Program Announcement

Defense Health Program

Defense Medical Research and Development Program

Department of Defense

Combat Casualty Care Joint Program Committee 6

Military Operational Medicine Joint Program Committee 5

Clinical and Rehabilitative Medicine Joint Program Committee 8

Psychological Health/Traumatic Brain Injury Research Program

Applied Neurotrauma Research Award

(Traumatic Brain Injury Emphasis)

Funding Opportunity Number: W81XWH-11-PHTBI-ANRA

Catalog of Federal Domestic Assistance Number: 12.420

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-application Submission Deadline:** 5:00 p.m. Eastern time (ET)**,** November 4, 2011
- **Invitation to Submit an Application:** December 2011
- **Application Submission Deadline:** 11:59 p.m. ET, February 1, 2012
- **Scientific Peer Review:** March 2012
- **Applicant Response to Scientific Peer Review Summary Statement (if applicable):** April, 2012
- **Programmatic Review:** May 2012

New for fiscal year 2011 (FY11): The Grants.gov Research & Related Budget form is a mandatory component of all Grants.gov application packages.

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I. FUNDING OPPORTUNITY DESCRIPTION

A. Program Description

Applications for the Psychological Health and Traumatic Brain Injury (PH/TBI) Research Program are being solicited by the Assistant Secretary of Defense for Health Affairs, Defense Health Program (DHP). The PH/TBI Research Program was established in FY07 for the purpose of complementing ongoing Department of Defense (DOD) efforts towards promoting a better standard of care for PH (including post-traumatic stress disorder [PTSD]) and TBI in the areas of prevention, detection, diagnosis, treatment, and rehabilitation. This includes research to benefit service members, their family members, veterans, and other beneficiaries of the Military Health System (MHS).

A total of $686 million (M) has been appropriated to support biomedical research focused on PH/TBI research efforts from FY07 through FY11. The FY11 appropriation that has been assigned to US Army Medical Research and Materiel Command (USAMRMC) is $100M. Approximately $25.5M of this appropriation has been assigned to the USAMRMC, Combat Casualty Care Joint Program Committee 6 (CCC JPC-6), Military Operational Medicine Joint Program Committee 5 (MOM JPC-5), and Clinical and Rehabilitative Medicine Joint Program Committee 8 (CRM JPC-8) for this Program Announcement/Funding Opportunity. The executing agent for this solicitation is the office of the Congressionally Directed Medical Research Programs (CDMRP). The Government reserves the right to increase this amount, should additional funds become available.

B. Award Information

The PH/TBI Research Program Applied Neurotrauma Research Award mechanism is being offered for the first time in FY11.

Applied Research is defined as work that refines concepts and ideas into potential solutions with a view toward evaluating technical feasibility of promising new products, pharmacologic agents, behavioral and rehabilitation interventions, diagnostic and therapeutic techniques, clinical guidance, and/or emerging approaches and technologies. Applications may include clinical trials.

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

If the study proposed involves the use of a drug that has not been approved by the Food and Drug Administration (FDA) for its investigational use, then an Investigational New Drug (IND) application to the FDA may be required and must be submitted to the FDA prior to the grant submission. If the proposed study involves an Investigational Device that has not been approved or cleared by the FDA for its investigational clinical use, the study may be required to comply with the FDA Investigational Device Exemption (IDE) regulations. If applicable, the IDE

application must be submitted prior to the grant submission. The Government reserves the right to withdraw funding if the documented status of the IND or IDE has not been obtained within 6 months of the award date.

Investigators must demonstrate logical reasoning and a sound scientific rationale established through a critical review and analysis of the literature for the proposal to be competitive. Research projects should include a well-formulated, testable hypothesis based on a strong scientific rationale.

Intramural (DOD) and extramural investigators are encouraged to apply to this Program Announcement/Funding Opportunity. Funding cannot be applied toward government or federal salaries. Therefore, intramural investigators wishing to submit independently, or with an extramural partner must have a non-profit foundation/organization submit the application. In addition, non-DOD federal agency investigators wishing to submit independently, or with an extramural partner, must have a non-profit foundation/organization submit the application.

Direct transfer of funds to a government organization or agency is not allowed except under very limited circumstances.

C. Research Areas

All applications for the DHP PH/TBI Research Program funding opportunity must specifically address one or more of the following identified areas of research and specific research needs. Applications for research on areas other than those listed should NOT be submitted in response to this Program Announcement/Funding Opportunity. If the proposed research is not relevant to the advertised projects/tasks, the government reserves the right to administratively withdraw the application.

