# Program Announcement

**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)

## Chronic Effects of Neurotrauma Consortium (CENC) Award

**Funding Opportunity Number: W81XWH-12-PHTBI-CENC**

**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

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# 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) Chronic Effects of Neurotrauma Consortium (CENC) 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 $37.175 million (M) of the $135.5M FY12 Peer Reviewed Traumatic Brain Injury and Psychological Health Research appropriation to support the CENC Award. 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 $62.175M. A single Consortium, consisting of a Coordinating Center and multiple Study Sites, will be supported through this DoD/VA collaborative effort.

Funds added by the VA will only be utilized to support research at VA sites; such funding will be coordinated through the VA Office of Research and Development. All collaborators may be eligible for additional DoD and VA funding (if eligible for VA funding) should additional funds become available. Leveraging existing resources, including infrastructure and/or research funding, is highly encouraged. The maximum period of performance is 5 years. A DoD/VA co-chaired Government Steering Committee (GSC) will provide Consortium oversight of research activities. Relevance to the health care needs of the Armed Forces and/or the US Veteran population is a key feature of the CENC Award. Therefore, applications with collaborations that partner extramural academic, industry, and non-DoD Federal investigators with Intramural investigators (especially PIs at MTFs) are highly encouraged.

## B. Award Information

Recent research has indicated that TBI, including mild TBI (mTBI)/concussion with repeated exposures, leads to neuronal changes, and cognitive, behavioral, psychological, and sensory impairments. Further, research suggests that TBI, including mTBI, leads to chronic consequences (lasting 3 months or greater) in some individuals having experienced a TBI. Three critical issues related to the chronic effects of neurotrauma (over the lifespan of the patient) remain:

(1) identification and characterization of the anatomic, molecular, and physiological mechanisms;

(2) evaluation of how comorbidities are associated with and exacerbated by neurotrauma; and

(3) appropriate treatment and rehabilitative strategies.

This Consortium effort will be dedicated to establishing a comprehensive understanding of the chronic sequelae associated with neurotrauma, primarily focused on mTBI/concussion as defined by the DoD/VA. Briefly, the DoD/VA defines mTBI as associated with normal structural imaging (excluding DTI, fMRI, etc.), loss of consciousness lasting 30 minutes or less, alteration

of consciousness/mental state from a moment up to 24 hours, and post-traumatic amnesia lasting 1 day or less. (The full DoD/VA mTBI definition is provided in the General Application Instructions, Appendix 7.) A key priority of this Consortium is the development of diagnostics, including a broad range of biomarkers, and novel treatment and rehabilitative strategies to improve the long-term health and well-being of Service Members and Veterans. The Consortium will coordinate research activities, including translational preclinical and clinical studies, as well as the collection, storage, use, and analyses of data and anatomical specimens, with an emphasis on basic and preclinical studies to address the anatomic, molecular, and physiological mechanisms issues and a heavy emphasis on clinical studies to address the comorbidities issues. There must be an emphasis on and progression toward translational/clinical work over the course of the Consortium. In the case of studies involving animal models, justification of validation is required at the time of application submission. Introduction of any new animal models will require clear justification. For applications studying blast-related TBI, teams should have access to an expert in the study of blast physics. The GSC must concur on blast or animal models.

CENC efforts will provide critical information to benefit Service Members and Veterans by enhancing diagnosis, treatment, and rehabilitation strategies. The 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]). The Coordinating Center will execute awards to Study Sites slated to be supported through DoD funding.

Consortium Study Sites approved for VA support will be funded directly through the VA Office of Research and Development, not through the Consortium Coordinating Center. However, all DoD and VA-supported projects will be executed within the Consortium infrastructure with oversight by an appointed GSC. Consortium execution will include review of research priorities and making recommendations to the Grants Officer's Representative (GOR); the ultimate approval authority is the USAMRAA Grants Officer (GO).

## C. Consortium Objectives

**(1)** To establish the association (onset, prevalence, and severity) of the chronic effects of mTBI and common comorbidities as described below under Focus Areas.

