the primary award. Up to an additional $5M per year for 5 years will be provided by the VA to VA sites, depending upon availability of funds. Requests for VA funds will be detailed either in separate applications to VA as Service Directed Research programs.
- The applicant may request the entire maximum funding amount for a project that may have a period of performance less than the maximum 5 years.
- The Coordinating Center is expected to provide a mechanism to transfer resources such as supplies and support necessary to the MTFs, DoD laboratories, or DoD activities embedded within a civilian medical center to support their participation in Consortium studies. Direct transfer of funds to a Government organization or agency is not allowed except under very limited circumstances and as subject to the prior GO approval. ***DoD funds provided through this award may not be used to support Government salaries.*** Details on exceptions to the prohibition of direct fund transfer to Government entities can be found in the General Application Instructions, Section II.C., Content and Form of Application Submission, Budget Instructions, Section K (Federal Agency Financial Plan).

  Refer to the General Application Instructions, Section II.C., Content and Form of Application Submission, for budget regulations and instructions for the Research & Related Budget. In addition, for this award mechanism, direct costs include:

  - **Consortium Core Facilities' Budgets**
    - Personnel
    - All other costs

  Note: Up to $100,000 may be requested for equipment for VA studies or within core facilities that will be used and housed at VA sites only. Equipment under non-VA portion is not allowed.

- **Study-Specific Budgets**
  - Salary; VA salary should be requested on VA subaward (under a research study or core laboratory facility). Government salary is not allowed on non-VA funded work.
  - Research study costs including related subject costs
  - Clinical research costs (as applicable)
  - Support for multidisciplinary collaborations
  - Research supplies to be justified
- **Travel, as described below**
  - Travel funds for the Coordinating Center PI to attend 1-2 day briefings with the GSC, USAMRAA, and VA staff as determined by the GSC.
  - Travel for attendance of one DoD-VA sponsored meeting
  - Travel between collaborating organizations
  - Note: Travel costs should be within allowable DoD and/or VA limits (as appropriate)

K. Consortium Oversight

a. ***GSC***: (SOP required, to be developed after award is made):

The GSC is co-chaired by DoD and VA representatives and is comprised of appropriate Government representatives and non-DoD and VA subject matter experts (as appropriate).

The GSC:

- Approves all studies to be conducted;
- Recommends new studies (but it is the primary role of the Consortium to work out the details and the Consortium can propose and recommend studies to the GSC); and
- Identifies existing and new requirements as they arise.

b. ***Independent Scientific Merit Review (SMR):*** An independent scientific review process will be established (approved by the GSC) to advise on the scientific merit of studies proposed post-award. The SMR is responsible for vetting all studies produced by the research program, ensuring unbiased rigorous scientific review in a timely manner. Specifically, an independent review panel of sufficient expertise will be established. A rating/scoring system by which study reviews are evaluated will guide the reviews. Each study will be evaluated, at a minimum, in terms of scientific significance, the proposed approach (i.e., methodology), investigators/environment, completeness and accuracy of the study, and the appropriateness of the budget. The SMR provides final, written reviews, inclusive of constructive feedback for

recommended changes (and resubmissions/re-reviews, if requested), of individual submitted studies within 32 days of assignment to reviewers. A system for carrying out expedited reviews with a 21-day turn-around must be detailed in the Consortium SOP (for GSC approval). Studies may also be submitted in the out-years by eligible VA investigators directly to VA as Service Directed Programs, who will manage peer review directly, and recommend approval based upon evaluation of scientific merit. Any studies submitted to the VA for funding in this manner must have a letter of support from the Consortium included in the application.