For proposals utilizing animal models, such animal models should be operationally valid with a clear linkage to DOD clinical/operational populations. ONLY established animal models will be accepted. In proposals studying blast-related TBI, while the use of actual explosives such as RDX or Oxyhydrogen is preferable, compressed air and hydrogen are acceptable so long as the research team is aware and accounts for the unique aspects of each type of approach, and has validated their model with respect to native blast. Additionally, teams should have access to an expert in the study of blast physics. Static and dynamic pressures should be measured. Mice should only be utilized in blast models if they are required for study of genetic modifications. Clinical researchers must plan on utilizing the NINDS Common Data Elements (see http://www.commondataelements.ninds.nih.gov/) and should plan to use the DOD definition of TBI (see definitions and classifications in http://www.dcoe.health.mil/Content/navigation/documents/VA%20Dod%20Management%20of%20Concussion%20mild%20Traumatic%20Brain%20Injury%20Summary.pdf)

Areas of interest for each Research Area are provided below:

Applied Science Areas:

- **The identification, role, and possible management (upstream of or at the point of phosphorylation) of phosphorylated Tau in TBI.** Tau has been shown to have an

important role in chronic traumatic encephalopathy. Proposals are sought for efforts developing an in vivo biomarker of Tau that can be used in research and in clinical applications. Proposals are also sought for studies of the role of Tau in the spectrum of TBI − particularly in mTBI/concussion. Studies of the role of Tau may also point to potential targets for therapy.

- **Investigation of the role of blast-induced hyperacceleration upon the generation of TBI.** Proposals are sought that address the role of blast wave spectral content and the assessment of skull and brain responses to blast loading and transiting blast energy. The question of whether cerebrospinal fluid cavitation and/or damage to the blood brain barrier is a source of brain injury related to effects of primary blast is also of interest. Investigators should be prepared to demonstrate that their blast models are validated with respect to native blast, that they have access to a specialist in blast physics and/or explosive ordinance disposal, and they should be prepared to measure both static and dynamic pressures at the point of impact of the blast wave with the animal.
- **The development of a valid animal model of anterior spinal cord injury as associated with burst or simulated burst/multi-level burst fracture of the spine.** Of particular interest is the thoracolumbar junction of the spine.

Applied/Clinical Science Areas: Emphasis will be placed on near term translation to clinical use.

- **Impact of field management and evacuation on the neurotrauma casualty**: Proposals are sought that characterize and offer solutions for secondary injury to the central nervous system as a result of hypotensive resuscitation as well as the MEDEVAC-related effects of hypobaria, noise, shock and vibration, and high G-Forces on the TBI and/or spinal cord injury (SCI) casualty. This research will result in improved early management and safe evacuation of brain and spinal cord casualties.
- **Characterization of functional changes in mTBI in casualties and operational forces and animal models of mTBI.** Proposals are sought for the characterization of functional changes in mTBI in casualties and operational forces and animal models of mTBI. Modalities can include, but are not limited to, advanced MRI techniques (DTI, resting fMRI, DSI), EEG and qEEG, and serum or tissue-based biomarkers of injury.
- **Prevention or reduction of training and combat-related brain injuries (specifically, mTBI/concussion) and mitigation of negative impact of concussion on cognitive and behavioral health.**

  Specific areas of interest include, but are not limited to:

  - Identification of mechanisms of neuroprotection in Warfighters with positive outcomes following exposure to mTBI event(s).
  - Develop an understanding of the time course of recovery using longitudinal studies with appropriate controls, starting from the mTBI event in theatre through evacuation, treatment, and recovery, as well as the interplay between concussion and other behavioral health issues and risk behaviors.

- Develop and validate standardized injury prediction algorithms, and integrate various prediction models into a single platform.
- Improve and validate neurocognitive assessment measures and metrics, and inform return-to-duty standards.
- Develop and validate evidence-based effective acute management therapies/ interventions.
- Assess the role of non-invasive/non-pharmacological interventions (e.g., sleep, exercise) in recovery from impact and/or blast-induced brain injury.

- **Development of field-deliverable forms or carriers of progesterone and related compounds that may be promising initial therapies for TBI.**
- **The role of pain in peripheral nerve trauma.**

  Areas of focus should include but are not limited to:

  - Post-amputation pain and pain syndromes of the mangled limb.
  - Assessment of the long-term effects of local anesthetic infusion (regional anesthesia) on peripheral nerves and muscles.
- **The discovery and development of restorative and rehabilitative concepts, technologies, and strategies for TBI-related hearing and balance injury and dysfunction that could support a full recovery to pre-injury functional capability (i.e., that of a deployable Warfighter).**

  Areas of focus include:

  - Studies to identify and characterize mechanisms associated with injury and dysfunction to exploit for treatment strategies.
  - Proof-of-concept studies in appropriate model systems of candidate technologies and strategies for restoration/rehabilitation.
  - Pre-clinical studies to advance candidate strategies and technologies to the point of readiness for clinical evaluations of safety and effectiveness. Device, biological, and pharmaceutical-based restoration/rehabilitation technologies will be considered.
  - Development of technologies for diagnostic tools, particularly those that would provide information to support treatment strategy selection.
  - Diagnostics
    1. Objective diagnosis and characterization of tinnitus
    2. Diagnosis and characterization of vestibular dysfunction
  - Restoration/Rehabilitation
    1. Treatment of tinnitus
    2. Rehabilitation of balance disorders, particularly using portable means