**(2)** To determine whether there is a causative effect of chronic mTBI/concussion on neurodegenerative disease and other comorbidities.

**(3)** To identify diagnostic and prognostic indicators of neurodegenerative disease and other comorbidities associated with mTBI/concussion.

**(4)** To develop and advance methods to treat and rehabilitate chronic neurodegenerative disease and comorbid effects of mTBI/concussion.

## D. Focus Areas

The CENC will be responsible for the collection, storage, use, and analyses of data and anatomical specimens and will coordinate specific research studies focused on the objectives of

the Consortium. The research studies must evaluate chronic (defined as greater than 3 months for the purpose of this Program Announcement/Funding Opportunity) anatomic, molecular, and physiological changes related to neurotrauma.

The Consortium must also propose activites that include the majority of comorbidities associated with the chronic effects of neurotrauma including:

- Psychological
- Neurological (including, memory, seizure, autonomic dysfunction, and sleep disorders)
- Sensory deficits (including visual, auditory, and vestibular dysfunction)
- Movement disorders
- Pain (including headache)
- Cognitive
- Neuro-endocrine deficits

***Applications must at a minimum include studies addressing pain, neurosensory, and psychological comorbidities.***

## E. General Consortium Requirements

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. Ultimately, the projects approved for execution via the Consortium will be balanced across the spectrum of the Focus Areas.

The Consortium framework (Figure 1) will consist of a Coordinating Center collaborating with multiple research sites. The Consortium will leverage existing infrastructure and collaborations. It is expected that each research site will consist of collaborating partners, namely, a VA and/or DoD Treatment Facilities and one or more strongly relevant non-Federal entities, including academic institutions and industry (e.g., private clinics and rehabilitation centers). Priority will be given to applications with established collaborations between research sites and the Coordinating Center.