L. Use of Human Subjects and Human Biological/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), 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 are rigorous and detailed, and will require information in addition to that supplied to the local IRB. Allow a minimum of 4 months for regulatory review and approval processes. The link to the DoD HRPO site is: https://mrmc.detrick.army.mil/index.cfm?pageid=research_protections. hrpo. Refer to the General Application Instructions, Appendix 5, for more information. 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 proposed clinical studies. All VA-funded and non-VA funded studies at VAs involving human subjects and human biological/anatomical substance must be reviewed by a VA IRB. The link to VA requirements for the Protection of Human Subjects in Research is: http://www1.va.gov/vhapublications/ViewPublication.asp?pub_ID=2531. The link to the VA Central IRB is http://www.research.va.gov/vacentralirb/.

M. Pre-Submission Question and Answer Process

An electronic Question and Answer (Q&A) forum will be provided prior to the application submission deadline. Details on the electronic process will be included with all invitations to submit a full application (following the pre-application screening process outlined in Section II.B). Questions will be accepted until December 30, 2012. Questions and answers will be posted on the Congressionally Directed Medical Research Programs (CDMRP) eReceipt website (https://cdmrp.org). In addition, questions about the CAP Award may be sent to cdmrp.reporting@amedd.army.mil.

II. SUBMISSION INFORMATION

Submission is a multi-step process requiring both (1) pre-application submission through the CDMRP eReceipt System (https://cdmrp.org/) and (2) application submission through Grants.gov. PIs and organizations identified in the application should be the same as those identified in the pre-application. If a change in PI or organization is necessary after submission of the pre-application, the PI must contact the CDMRP Help Desk at help@cdmrp.org or 301-682-5507.

A. Step 1 – Pre-Application Components

All pre-application components must be submitted through the CDMRP eReceipt system by ***5:00 p.m. ET on the deadline***. 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.

The pre-application consists of the following components, which are organized in the CDMRP eReceipt system 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**
- **Collaborators and Conflicts of Interest (COI) – Tab 3**
- **Required Files – Tab 4**
- **Preproposal Narrative (10-page limit):** The Preproposal Narrative is inclusive of any figures, tables, graphs, photographs, diagrams, chemical structures, pictures, pictorials, and cartoons.
- **The Preproposal Narrative should include the following:**
    - **Overarching Goals:** Describe the overarching research strategy to address all of the objectives of the Consortium. Provide a brief description of the initial four studies to be proposed and participating sites. Describe the reasoning on which the studies are based, the specific aims to be accomplished, the outcomes to be measured, and the contribution towards achieving overall goals of the Consortium. Provide a brief description of how the proposed Consortium will be organized to meet the overall goals. Identify the critical research questions required to address each of the Consortium Objectives and describe the research question(s) appropriate for generating outcomes responsive to each of these objectives.
    - **Consortium Structure:** Outline the Consortium infrastructure organization, including any organizations that will participate in the Consortium. Briefly discuss the qualifications of key in the coordinating center, core facilities, and research studies. Describe elements of the Consortium that will promote synergy and achieve the overarching goals. Describe the proposed decision making structure.
    - **Research Plan:** Describe the overarching research strategy to address all of the objectives of the Consortium. Provide a brief description of the initial four studies

to be proposed and participating sites. Describe the reasoning on which the studies are based, the specific aims to be accomplished, the outcomes to be measured, and the contribution toward achieving overall goals of the Consortium.

- **Pre-Application Supporting Documentation:** The items to be included as supporting documentation for the pre-application (not included in the 10-page limit noted above) are limited to:
  - **References** (three-page limit): List relevant references using a standard reference format that includes the full citation (i.e., author(s), year published, and title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate). The inclusion of Internet URLs to references is encouraged.
  - **PI and Key Personnel Biographical Sketches** (two-page limit per individual): VA investigators should highlight their VA affiliation/appointment; highlight what each key personnel will bring to the Consortium effort.
- **Submit Pre-Application – Tab 5**
- **Other Documents Tab –** This tab is not applicable.