3. Restoration of auditory and vestibular function
4. Treatment of central auditory and vestibular processing disorders

- **Pain management associated with TBI.**

  Areas of focus include:

  - Research to support the development of best practices for assessing and managing acute pain and chronic pain in the battlefield and clinical environments (including novel pain control methods, complementary and alternative medicine techniques, and epidemiology of incidents of acute and chronic pain with respect to functional outcomes associated with TBI).
  - Strategies to identify and treat pain generators (including the pathophysiology of TBI associated pain, improved objective diagnostic tools for pain and development of predictors of pain development).
  - Addressing psychosocial aspects of managing pain (including improved understanding of and treatment implications of behavioral co-morbidities associated with TBI, patient empowerment, and family and other support systems).
  - Management of acute pain and chronic pain due to TBI. Of interest also are devices and therapies that can relieve pain with minimal effects on physical and cognitive performance, and that have minimal or no potential for addictions.

Clinical Science Areas:

- **Phase I/II clinical trials of neutraceuticals (e.g., DHA, Omega 3FFA) or promising pharmaceuticals for the treatment of the spectrum of TBI.** Combination therapies may also be considered.

Use of Human Subjects and Human Anatomical Substances: All DOD-funded research involving new and ongoing research with human subjects and human anatomical substances must be reviewed and approved by the USAMRMC Office of Research Protections (ORP), Human Research Protection Office (HRPO), in addition to the local Institutional Review Board (IRB) of record. Local IRB approval at the time of submission is not required. The HRPO is mandated to comply with specific laws and 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. Refer to the General Application Instructions, Appendix 5, for more information.

Data Management: The terms of assistance agreements initiated through this Program Announcement/ Funding Opportunity will require that investigators be prepared to submit TBI and SCI data from human subjects to a DOD/NIH Neurotrauma database (Federal Interagency Traumatic Brain Injury Research [FITBIR] Informatics System) utilizing the NINDS Common Data Element formats (see http://www.commondataelements.ninds.nih.gov/), along with appropriate supporting documentation. The goal of this data-sharing policy is to facilitate TBI and SCI research, and foster collaboration by providing the broader research community access

to publicly available high-quality data. The data-sharing policy for use with this database currently is being developed. Further information will be available for applicants in the near future**.**

Multi-institutional research: Multidisciplinary and multi-institutional projects are allowed. If the proposed research is multi-institutional, plans for communication and data transfer between the collaborating institutions, as well as how data, specimens, and/or imaging products obtained during the study will be handled, should be included in the Project Narrative. A separate intellectual and material property plan agreed upon by all participating institutions is also required for multi-institutional research. Participating institutions must be willing to resolve potential intellectual and material property issues, and to remove any barriers that may interfere with achieving high levels of cooperation to ensure successful completion of this award.

Encouraged DOD collaboration and alignment: Military relevance is a key feature of this award. Therefore, PIs are strongly encouraged to collaborate, integrate, and/or align their research projects with military and/or the U.S. Department of Veterans Affairs (VA) research laboratories and programs. The following websites may be useful in identifying information about ongoing DOD areas of research interest.

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

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

Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury
http://www.dcoe.health.mil

Defense and Veterans Brain Injury Center
http://www.dvbic.org/

Center for Deployment Psychology
http://www.deploymentpsych.org/

Deployment Health Clinical Center
http://www.pdhealth.mil/

DOD PH/TBI Research Program Investigator-Initiated Research Award 7 Center for the Study of Traumatic Stress
http://www.centerforthestudyoftraumaticstress.org/

National Center for Telehealth and Technology
http://www.t2health.org/

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

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

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

Navy and Marine Corps Public Health Center
http://www.nmcphc.med.navy.mil/

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

Office of Naval Research
http://www.onr.navy.mil/

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

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

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

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

Naval Health Research Center
http://www.nhrc.navy.mil/

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

Office of the Under Secretary of Defense for Acquisition, Technology and Logistics
http://www.acq.osd.mil/

Use of Active Duty Military and VA Populations: If the proposed research plan involves access to Active Duty Military and/or VA patient population(s), the Principal Investigator (PI) is responsible for establishing access to such populations. If possible, access to target Active Duty Military and/or VA patient population(s) should be confirmed at the time of application submission. A letter of support, signed by the lowest ranking person with approval authority, should be included for studies involving Active Duty military, veterans, military and/or VA controlled study materials, and military and/or VA databases.

D. Eligibility Information

- Independent investigators at all academic levels (or equivalent).
- Cost sharing/matching is not an eligibility requirement.
- Refer to the General Application Instructions, Appendix 1, for general eligibility information.