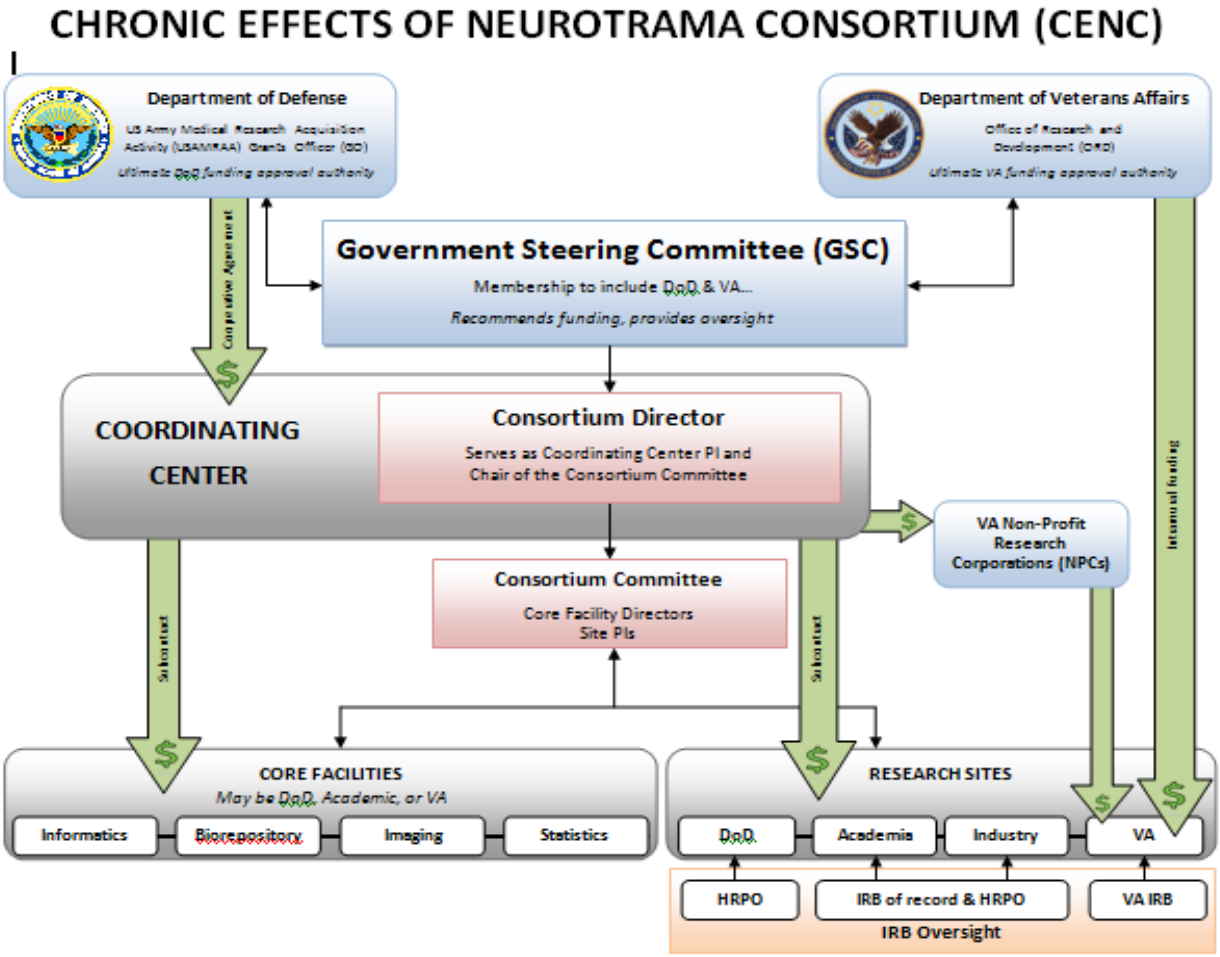


**Figure 1**

The Coordinating Center and any associated Study Sites must apply to this Program Announcement/Funding Opportunity through a single application. A single award will be made to the selected Coordinating Center to support the Coordinating Center's efforts as well as Consortium-associated Study Sites slated for receipt of DoD funding. Those Consortium Study Sites slated for support via the VA will be executed directly through the VA Office of Research and Development.

CENC Award applications should name and describe individual core facilities at member organizations that will serve as official Consortium research core facilities, which may include informatics, biorepository, imaging, and statistical laboratories. 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 availability of specimens for planned and future analyses. Proposed studies could address ways to effectively use specimens to develop effective diagnostics and/or indicators of treatment response.

In addition to the proposed structure and core laboratory organization, CENC Award applications must include an initial set of proposed studies agreed upon by the Consortium participants, which are reflective of the Consortium Objectives and aligned Focus Areas (as noted above in Sections I.C. and I.D., respectively) for consideration during the review and selection process. Some or all may be carried out if recommended for funding by the GSC and approved for funding by the USAMRAA GO or VA Office of Research and Development. Proposed studies should include a range of scope, size, and type designed to meet the overall focus of the Consortium. The proposed set of studies must address all four Consortium Objectives (see Section I.C.). Additionally, performance metrics and execution milestones must be provided for each study. Studies submitted for VA research support should be clearly identified, and the VA investigator must be eligible to submit for VA funding (see Section I.G., Eligibility Information).

Funding selection will depend upon evaluation of the proposed Coordinating Center structure, core laboratories, scientific studies, record of productivity, evidence of VA and DoD collaboration, available capabilities, access to military and/or Veteran populations, 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. The GSC may also recommend additional studies. 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.

It is anticipated that the Consortium budget will support the Coordinating Center, core laboratories/facilities, and DoD-funded research Study Sites. 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. In some cases, studies may include civilian sites/populations; however, this 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 organization and use, as well as specimen collection, storage, and use. The Coordinating Center will coordinate highly relevant translational preclinical studies and clinical research 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 enhancing diagnosis, treatment, and rehabilitation strategies. The Principal Investigator (PI) of

the Coordinating Center shall provide evidence of prior experience with the design and administration of multi-institutional research studies.