B. Pre-Application Screening: Pre-applications will be screened based on the following criteria:

- **Overarching Goals:** How well the goals are aligned with the objectives of the CAP Award.
- **Consortium Structure:** How well the outlined Consortium organization, personnel, and structure will support the study coordination and core facilities required to achieve the stated goals. The appropriateness of the administrative and research teams' background and expertise with respect to their ability to oversee studies and evidence of their ability to work collaboratively. Whether there is evidence for collaboration across and between Government agency entities, academia and industry partners. Whether potential leveraging is evident.
- **Research Plan:** The clarity of the overarching research strategy to adequately address all of the objectives of the Consortium. Clear strategy for identifying and executing the studies (in addition to the four initial studies being proposed) that will need to be done to address the objectives. How well the proposed initial studies will meet the overall objectives of the Consortium according to a defined timeline. The degree to which the proposed studies address important questions collaboratively.

Following the pre-application screening, PIs will be notified of whether or not they are invited to submit an application; however, they will not receive feedback (e.g., strengths and weaknesses) on their pre-application.

C. Step 2 – Application Components

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

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

The Grants.gov application package consists of 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 Forms

- **Attachment 1: Project Narrative (30-page limit):** Upload as "ProjectNarrative.pdf."

  Describe the qualifications of the group and the key features of the Consortium using the following general outline:

  - **Overall Research Plan:** The narrative should include a description of the scientific rationale behind the approach the Consortium proposes. The section should also describe in detail how the overall research plan will integrate the key Consortium and research projects to meet the overarching objectives of the Consortium. A timeline that aligns milestones and deliverables with objectives for the Consortium should be provided. A projection of the types of studies (including size and scope) to be conducted by the Consortium over the entire award period should be presented. This section must detail the overall plan and rationale for inclusion of four initial studies selected and a plan and rationale for additional studies. A separate section ("Research Plan") will be for applicants to propose four initial studies.
  - **Consortium Expertise and Resources**
    - Outline the structure of the proposed Consortium. Identify key personnel, unique expertise, and ability to collaborate with diverse facilities, and administrative organization/oversight, including decision-making procedure.
    - Describe the experience of the PI and other key personnel within the Coordinating Center with the design, implementation, and administration of relevant research studies and collaborative experience in multi-site efforts. Specify scientific and technical expertise. In Attachment 2, reference relevant publications and submit reprints with the application supporting documentation.

- Describe the resources and facilities that will be available for this effort, including description of leveraged activities, distinguishing between what is already established versus what would be new requests to be supported.
- Describe the resources and expertise for data collection, management, quality control, and maintenance of data security/confidentiality.
- Provide evidence of organizational commitment for the Coordinating Center, core laboratory facilities, and each participating Study Site for the use of facilities and resources in the conduct of Consortium.

- **Consortium Plan of Operations**
  - **Site Coordination and Communication Plan:** Describe plans to communicate and partner with the proposed MTFs, VA, and other sites. Explain the contribution of each Study Site and how these site PIs will provide input on all Consortium procedures and studies to a level commensurate with all other Study Sites. Outline a plan for providing resources to the MTF and VA sites and establishing the research capabilities needed at the MTF and VA sites for full Consortium participation.
  - **New Study Proposal Procedures:** Outline a plan for the solicitation, design, evaluation, and prioritization of potential future Consortium studies for presentation to the GSC (including independent scientific review process and progress reviews) following initial study implementation. Include a mechanism for determining Study Site participation and approval for new study ideas within the approved Consortium award, VA funding in out-years, and other funding sources.
  - **Study Management and Monitoring:** Describe plans for real-time communication among all organizations participating in the Consortium (including the rapid dissemination of adverse events). Include a named Consortium Research Manager (if applicable) who will interact with other individual site clinical coordinators to guide clinical protocols through the regulatory approval processes, coordinate participant accrual, and coordinate study activities across sites. Outline procedures for quality assurance, quality control, safety, and study monitoring.
  - **Core Facilities:** Describe functions and responsibilities of each core facility and how the core facilities will be utilized and integrated across all Study Sites.
  - **Protocol Development and Human Subjects Protection (as applicable):** Describe plans for coordinating the development of clinical protocols and associated clinical documents that include HRPO-prescribed content. Outline a plan for the external peer review of all Consortium clinical protocols and the coordination of IRB submissions and approvals. Describe the development of a plan for addressing human subjects protection requirements as outlined by HRPO at https://mrmc.detrick.army.mil/index.cfm?pageid=research_protections. hrpo. The link to VA requirements for the Protection of Human Subjects in Research is http://www1.va.gov/vhapublications/ViewPublication.asp?pub_ID=2531. The