E. Funding

- The maximum period of performance is **4** years.
- The maximum allowable direct costs for the entire period of performance is **$2.0M** plus indirect costs.
- All direct and indirect costs of any subaward (subgrant or subcontract) must be included in the total direct costs of the primary award.
- Regardless of the period of performance proposed, the applicant should generally not exceed the maximum allowable direct costs. However, this is a general guideline and proposals will be assessed on potential for near-term benefit and cost-effectiveness of the investment along with the other stated screening criteria. Indirect costs shall be proposed in accordance with the organization's negotiated rate agreement.

Applications with the Partnering PI Option:

- For the Partnering PI Option, no additional funds will be provided. A separate award will be made to each PI's organization. The PIs are expected to be equal partners in the research, and direct cost funding should be divided accordingly unless otherwise warranted and clearly justified.
- The maximum period of performance is **4** years.
- The maximum allowable direct costs for the entire period of performance is **$2.0M** plus indirect costs.
- All direct and indirect costs of any subaward (subgrant or subcontract) must be included in the total direct costs of the primary award.

- Regardless of the period of performance proposed, the applicant may not exceed the maximum allowable direct costs. Indirect costs shall be proposed in accordance with the organization's negotiated rate agreement.

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

May be requested for (not all-inclusive):

- Salary
- Research-related subject costs
- Clinical research costs
- Equipment
- Research supplies
- Travel between collaborating organizations
- Travel costs of up to $1,800 per year to attend scientific/technical meetings
- Required travel costs:
    - Each PI must request travel funds to attend one program review per year during the award period of performance. For planning purposes, it may be assumed that program reviews will be held in the National Capitol Region.
    - In addition, each PI must request travel funds, up to $1,800, to attend one Military Health Research Forum (MHRF) or another DOD-sponsored meeting during the award period of performance. The MHRF is a DOD-sponsored meeting that is typically held every 2-3 years.

The Combat Casualty Care Joint Program Committee 6, Military Operational Medicine Joint Program Committee 5, and Clinical and Rehabilitative Medicine Joint Program Committee 8 expects to allot approximately $25.5M of the $100M FY11 PH/TBI Research Program appropriation to fund approximately 7-8 Applied Neurotrauma Research Award applications, depending on the quality and number of applications received. Funding of applications received in response to this Program Announcement/Funding Opportunity is contingent upon the availability of Federal funds for this program.

II. SUBMISSION INFORMATION

Submission is a multi-step process requiring both (1) pre-application submission through the CDMRP eReceipt System (https://cdmrp.org/) and (2) application submission through Grants.gov (http://www.grants.gov/).

The Applied Neurotrauma Research Award mechanism is structured to accommodate up to two PIs. One partner will be identified as the Initiating PI and will be responsible for the majority of the administrative tasks associated with application submission. The other PI(s) will be identified as the Partnering PI. Initiating and Partnering PIs each have different submission requirements; however, all PIs should contribute significantly to the development of the

proposed research project including the Project Narrative, Statement of Work, and other required components. The Initiating PI must complete the pre-application submission process and submit the contact information for each Partnering PI. The Partnering PI will then be notified separately by email. Please note that each Partnering PI must follow the link in this email and register with CDMRP eReceipt in order to associate his/her grant application package with that of the Initiating PI. If an application is invited, only the Initiating PI will receive a letter of invitation via email from CDMRP. The letter will provide the information necessary to begin application submission through Grants.gov.

A. Where to Obtain the Application Package

To obtain the complete application package, including all required forms, perform a Grants.gov (http://www.grants.gov/) basic search using the Funding Opportunity Number: W81XWH-11-PHTBI-ANRA.

B. Pre-Application Submission Content and Form

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

PIs and organizations identified in the 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.

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**

  The Initiating PI must enter the contact information for the Partnering PI in the Partnering PI section**.**

- **Required Files – Tab 4**

  Preproposal Narrative (three-page limit): The Preproposal Narrative page limit applies to text and any figures, tables, graphs, photographs, diagrams, chemical structures, pictures, pictorials, and cartoons.

  The Preproposal Narrative should include the following:

  - **Rationale:** Present the ideas and reasoning behind the proposed study, to include relevant literature citations. State how this project meets the intent of the award mechanism and the intent of the program.

- **Hypothesis or Objective:** State the hypothesis to be tested or the objective to be reached.
- **Research Strategy:** Concisely state the project's objective and specific aims. Describe the proposed methods and how they will accomplish the project's aims.
- **Research Area:** Explain how the proposed work addresses one or more of the required research areas.
- **Military Benefit:** State explicitly how the proposed work will have an impact on the prevention, detection, diagnosis, and/or treatment of military-relevant TBI issues. Describe how the proposed work is responsive to the health care needs of warriors, veterans, families, caregivers, and/or communities.