CENC Award applications should include a description of plans to coordinate with the Study Sites to propose, design, externally peer review, and prioritize the most relevant initial studies for review and selection by the GSC. Additional studies will be presented to the GSC for review and approval of recommendations prior to implementation. While the Consortium and initially proposed sites may be approved to conduct specific studies, additional applications may be considered and approved should funding be available, thus allowing additional participation from investigators/institutions after the initial award. Such may be targeted via new solicitation(s) or via existing Study Sites. See Section I.K. 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 CENC 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 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 will:

- 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 DoD and VA during the pre-award planning meeting, are initiated within 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 military treatment facility (MTF) and VA sites with resources not to include funding necessary for participation in the Consortium. Details 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);
- 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;
- Establish and manage a communications plan and a real-time communications system between the Coordinating Center 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 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 performance period of the award, identify potential studies and 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 on-site monitoring program to be managed by the Coordinating Center;
    - Implement the Consortium-developed management plan for acquisition and aggregation of protocol-specified specimens, biological/anatomical fluids, and relevant clinical data to the appropriate laboratories for testing or storage necessary for the conduct and analyses of clinical studies during the performance period 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, and therapeutic use);
- 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 substance 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;
- 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 the USAMRMC and VA;

- Assist with the preparation of quarterly written progress reports and a final written comprehensive report; and
- Prepare for a site visit audit, if applicable. 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. At a minimum, data will be reported via core measures of the National Institute of Neurological Disorders and Stroke TBI Common Data Elements (CDE) (http://www.commondataelements.ninds.nih.gov). If the proposed research is not compatible with the core CDEs, the investigators must supply a detailed justification why these measures will not be incorporated into the research. Additionally, reporting is expected via the Federal Interagency Traumatic Brain Injury Research http://www.nih.gov/news/health/aug2011/ninds-29.htm (http://fitbir.nih.gov/tbi-portal) database, and others as appropriate. 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 the VA eligibility at the pre-application step. To be eligible for VA funding (salary, equipment, site or core 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, USAMRAA). Elements selected for VA funding will be supported as Service Directed Research

programs under VA Biomedical, Clinical, Rehabilitation, or Health Services Research and Development.

## I. Performance Metrics

Applicants should lay out a plan for the number and types of studies the Consortium expects to execute. While no set number of studies that will be coordinated 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, GSC, VA, and USAMRMC, shall be initiated. A timeline outlining the overall plan for study initiation, performance, and analyses shall be developed, with clear milestones to which the Consortium will be held accountable. The Consortium SOP should contain 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 will 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 **$37.175M** 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 in 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 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., for budget regulations and instructions for the Research & Related Budget. In addition, for this award mechanism, direct costs include:

- Salary
- Research-related subject costs
- Clinical research costs (as applicable)
- Support for multidisciplinary collaborations
- Travel between collaborating organizations
- Travel funds for the Coordinating Center PI to attend quarterly 1-2 day briefings with the GSC and the USAMRMC and VA staff
- Travel costs for attendance at one DoD-VA sponsored meeting
- Note that travel costs should be within allowable DoD or VA limits (as appropriate)

## K. Consortium Oversight

**a.** ***GSC:*** (SOP/Charter Required):

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.** ***Peer Review Program (PRP):*** The Coordinating Center will establish a PRP (to be approved by the GSC) to advise on the scientific merits of studies proposed post-award. The PRP is responsible for vetting all projects produced by the Consortium, ensuring unbiased rigorous scientific review in a timely manner. Specifically, a peer review panel of between 9 and 15 selected reviewers will be recruited. A rating/scoring system by which project reviews are evaluated will guide the reviewers' work. Each project will be evaluated at a minimum in terms of scientific significance, the proposed approach (i.e., methodology), investigators/environment, completeness, and accuracy of the project, and the budget. The PRP provides final written reviews, inclusive of constructive feedback for recommended changes (and resubmissions/reviews, if requested), of individual submitted projects within 32 days of assignment to peer reviewers. A system for carrying out expedited reviews with a 21-day turn-around will also be required.