link to the VA Central IRB is http://www.research.va.gov/vacentralirb/. Outline plans for developing procedures to ensure compliance with FDA requirements for investigational agents, as appropriate.

- **Data Management:** Outline a strategy for the development and implementation of a Consortium-wide data management plan, including (1) descriptions of the overall approach to data collection and management, (2) a statistical plan that includes methods to monitor quality and consistency of data collection and methods to measure outcomes, (3) a plan for real-time data transfer, (4) data security measures, and (5) a description of how to use/apply findings for future studies.
  - **Specimen Handling and Distribution:** Describe plans for the development of methods for the handling, distribution, analysis, banking, and security of any specimens and/or imaging products generated from Consortium-sponsored studies. Include a named coordinator responsible for managing and resolving material and intellectual property issues among Consortium organizations.
  - **Information Technology (IT) Resources:** Since the Consortium will rely heavily on information technology, provide the name and key personnel description of the individual who will be responsible for database and information infrastructure. Describe relevant personnel and organizational experience with implementing multi-institutional real-time communications.
  - **Publication and Data Dissemination:** Describe plans for ensuring rapid publication and other public dissemination of data while maintaining participant privacy. Ensure that all Data Sharing requirements have been considered and addressed (note Data Sharing, Section I.F.). Describe plans for rapid responding to GSC inquiries.
  - **Fiscal and Legal Administration:** Describe the fiscal organization necessary for the proper distribution of funds between Study Sites for performance of studies.
- **Research Plan: (12-page limit for *each* Proposed Research Project):** The Research Plan must include an initial set of proposed studies agreed upon by the Consortium participants, which are reflective of Consortium Objectives and Focus Areas. Applicants must provide a description of a ***minimum of four*** studies in sufficient detail to allow for evaluation of the scientific merit alone and in relation to meeting the overall objectives of the Consortium. Details about each proposed project must include the following:
  - **Background:** Present the theoretical background and rationale supporting the proposed work. Cite relevant literature and any available preliminary data. Describe previous experience most pertinent to this project.
  - **Objectives/Specific Aims/Hypotheses:** Provide a description of the purpose and objectives of the study with detailed specific aims and/or study questions/hypotheses. Provide a clear description of what the study deliverables will be and the timeline for each study.

- **Research Strategy:** Describe the study design, methods, and analyses, including appropriate controls and/or comparison groups, in sufficient detail for analysis. Address potential problem areas and present alternative methods and approaches. If human subjects or human anatomical samples will be used, include a detailed plan for the recruitment of subjects or the acquisition of samples. Clinical trial projects should clearly define the primary clinical outcome measure. Describe the patient populations and Study Sites that will be utilized for each study. Provide sufficient information on the methods, metrics, and statistical power for each study to allow for an evaluation of the proposed design and study budget.

  - **Military and Veterans Benefit:** Describe how the proposed studies build on the research goals of the named MTF and VA collaborators in order to maximally benefit Service Members and Veterans. Describe how the studies will have impact on accelerating the movement of promising treatments for the required and/or additional focus areas and objective(s). Describe how the proposed studies will support identification and confirmation of clinically relevant biomarkers as diagnostic and prognostic indicators of PTSD and co-occurring disorders.
  - **Study Personnel:** Describe the background and expertise of investigators. Briefly describe their roles on the project.