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

- **Quad Chart:** 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:
  - 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.
- References Cited (one-page limit)
- Key Personnel Biographical Sketches (four-page limit per individual)

- **Submit Pre-application – Tab 5**
- **Other Documents Tab**

  No additional documents are required**.**

Pre-Application Screening

- **Pre-Application Screening Criteria**

  To determine the technical merits of the pre-application and the relevance to the mission of the DOD, CCC JPC-6, MOM JPC-5, and CRM JPC-8, pre-applications will be screened based on the following criteria:

- **Military Benefit:** What impact these studies will have on the outcomes of Service Members and/or veterans.
- **Research Idea:** How the proposed project addresses the intent of the award mechanism and the program. How well delineated and appropriate is/are the hypothesis(-es) to be tested or the objective(s) to be reached.
- **Research Strategy**: How the rationale and specific aims support the project's objective. How appropriate are the proposed methods and how will they accomplish the project's aims.
- **Personnel:** How the personnel's background and expertise are appropriate to accomplish the proposed research.

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

  Following the pre-application screening, Initiating PIs will be notified of whether or not they are invited to submit an application, and they will not receive feedback (e.g., a critique of strengths and weaknesses) on their pre-application. Pre-application notification dates are indicated on the title page of this Program Announcement/ Funding Opportunity.

C. Application Submission Content and Form

Applications will not be accepted unless the PI or the Initiating 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 the Grants.gov portal (http://www.grants.gov/). For the FY11 PH/TBI Applied Neurotrauma Research Award, additional application components are also required and should be submitted as directed below.

For the Partnering PI Option: The CDMRP requires separate Grants.gov application package submissions for the Initiating PI and each Partnering PI. Initiating and Partnering PIs will each be assigned unique and separate log numbers by the CDMRP eReceipt System. Each Grants.gov application package must be submitted using the unique log number.

Application Components for Single PIs or for Initiating PIs under the Partnering PI Option:

Grants.gov application package components: For the FY11 PH/TBI Applied Neurotrauma Research Award, the Grants.gov application package includes the following components (refer to the General Application Instructions, Section II.C., for additional information on application submission):

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

2. Attachments Form

- **Attachment 1: Project Narrative (15-page limit):** Upload as "ProjectNarrative.pdf."

  Describe the proposed project in detail using the outline below.

  - **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.
  - **Hypothesis or Objective:** 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.

  Submissions that include clinical interventions and/or clinical research:

  Submissions that include clinical research will be evaluated using additional review criteria, which are outlined in Section III.B.1. of this Program Announcement/Funding Opportunity. Therefore, the following items should also be described within the Project Narrative:

  - **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.

- **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: List the references cited (including URLs if available) in the project narrative using a standard reference format that includes the full citation (i.e., author[s], year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).
    - List of Abbreviations, Acronyms, and Symbols: Provide a list of abbreviations, acronyms, and symbols.
    - Facilities, Existing Equipment, and Other Resources: Describe the facilities and equipment available for performance of the proposed project, and any additional facilities or equipment proposed for acquisition at no cost to the USAMRMC. 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 (five-page limit): Include relevant publication URLs and/or patent abstracts. If publications are not publicly available, then they must be included. 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 or appropriate organization official, reflecting the laboratory space, equipment, and other resources available for the project.
    - Letters of Collaboration (if applicable) (two-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.
    - Data and Research Resources Sharing Plan: Describe how data and resources generated during the performance of the project will be shared with the research community. Refer to the General Application Instructions, Appendix 4, for more information about the CDMRP expectations for making data and research resources publically available.
- **Attachment 3: Technical Abstract (one-page limit):** Upload as "TechAbs.pdf."

  Technical abstracts should be written using the outline below.
    - Background: Present the ideas and reasoning behind the proposed work.

- Objective/Hypothesis: State the objective/hypothesis to be tested. Provide evidence or rationale that supports the objective/hypothesis.
- Specific Aims: State the specific aims of the study.
- Study Design: Briefly describe the study design including appropriate controls.
- Innovation: Briefly describe how the proposed project is innovative.
- Impact: Briefly describe how the proposed project will have an impact on TBI research or patient care.

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

  Public abstracts should be written using the outline below.

  - Clearly describe, in a manner readily understood by lay persons, the rationale and objective for the proposed work.
    - Do not duplicate the technical abstract.
  - Describe the ultimate applicability of the research.
    - What types of patients will it help, and how will it help them?
    - What are the potential clinical applications, benefits, and risks?
    - What is the projected time it may take to achieve a patient-related outcome?
  - If the research is too basic for clinical applicability, describe the interim outcomes.
  - What are the likely contributions of this study to advancing the field of TBI research or patient care?

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

  Each PI must submit an identical copy of a jointly created SOW. The contributions of the Initiating PI and Partnering PI should be noted for each task.