## 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. GSC justification is required if longer than 6 months. 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 trials. All VA-funded studies 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/.

All subject recruitment at VA facilities must follow VA human subject guidelines for both VA and non-VA investigators. Recruitment at VA facilities must be done through VA investigators who are members of the Consortium.

## M. Research Involving Animal Use

Specific documents relating to the use of animals in the proposed research will be requested if the application is selected for funding (these documents should not be submitted with the application). The Animal Care and Use Review Office (ACURO), a component of the USAMRMC ORP, must review and approve all animal use prior to the start of working with animals. PIs must submit the institutional animal use protocol, Institutional Animal Care and Use Committee approval of that protocol, and a version the animal use appendix entitled "Research Involving Animals." For guidance on which version of the appendix to use as well as links to both, visit the ACURO website at: https://mrmc.amedd.army.mil/index.cfm?pageid=Research_Protections.acuro_Animalappendix. Allow 2 to 4 months for regulatory review and approval processes for animal studies. For additional information, send an email with questions to the ORP ACURO at (ACURO@amedd.army.mil). VA processes apply when funding is via the VA. Details on VA requirements are provided at: http://www1.va.gov/vhapublications/ViewPublication.asp?pub_ID=2464.

## N. DoD and VA Aligned Organizations Encouraged

Relevance to the health care needs of the Armed Forces and/or the US Veteran population is a key feature of the CENC Award. Therefore, applications with collaborations that partner extramural academic industry and non-DoD Federal investigators with Intramural investigators (especially PIs at MTFs) are highly encouraged.

## O. 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 CENC 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 mailto: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 (20-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:**
    - **Road Map:** Identify the critical research questions required to address each of the Consortium Objectives and prescribe the research question(s) appropriate for generating outcomes responsive to each of these objectives. The Consortium will be focused on basic and preclinical studies to address the biologic/anatomic, molecular, and physiological mechanisms issues and a heavy emphasis on clinical

studies to address the comorbidities issues. There must be an emphasis and progression toward clinical/translational work over the course of the Consortium.

- **Overarching Goals:** Provide a brief description of the overall goals of the proposed research.
- **Consortium Structure:** Outline the organizations that will participate in the Consortium. Briefly discuss the qualifications of key personnel in the administration and their ability to oversee studies. Discuss potential core facilities and shared resources.
- **Management Approach and Processes**, to include:
  - Description of management processes to be implemented (to include the approach as to how to achieve maximum synergy between the elements of CENC).
  - Description of the process to terminate research (to include early termination for non-performance or to direct funds to new or more promising lines of approach).
  - Description of Clinical Trials management (as applicable).
- **Research Plan:** Provide a brief description of the initial studies to be proposed and potential future studies. Identify target focus area(s) relevant to each study. Describe the reasoning on which the studies are based, the target patient population(s), and the outcomes to be measured.
  - Discussion of maturity and feasibility of each research project and the overall research approach, including approval and technical process to move steps forward.
  - Schedule (Gantt-like format) for each proposed therapy or major proposed research aim that answers to one of the four CENC Objectives showing major tasks and key milestones/timelines, with responsible organization and people, key decision points, and key communication points (within CENC and between the FDA, the VA, and the DoD).
  - How any non-CENC resources can/will be leveraged to support the CENC projects.
- **Relevance:** Describe how the Consortium will have an impact on the lives of Service Member and Veteran populations and their family members.
  - Discussion of how the Consortium objectives and Focus Areas will be addressed and the potential impact on the health care needs of the Armed Forces and/or the US Veteran population.
- **Leveraging Resources:** Describe the offeror's ability to leverage non-CENC resources (research or funding, or both).

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

- **Quad Charts (one per proposed project):** This document must be submitted by the pre-application submission deadline. The Quad Chart is a PowerPoint file that must be downloaded from the CDMRP eReceipt System and saved using Adobe Acrobat Reader as a PDF file. The Quad Chart must include the following sections:
  - Objective(s)
  - Focus Area(s)
  - Problem and Relevance: Provide a bulleted summary of the problem to be studied and its 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.
  - 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.
- **References Cited (five-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 (four-page limit per individual):** VA investigators should highlight their VA affiliation/appointment.