- **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. ***Each component has no page limit unless otherwise noted.***
  - References Cited (four-page limit): 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 Acronyms and Symbols (one-page limit): Provide a list of acronyms and symbols (e.g., PCR = polymerase chain reaction).
  - 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 if Government-owned facilities or equipment are proposed for use. Reference should be made to the original or present contract under which the facilities or equipment items are now accountable. There is no form for this information.
  - Publications and/or Patent Abstracts (10-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 (two-page limit per letter): Provide a letter (or letters if applicable), of organizational support.

- Quad Charts for Each Proposed Study. The Quad Chart template will be provided via Grants.gov. file that must be downloaded from the CDMRP eReceipt System (https://cdmrp.org) and saved using Adobe Acrobat Reader as a PDF file. The Quad Chart must include the following sections:
  - Problem and Military Relevance – Provide a bulleted summary of the problem to be studied and its military relevance.
  - Proposed Solution – Provide a bulleted summary of the objectives of the work based on the Preproposal Narrative.
  - Picture – Insert a picture or other graphic that is representative of the work to be performed; this may, for example, show some aspect of the research to be performed, the expected technology outcome of the work, or the military problem that is being addressed.
  - Timeline and Cost – Identify the major planned activities or phases of the work and their duration on the chart provided, and provide the estimated direct costs by year.
- Letters of Collaboration (if applicable) (no page limit per letter): 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.
- Intellectual and Material Property Plan (if applicable): Provide a plan for resolving intellectual and material property issues among participating organizations and how any conflicts will be resolved.

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

  Technical abstracts should be written using the outline below. 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.

  - **Background:** Describe the general management and organizational structure of the Consortium. Outline the management and expertise of Consortium personnel at the Coordinating Center and Study Sites.
  - **Objectives:** Describe the Consortium's overall research goals and agenda, including detailing the public purpose to be derived from the proposed research.
  - **Research Plan:** Briefly describe the studies the Consortium plans to pursue during the performance period. State how the proposed projects address the CAP Award Focus Areas.
  - **Military/VA Benefit:** Briefly describe how the expected results will have a significant impact on ***PTSD and associated chronic sequelae (including depression, anger/aggression, and substance use/abuse, etc.)*** experienced by Service Members and Veterans.

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

  Lay abstracts should be written using the outline below. Do not duplicate the technical abstract. The lay abstract is used by consumer peer reviewers along with other components of the application package.

  - Describe the ultimate applicability of the Consortium's research. What types of patients will it help and how will it help them?
  - What are the potential applications, benefits, and risks?
  - What is the projected time it may take to achieve a relevant outcome?
  - What are the likely contributions of this study to advancing the field of research?
  - How will the outcomes benefit the public?

- **Attachment 5: Statement of Work (SOW) (10-page limit):** Upload as "SOW.pdf." Refer to the General Application Instructions, Section II.C., for detailed information.

- **Attachment 6: Military and VA Benefit Statement (two-page limit):** Upload as "MilBen.pdf." State explicitly how the proposed work, if successful, will have a significant impact on ***PTSD and common co-occurring psychiatric and medical disorders*** experienced by Service Members and Veterans.

  - Describe how the proposed studies are responsive to the health care needs of the Armed Forces and/or the US Veteran population.
  - Describe the military or Veteran population(s) that are to be utilized and their appropriateness for the proposed studies.
  - If non-military populations will be used for the proposed research, explain how the populations simulate the targeted population (i.e., Armed Forces and/or the US Veteran population).