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

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

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

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

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

- Describe the recruitment process in detail. Address who will identify potential human subjects, who will recruit them, and what methods will be used to recruit them.
- Include a detailed description of and justification for the compensation plan if the human subjects will be compensated for participation in the study.
- Describe the recruitment and advertisement materials. The recruitment materials should not be coercive or offer undue inducements, and should accurately reflect the study.

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

- Identify who is responsible for explaining the study, answering questions, and obtaining informed consent.
- Include information regarding the timing and location of the consent process.
- Address issues relevant to the mental capacity of the potential human subject (e.g., altered capacity due to administration of any mind-altering substances such as tranquilizers, conscious sedation or anesthesia, brain injury, stress/life situations, or human subject age), if applicable.
- Address how privacy and time for decision making will be provided, and whether or not the potential human subject will be allowed to discuss the study with anyone before making a decision.
- Consider the need for obtaining ongoing consent or for re-assessing capacity over the course of a long-term study, and describe any relevant procedures to assure continued consent.
- Describe the plan for the consent of the individual's Legally Authorized Representative (LAR) to be obtained prior to the human subject's participation in the study. State law defines who may act as the LAR. The

local IRB of record should be consulted for guidance regarding who can serve as LAR for research at the study site. Note: The PI must describe a clear intent to benefit for human subjects who cannot give their own consent to participate in the proposed clinical trial to be in compliance with Title 10 United States Code Section 980 (10 USC 980) (http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=browse_usc&docid=Cite:+10USC980. If applicable, please refer to the General Application Instructions, Appendix 5, for more information.

- Provide a draft in English of the proposed Informed Consent Form. A plan for ensuring that human subjects' questions will be addressed during the consent process and throughout the trial should be included.
- ***Assent.*** If minors or other populations that cannot provide informed consent are included in the proposed clinical trial, a plan to obtain assent (agreement) from those with capacity to provide it, or a justification for a waiver of assent should be provided. PIs should consult with their local IRB to identify the conditions necessary for obtaining assent.

e. Screening Procedures: List and describe any evaluations (e.g., laboratory procedures, history, or physical examination) that are required to determine eligibility/suitability for study participation and the diagnostic criteria for entry. Please note that some screening procedures may require a separate consent or a two-stage consent process. Informed consent must be obtained prior to initiation of any procedures for the purpose of determining eligibility.

f. Risks/Benefits Assessment:

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

to drive) or equipment (e.g., thermometers, telemedicine equipment) needed for human subjects enrolled in the study.

- **Potential benefits:** Describe known and potential benefits of the study to the human subject, a specific community, or society.

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

  a. Description of the Intervention: As applicable, the description of the intervention should include the following components: source, dose, schedule, administration route, washout period, duration of the intervention, and concomitant medications allowed. Description of devices should include detailed operational instructions, and any potential risks to users, and intended benefits. Other types of interventions should be fully described.

  b. Study Procedures: Describe the interaction with the human subject to include the study intervention that he/she will experience. Provide sufficient detail in chronological order for a person uninvolved in the study to understand what the human subject will experience. Provide a schedule (e.g., flowchart or diagram) of study evaluations and follow-up procedures.

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

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

  - **Identifiers:** Describe the unique identifiers or specific code system to be used to identify human subjects, if applicable.
  - **Confidentiality:**
    - Explain measures taken to protect the privacy of human subjects in the study and to maintain confidentiality of study data. Strategies to protect the privacy and confidentiality of study records, particularly those containing identifying information, should be addressed.
    - Address who will have access to study records, data, and specimens, including an acknowledgment that representatives of USAMRMC are eligible to review study records.
    - Address requirements for reporting sensitive information to state or local authorities.
  - **Disposition of data:** Describe where data (both electronic and hard copy) will be stored, who will keep the data, how the data will be stored, and the length of time data will be stored.
  - **Sharing study results:** In cases where the human subject could possibly benefit medically or otherwise from the information, explain whether or not the results of screening and/or study participation will be shared with human

subjects or their primary care provider, to include results from any screening or diagnostic tests performed as part of the study.

b. Laboratory Evaluations:

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

- **Attachment 9: Study Personnel and Organization (if applicable) (no page limit):** Upload as "Personnel.pdf." The Study Personnel and Organization attachment should include the components listed below.

a. Principal Investigator/Study Staff: Provide an organizational chart identifying key members of the study team including institution/center/ department. Briefly describe their roles on the project. For clinical projects, a medical monitor (external to the study and not reimbursed by the study) and study coordinator(s) should be included.

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

- **Attachment 10: Surveys, Questionnaires, and Other Data Collection Instruments, if applicable (no page limit):** Upload as "Surveys.pdf." The Surveys, Questionnaires, and Other Data Collection Instruments attachment should include a copy of the most recent version of surveys, questionnaires, data collection forms, rating scales, interview guides, or other instruments. For each instrument, describe how the information collected is related to the objectives of the study.