- **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:

- **Road Map:** How well the proposed Road Map addresses Consortium Objectives.
- **Consortium Structure:** How well the outlined Consortium structure will support efficient infrastructure designed to support the study coordination and core facilities required to conduct multi-institutional studies of varying scope and size. The appropriateness of the administrative and research teams' background and expertise with respect to their ability to oversee studies.
- **Military/VA Benefit:** The degree to which the proposed research, if successful, will have a significant impact on mTBI/concussion and common chronic comorbidities experienced by Service Members and Veterans.
- **Research Plan:** How well the proposed initial studies will meet the overall objectives of the Consortium in a reasonable representative scope and size. 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 provided in Grants.gov for this Program Announcement/Funding Opportunity. The application package is 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 (no page limit):** Upload as "ProjectNarrative.pdf."

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

  - **Consortium Road Map:** Identify the critical research questions required to address each of the Consortium Objectives and prescribe the research question(s) appropriate for generating outcomes responsive to each of these objectives. The Consortium will be focused on basic and preclinical studies to address the anatomic, molecular, and physiological mechanisms issues and a heavy emphasis on clinical studies to address the comorbidities issues. There must be an emphasis on and progression toward clinical/translational work over the course of the Consortium.
  - **Consortium Expertise, Resources, and Previous Collaborations among Study Site Entities and between Study Site Entities and the Coordinating Center**
    - Outline the structure of the proposed Consortium and identify key personnel.
    - Describe the previous experience of the PI and other key personnel within the Coordinating Center with the design and administration of multi-institutional relevant studies. Reference relevant publications and submit reprints with the application supporting documentation.
    - Describe the previous experience of key personnel at each Study Site with the development and conduct of relevant studies. Reference relevant

publications and submit reprints with the application supporting documentation.

- Describe the appropriate patient populations at relevant Clinical Study Site and provide evidence of the ability to enroll adequate patient numbers into Consortium-sponsored studies. Provide an estimate of case enrollment/ patient load and the track record of research in this area for each Clinical Study Site and each Site PI.
- Describe the resources and facilities available within each Study Site for execution of relevant research projects.
- Describe the resources and expertise in each participating Study Site for data management and maintenance of data security/confidentiality.
- Provide evidence of organizational commitment for the Coordinating Center and each participating Study Site for the use of facilities and resources in the conduct of Consortium operations.
- Describe any plans to leverage existing or translational funding programs and infrastructure for the proposed Consortium.
- Describe ongoing and previous collaborations between Study Site entities related to the current effort(s).
- Describe ongoing and previous collaborations between Study Site entities and the Coordinating Center related to the current effort(s).

o **Plan of Operations**

- **Government Coordination:** Describe plans to communicate and partner with the named MTFs and VA sites. Explain 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.
- **Study Identification:** Outline a plan for the proposed project, design, and prioritization of potential future Consortium studies for presentation to the GSC (including peer review process) following initial study implementation. Include a mechanism for determining Study Site participation.
- **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:** Outline essential cores and other facilities to be shared that will be necessary for facilitation of Consortium success. Discuss 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/VA IRB-prescribed content (as applicable). 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/VA IRB. The link to the DoD HRPO site is https://mrmc.detrick.army.mil/index.cfm?pageid=research_protections. hrpo. Outline plans for developing procedures to ensure compliance with FDA requirements for investigational agents, as appropriate. 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/.

o **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 IT, provide the name 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 in Section I.F.). A forum on data sharing will be required at year 3 of the Period of Performance. Details will be worked out during the pre-award meeting.
- **Fiscal and Legal Administration:** Describe the fiscal organization necessary for the proper distribution of funds between Study Sites for performance of studies.