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

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

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

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

D. 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 any one of the deadlines will result in application rejection.

E. Other Submission Requirements

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

All applications must be submitted through Grants.gov. Organizations are required to provide a Data Universal Numbering System (DUNS) number and register with the Central Contractor Registry (CCR) 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 Overview

All applications are evaluated by scientists, clinicians, and consumer advocates using a two-tier review process. The first tier is a scientific peer review of applications against established criteria for determining scientific merit. The second tier is a programmatic review that compares applications to each other and makes recommendations for funding to the Identified Approval Authority, based on scientific merit, the overall goals of the program, and 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 review process used by the CDMRP may 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. Each level of review requires panelists to sign a non-disclosure statement attesting that application and evaluation information will not be disclosed outside the panel. Violations of the non-disclosure statement can result in the dissolving of a panel(s) and other corrective actions. Organizational personnel and PIs 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 panelists or PIs that compromise the confidentiality of the review process may also result in suspension or debarment of their employing organizations 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 Criteria

1. Scientific Merit Review: To determine technical merit, all applications will be evaluated according to the following **bolded** scored criteria, which are of equal importance:

- **Overall Research Plan**
  - The strength of the scientific rationale behind the approach the Consortium proposes.
  - How well the overall research plan integrates the key components and research projects to meet the overarching objectives of the Consortium.
  - The feasibility of the timeline that aligns milestones and deliverables with objectives for the Consortium.
  - How the scientific projection of the types of studies (including size and scope) to be conducted by the Consortium over the entire period of performance supports the overall research strategy and aims of the Consortium.
- **Consortium Infrastructure**
  - **Consortium Expertise, Resources, and Previous Collaborations among Study Site Entities and between Study Site Entities and the Coordinating Center**
    - Expertise and experience of proposed PI.
    - To what extent the Coordinating Center personnel's background, track record, and expertise are appropriate with respect to the ability to manage and oversee Consortium.
    - To what extent the levels of effort of key personnel are appropriate for successful conduct of the proposed work.
    - The degree to which the ability and experience of the organization with the financial management of multi-institutional research studies is appropriate.
    - Ongoing and previous collaborations between Study Site entities and Coordinating Center related to the current effort(s).
  - **Coordination of Consortium Components**
    - To what extent the proposed overall organizational structure of the Consortium is appropriate.
    - How well the Coordinating Center addresses a plan to oversee and coordinate all Consortium Sites.
    - How well the plan for the establishment and maintenance of core facilities will effectively support Consortium activities.
    - How well each Consortium Site will function as an integrated unit.

- How well the proposed Consortium structure and research integrates the MTF and VA sites, and other sites with their stated research goals.
- To what degree the appropriate resources are provided for full participation at each Consortium Site.

o **Study Management and Monitoring**

- How the plans for real-time communication among all organizations participating in the Consortium, including complete and timely reporting of adverse events, are appropriate to facilitate Consortium activities.
- The extent of the named Consortium Clinical Research Manager's experience with guiding clinical protocols through the regulatory approval processes, coordinating participant accrual, and coordinating study activities across sites (if applicable).
- How the outlined procedures for quality assurance, quality control, safety, and study monitoring are adequate for conducting multi-institutional studies.
- How the plans for specimen handling, distribution, analysis, banking, and security are appropriate to facilitate Consortium activities.

o **Data Management**

- The degree to which the overall approach to data collection, management, analysis, and security measures is appropriate.
- How clearly the effective application of methods to monitor quality and consistency of data collection and methods to measure outcomes in previous trials conducted have been demonstrated by the PI and key personnel.
- How the plan for real-time data transfer is adequate for supporting the Consortium-associated activities.
- The degree to which plans for the publication and other dissemination of data are appropriate.

o **Clinical Protocol Development and Human Subjects' Protections**

- The degree to which plans for the proposed clinical protocols and associated clinical documents within the performance period are appropriate.
- To what extent the plans for addressing human subjects' protection requirements as described by HRPO, VA as applicable, and coordinating IRB submissions and approvals at participating sites are appropriate.
- How well appropriate plans for developing procedures to ensure compliance with FDA regulations for investigational agents are considered when relevant.

o **Organizational Resources and Commitment**

- The degree of organizational commitment for the use of facilities and resources in the conduct of Consortium operations.