- **Attachment 11: Impact Statement (one-page limit).** Upload as "Impact.pdf."

  State explicitly how the proposed work will have an impact on the prevention, detection, diagnosis, and/or treatment of military-relevant TBI issues. Describe how the proposed work is responsive to the health care needs of warriors, Veterans, families, caregivers, and/or communities.

  For Clinical Trials and/or Clinical Research

  - Identify the volunteer population(s) that will participate in the proposed intervention, and describe the potential impact of the proposed clinical trial on the health and well-being of military personnel and their families.
  - Describe the short-term impact: Detail the anticipated outcomes that will be directly attributed to the results of the proposed clinical trial.
  - Describe the long-term impact: Explain the long-range vision for implementation of the intervention in the clinic or field, and describe the anticipated long-term benefits for the targeted population.
  - Compare the proposed intervention to pharmacologic agents, devices, and/or clinical guidance currently available, if applicable.

- **Attachment 12: Transition Plan (one-page limit).** Upload as "Transition.pdf." Provide information on the methods and strategies proposed to move the product to the next phase of clinical trials and/or delivery to the military or civilian market after successful completion of the award. The transition plan should include the components listed below.
  - Details of the funding strategy that will be used to bring the outcomes to the next level of clinical trials and/or delivery to the military or civilian market (e.g., specific potential industry partners, specific funding opportunities to be applied for).
  - A description of collaborations and other resources that will be used to provide continuity of development.
  - A brief schedule and milestones for bringing the outcome(s) to the next phase of clinical trials and/or delivery to the military or civilian market.
  - A risk analysis for cost, schedule, manufacturability, and sustainability.

- **Attachment 13: Military Benefit Statement (one-page limit):** Upload as "MilBen.pdf."

  State explicitly how the proposed work, if successful, will have an impact on the movement of promising treatments into clinical practice for service members and/or veterans with deployment-related TBI problems.

  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. Show how the proposed studies complement ongoing DOD and VA areas of research interest.

- **Attachment 14: Letters Confirming Access to Target Military or VA Patient Population(s) (one-page limit):** Upload as "Access.pdf."

  If applicable, provide a letter(s) signed by the lowest ranking person with approval authority for studies involving Active Duty military, veterans, military and/or VA-controlled study materials, and military and/or VA databases.

- **Attachment 15: Current Quad Chart (one-page limit):** Upload as "Quad.pdf."

  Provide a current Quad Chart in the same format as in the pre-application. If no changes have been made to the project, the same Quad Chart submitted with the pre-application may be used.

3. **Research & Related Senior/Key Person Profile (Expanded) Form:** 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."

   For the Partnering PI Option: Initiating and Partnering PIs must each submit a budget and justification as part of their separate Grants.gov application packages. The Research & Related Budget form for the Initiating PI should not include budget information for the Partnering PIs, even if they are at the same organization.

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.

Application Components for the Partnering PI:

The Partnering PI must follow the link in the email from CDMRP eReceipt and complete the registration process prior to the application submission deadline in order to associate his/her grant application package with that of the Initiating PI.

The application submission process for the Partnering PI uses an abbreviated application package of forms and attachments from Grants.gov that includes:

1. **SF 424 (R&R) Application for Federal Assistance Form**

2. **Attachments Form**

   - **Attachment 5: Statement of Work (SOW) (three-page limit):** Upload as "SOW.pdf." Refer to the General Application Instructions, Section II.C., for detailed information on completing the SOW. ***Each PI must submit an identical copy of a jointly created SOW. The contributions of the Initiating PI and Partnering PI should be noted for each task.***

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

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

   Initiating and Partnering PIs must each submit a budget and justification as part of their separate Grants.gov application packages. The Research & Related Budget form for the Initiating PI should not include budget information for the Partnering PIs, even if they are at the same organization.

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

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

D. Applicant Response to Scientific Peer Review Summary Statement (if applicable) (five-page limit):

The Grants Officer reserves the right to require that ALL applicants provide written responses to issues or concerns identified by reviewers in the Scientific Peer Review Summary Statements. In the event that the DOD determines that such is required, a response template will be provided to applicants (for use in crafting replies) at the time of Summary Statement distribution to applicants via the CDMRP eReceipt System.

This will not be an opportunity to introduce new elements to the application, only clarify elements of the original submission. Every section of the response template must have a statement provided.

All responses will be reviewed by the primary, secondary, and tertiary peer reviewers responsible for the original scientific review. Reviewers' supplemental comments will be forwarded to Programmatic Review for consideration along with the original Summary Statements. Failure by applicants to submit the responses by the deadline identified in the email notification of the requirement will result in administrative withdrawal of the application.