- **Research Plan: (20-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. Details about each proposed project must include the following:
  - **Background:** Present the ideas and reasoning behind 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.
  - **Research Strategy:** Describe the study design, methods, and analyses, including appropriate controls, 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. Describe the statistical plan, if appropriate, for the research proposed.
- **For submissions that include clinical interventions and/or clinical research, the following are also required:**
  - **Study Design:** Describe the type of study to be performed and outline the proposed methodology in sufficient detail to show a clear course of action:
    - 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).
    - Describe the reliability and validity of psychometric measures, if applicable.
  - **Statistical Plan and Data Analysis:** Include a complete power analysis to demonstrate that the sample size is appropriate to meet the objectives of the study. Specify the approximate number of human subjects that will be enrolled.

        - If multiple Study Sites are involved, state the approximate number to be enrolled at each site. Describe the data analysis plan in a manner that is consistent with the study objectives.
    - **Military and VA Benefit:** Describe how the proposed studies build on the research goals in order to maximally benefit Service Members and Veterans. Describe how the studies will have impact on accelerating the movement of promising treatments for one or more of the target Focus Areas.
    - **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. ***There are no page limits for any component unless otherwise noted. Include only those components described below; inclusion of items not requested may result in administrative rejection 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 Acronyms and Symbols: 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 whether or not 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), signed by the Department Chair(s) or appropriate organization official(s), reflecting the institution's commitment to the completion of the project, including laboratory space, equipment, and other resources available for the project.
    - Current Quad Charts: Provide current Quad Charts in the same format as in the pre-application. If no changes have been made to the project, the same Quad Charts submitted with the pre-application may be used.
    - 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.

- **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.
  - **Research Plan:** Briefly describe the studies the Consortium plans to pursue during the performance period. State how the proposed projects address the CENC Award Objectives and Focus Areas.
  - **Military/VA Benefit:** Briefly describe how the expected results will have a significant impact on mTBI/concussion and common chronic comorbidities 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?

- **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 mTBI/concussion and common chronic comorbidities 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 DoD Office of the Assistant Secretary of Defense and the VA Office of Research and Development based on scientific merit, the overall goals of the program, specific intent of the award mechanism, and recommendation of the GSC. 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, it is a crime for Federal officials to disclose confidential information of one party to another third party is a crime in accordance with 18 USC 1905.

## B. Application Review Criteria

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

    - **Consortium Infrastructure**
        - **Consortium Roadmap**
            - How well the proposed Road Map provides a feasible plan for addressing all Consortium Objectives, including identification of appropriate research

question(s)/projects for generating outcomes responsive to each of these objectives.

- How well the proposed Road Map projects appropriate studies for addressing Consortium Objectives.

o **Overarching Management Plan**

- How well the Management Plan addresses the monitoring of the Consortium's research.
- How well the Management Plan addresses an ability to alter the course of the consortium's research to be able to terminate unsuccessful projects early and redirect funds to more promising avenues of approach.
- How well the management plan demonstrates a sound strategy for obtaining synergy throughout the Consortium.

- **Consortium Expertise, Resources, and Previous Collaborations among Study Site Entities and between Study Site Entities and the Coordinating Center**

  - To what extent the Coordinating Center personnel's background, track record, and expertise are appropriate with respect to the ability to manage and oversee the Consortium.
  - To what extent the levels of effort are appropriate for successful conduct of the proposed work.
  - The degree to which the level of organizational IT experience in implementing multi-institutional real-time communications is appropriate.
  - How the specific abilities and experience possessed by the named information technology lead will enable him/her to quickly and efficiently implement the electronic communications required by the Consortium.
  - The degree to which the ability and experience of the organization with the financial management of multi-institutional research studies are appropriate.
  - How well ongoing and previous collaborations between Study Site entities related to the current effort(s) are described.
  - How well ongoing and previous collaborations between Study Site entities and the Coordinating Center related to the current effort(s) are described.

o **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 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 Protection (if applicable)**

- The degree to which plans for the proposed project, development, and external peer review of 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 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.

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 the 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 proposed Research Site MTF/VA.