- Whether the organizations have demonstrated access to appropriate patient populations for conduct of Consortium studies.
- How the resources and expertise at each organization are appropriate for coordinating specimen collection and processing (as applicable).
- How the resources and expertise at each organization are appropriate for data management and maintaining security/confidentiality.
- The degree to which each organization demonstrates a willingness to resolve intellectual and material property issues with other organizations in the Consortium.
- The extent to which the intellectual and material property plan is developed and appropriate.
- Evidence of established collaborative relationship between Coordinating Center and each proposed Research Site/Research Site Unit.
- How well the commitment of the organizations to work with all Consortium Sites, is demonstrated.
- Evidence of an ongoing relationship between the proposed Research Site and MTF/VA.

- **Criteria for Evaluation of *Each* of the Proposed Projects**
  - **Impact**
    - How the proposed study addresses overarching and specific Consortium goals.
    - How the potential outcomes of the proposed work will provide/improve the short-term benefits for individuals.
    - How significantly the long-term benefits may impact patient care and/or quality of life.
  - **Research Strategy**
    - How well the preliminary data and scientific rationale supports the research project.
    - How well the hypotheses or objectives, aims, experimental design, methods, and analyses are developed and integrated into the project.
    - How the statistical plan, including sample size projections and power analysis, is adequate to achieve the study objectives and is appropriate to type and phase of study.
    - Acknowledgement of potential problems and addresses alternative approaches.
    - Description of the population(s) of interest, demonstrates access to these populations, and identifies sampling methods to gain a representative sample from the population(s) of interest.

- How well the proposed work utilizes the Consortium resources.

- **Innovation**
  - How the research proposes new paradigms or challenges existing paradigms.
  - How the proposed research represents more than an incremental advance upon published data.
- **Feasibility**
  - Whether there is sufficient evidence that the PI has the experience and resources to conduct the research successfully. Whether the described study population is feasible with respect to access, recruitment strategies, inclusion/exclusion criteria, etc.
- **Personnel**
  - How the background and expertise of the investigator(s) demonstrate their ability to perform the proposed work.
  - How the levels of effort by the investigator(s) are appropriate to ensure success of this project.
  - How the investigator(s) record(s) of accomplishment demonstrates his/her ability to accomplish the proposed work.
- **Ethical Considerations**
  - How the level of risk to human subjects is minimized.
  - 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.
  - How well safeguards are in place for vulnerable populations.

- ***The following unscored administrative bolded criterion will be considered as necessary following the above scored criteria:***
  - **Budget**
    - Whether the budget is appropriate for the proposed research and within the limitations of the award mechanism.

2. Programmatic: The following criteria are used by programmatic reviewers to make funding recommendations.

- **Stage 1:** During the first stage of programmatic review, applications will be reviewed using the following criteria:
  - Adherence to the intent of the award mechanism
  - Programmatic relevance in relation to the objectives of the PH/TBI RP CAP Award

- Ratings and evaluations of the peer reviewers
- Relative translational potential
- Military and VA benefit

- **Stage 2:** Applications that best meet the Stage 1 programmatic review criteria will be selected for the second stage, which will consist of an in-person oral presentation. The presentation format will be provided to Stage 2 invitees at the time of notification of selection for Stage 2 competition. During Stage 2, the following criteria will be used by programmatic reviewers to make funding recommendations:
  - Vision and leadership demonstrated in addressing discussion questions, which will be provided no later than 2 weeks prior to the date of the oral presentation.
  - Status of establishment of relevant collaborations

IV. ADMINISTRATIVE ACTIONS

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

A. Rejection

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

- Preproposal Narrative is missing.
- Page size is larger than 8.5 inches x 11.0 inches (approximately 21.59 cm x 27.94 cm).

The following will result in administrative rejection of the application:

- Project Narrative is missing.
- Budget is missing
- Page size is larger than 8.5 inches x 11.0 inches (approximately 21.59 cm x 27.94 cm).
- Submission of an application for which a letter of invitation was not received.

B. Modifications

- Pages exceeding the specified limits will be removed prior to review for all documents.
- Documents not requested will be removed.
- Following the application deadline, the PI may be contacted by CDMRP via email with a request to provide certain missing supporting documents (excluding those listed above in Section IV.A., Rejection). The missing documents must be provided by 5:00 p.m. ET on the second full business day following the date the email was sent. Otherwise, the application will be reviewed as submitted.

- No other post-submission modifications will be accepted.

C. Withdrawal

The following may result in administrative withdrawal of the application:

- FY12 PH/TBI RP CAP Award GSC member(s) is (are) found to be involved in the preapplication or application processes including, but not limited to, concept design, application development, budget preparation, and the development of any supporting document. A list of the FY12 PH/TBI RP CAP Award GSC members will be made available to all by October 5, 2012 at http://cdmrp.army.mil/phtbi/default.
- The application does not conform to this Program Announcement/Funding Opportunity description to an extent that precludes appropriate review.
- Inclusion of URLs with the exception of links to published references References Cited and Publication and/or Patent Abstract sections.
- The PI does not meet the eligibility criteria.

D. Withhold

Applications that appear to involve research misconduct will be administratively withheld from further consideration pending organizational investigation. The organization will be requested to provide the findings of the investigation to the USAMRAA Contracting/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, 2013. Refer to the General Application Instructions, Appendix 4, for additional award administration information.

B. Administrative and National Policy Requirements

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

C. Reporting

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

D. Award Transfers

Refer to the General Application Instructions, Appendix 4, Section F, 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 the CDMRP eReceipt System 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: 1-301-682-5507

Email: help@cdmrp.org

B. Grants.gov Contact Center

Questions related to application submission through the 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: 1-800-518-4726

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. If the application package is updated or changed, the original version of the application package may not be accepted by Grants.gov.

VII. REFERENCES

Friedman MJ, Keane TM, & Resick PA (Eds.). 2007. *Handbook of PTSD.* New York: Guilford Press.

Hoge CW, Castro CA, Messer SC, McGurk D, Cotting DI, & Koffman RL. 2004. Combat duty in Iraq and Afghanistan, mental health problems, and barriers to care. *New England Journal of Medicine* 351:13-22

Hoge CW, Terhakopian A, Castro CA, Messer SC, & Engel CC. 2007. Association of posttraumatic stress disorder with somatic symptoms, health care visits, and absenteeism among Iraq war veterans. *American Journal of Psychiatry* 164:150-153.

Vasterling JJ, Proctor SP, Amoroso P, Kane R, Heeren T, & White RF. 2006. Neuropsychological outcomes of Army personnel following deployment to the Iraq War. *Journal of the American Medical Association* 296:519-529.

VIII. APPLICATION SUBMISSION CHECKLIST

Grants.gov Application Components	Action	Completed
SF-424 (R&R) Application for Federal Assistance Form	Complete form as instructed.	
Attachments Form	Upload Project Narrative (ProjectNarrative.pdf) as Attachment 1.	
	Upload Supporting Documentation (Support.pdf) as Attachment 2.	
	Upload Technical Abstract (TechAbs.pdf) as Attachment 3.	
	Upload Lay Abstract (LayAbs.pdf) as Attachment 4.	
	Upload Statement of Work (SOW.pdf) as Attachment 5.	
	Upload Military and VA Benefit Statement (MilBen.pdf) as Attachment 6.	
Research & Related Senior/Key Person Profile (Expanded)	Attach PI Biographical Sketch (Biosketch_LastName.pdf) to the appropriate field.	
	Attach PI 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 Current & Pending Support (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.	