- **Criteria for Evaluation of *Each* of the Proposed Projects**

  ***Projects that do not include clinical interventions or clinical research will be evaluated according to the following scored criteria:***

  - **Impact**
    - How the proposed study addresses the specified Consortium Objective(s) and Focus Areas.
    - The potential contribution of the proposed study to research and/or patient care related to chronic neurotrauma.
  - **Research Strategy and Feasibility**
    - 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 well the PI acknowledges potential problems and addresses alternative approaches.
  - **Innovation (if applicable)**
    - How the research proposes new paradigms or challenges existing paradigms in one or more of the following ways: concept or question, research methods or technologies, adaptations of existing methods or technologies, and clinical interventions.

- How the proposed research represents more than an incremental advance upon published data
- How the potential gain justifies the perceived risk.

o **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.

***Applications that include clinical interventions or clinical research will be evaluated according to the following scored criteria:***

- **Clinical Impact**
  - How the proposed study addresses the Consortium Focus Areas.
  - How the results of the proposed clinical study will affect research and/or patient care related to chronic neurotrauma.
  - How well the sample population represents the targeted patient population that might benefit from the proposed intervention.
  - How the potential outcomes of the proposed clinical trial will provide/improve the 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.
- **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.
  - 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.
- **Intervention**
  - To what degree the intervention addresses the clinical need(s) described.
  - How the intervention advances patient care beyond the currently available interventions.
- **Recruitment, Accrual, and Feasibility**

- Whether the PI has demonstrated access to the proposed target population as listed above.
- How the recruitment, informed consent, screening, and retention processes for the target population will be conducted to meet the needs of the proposed clinical trial.
- Whether the PI has discussed possible delays in the trial (e.g., slow accrual, attrition) and provided evidence of an adequate contingency plan.
- To what extent the proposed clinical trial affects the daily lives of the target population participating in the study (e.g., Will human subjects still be able to take their regular medications while participating in the clinical trial?).

- **Research Strategy**
  - How well the scientific rationale for testing the hypothesis is supported by the preliminary data, critical review and analysis of the literature, and/or prior clinical evidence supporting the relationship to the chronic effects of neurotrauma.
  - How well the study aims, hypotheses or objectives, experimental design, methods, data collection procedures, and analyses are designed to clearly answer the clinical objective.
  - How well the research design incorporates treatment outcome as the metric of primary importance and compares factors including patient compliance, treatment satisfaction, optimizing patient match to treatment modality, ease of treatment delivery, provider/patient safety issues, cost, program management issues, and a resultant "best practice guide to implementation."
  - How appropriate are the questionnaires, surveys, and other tools included in the study, and how well described are their psychometrics.
  - How well the inclusion and randomization criteria meet the needs of the proposed clinical trial.
  - How well the exclusion criteria are justified.
- **Statistical Plan (as appropriate for the proposed clinical trial)**
  - 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.
- **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.

***The following unscored administrative bolded criteria will not be individually evaluated for clinical and non-clinical studies:***

- **Application Presentation**
  - How the writing and components of the application influenced the review.
- **Budget**
  - Whether the budget is appropriate for the proposed research and within the limitations of the award mechanism.

**2. Programmatic Review:** 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 goals/priorities of the PH/TBI RP CENC Award
  - Ratings and evaluations of the peer reviewers
  - Relative translational potential
  - Military and VA benefit
- **Stage 2:** The following criteria are used by programmatic reviewers to make funding recommendations. Applications that best meet the Stage 1 programmatic review criteria will be selected for the second stage, which will consist of an oral presentation. During Stage 2, the following criteria will be used:
  - Vision and leadership demonstrated in addressing discussion questions that will be provided to the selected applicants 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 CENC Award GSC member(s) is (are) found to be involved in the pre-application 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 CENC 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 References Cited and Publication and/or Patent Abstract sections..

- Inclusion of any employee of CDMRP review contractors in applications for funding without adequate plans to mitigate conflicts of interest. Refer to the General Applications Instructions, Section II.B., for further detailed information.
- 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. 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. | |