E. Submission Dates and Times

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

F. Other Submission Requirements

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

All applications must be submitted through Grants.gov. Organizations are required to provide a Data Universal Number 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 Process

All applications are evaluated by scientists, clinicians, and consumer advocates using a two-tier review process. The first tier is a peer review of applications against established criteria for determining technical merit. The second tier is a programmatic review that compares applications to each other and makes recommendations for funding to the Commanding General, USAMRMC, for concurrence, and then to the Office of the Assistant Secretary of Defense for Health Affairs for final approval, based on technical merit, the relevance to the mission of the DOD, CCC JPC-6, MOM JPC-5, and CRM JPC-8 and the specific intent of the award mechanism. The highest scoring applications from the first tier of review are not automatically recommended for funding. Additional information about the two-tier review process used by the CDMRP can be found at http://cdmrp.army.mil/about/fundingprocess.

All CCC JPC-6, MOM JPC-5, and CRM JPC-8 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 (Title 18 United States Code 1905).

B. Application Review Criteria

1. **Peer Review:** To determine technical merit, all applications will be evaluated according to the following scored criteria.

Applications that <u>do not include</u> clinical interventions or clinical research will be evaluated according to the following criteria, which are of equal importance.

- **Impact**
  - How the proposed study addresses at least one of the FY11 PH/TBI Applied Neurotrauma Research Award Research Areas.
  - The potential contribution of the proposed study to research and/or patient care in the FY11 PH/TBI Applied Neurotrauma Research Award Research Area(s) addressed.
- **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.
  - How the PI describes 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.
  - Are proposed animal models established/validated (if applicable).
- **Innovation**
  - 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.
- **Personnel**
  - How the background and expertise of the PI and other key personnel demonstrate their ability to perform the proposed work.
  - How the levels of effort by the PI and other key personnel are appropriate to ensure success of this project.
  - How the PI's record of accomplishment demonstrates his/her ability to accomplish the proposed work.

Applications that <u>include</u> clinical interventions or clinical research will be evaluated according to the following criteria, which are of equal importance.

- **Clinical Impact**
  - How the proposed study addresses at least one of the FY11 PH/TBI Applied Neurotrauma Research Award Research Areas.
  - How the results of the proposed clinical study will affect the magnitude and scope of potential clinical applications in the FY11 PH/TBI Applied Neurotrauma Research Award Research Areas(s) addressed.
  - 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 intervention is supported by the preliminary data, critical review and analysis of the literature, and/or prior clinical evidence.
    - 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, if applicable.
    - How well the inclusion and randomization criteria meet the needs of the proposed clinical trial, if applicable.
    - 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.
- **Transition Plan**
    - Whether the funding strategy described to bring the outcome(s) to the next level of clinical trials and/or delivery to the military and/or civilian market is appropriate.
    - Whether appropriate collaborations and other resources for providing continuity of development are established and/or well described.
    - How the schedule and milestones for bringing the outcome(s) to clinical trial and/or delivery to the military and/or civilian market is appropriate.
    - How well the potential risk analysis for cost, schedule, manufacturability and sustainability is developed.
- **Personnel**
    - How the background and expertise of the PI and other key personnel demonstrate their ability to perform the proposed work.
    - How the levels of effort by the PI and other key personnel are appropriate to ensure success of this project.
    - How the PI's record of accomplishment demonstrates his/her ability to accomplish the proposed work.

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

- **Environment**
  - The appropriateness of the scientific environment for the proposed research.
  - How the research requirements are supported by the availability of and accessibility to facilities and resources (including collaborative arrangements).
  - The quality and extent of institutional support are appropriate for the proposed research.
- **Budget**
  - Whether the budget is appropriate for the proposed research and within the limitations of this Program Announcement/Funding Opportunity.
- **Application Presentation**
  - To what extent the writing, clarity, and presentation of the application components influenced the review.

2. **Programmatic Review:** To determine the application's relevance to the mission of the DOD and JPC-6, JPC-5, and JPC-8, as well as to make funding recommendations, the following criteria are used by programmatic reviewers:

- **Responsiveness to Research Projects, Tasks, and Gaps**
  - How well the proposed study meets the Traumatic Brain Injury focused tasks within the project addressed, if successful.
  - How well the proposed study accelerates core research efforts.
- **Impact on Military Population**
  - How much the proposed project contributes to accelerating the fulfillment of military requirements, if successful.
  - How the plan to access the military populations, if applicable, is appropriate and feasible.
  - How well the research study solves a documented military problem.
- **Ratings and Evaluations of the Scientific Peer Reviewers**
  - Scientific merit of the proposed project will be considered in the context of the military relevance and programmatic review, and compared to all eligible applications under consideration.

C. Recipient Qualification

Refer to the General Application Instructions, Appendix 1, for additional information on organization and Government agency requirements.

D. Application Review Dates

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

E. Notification of Application Review Results

Each PI and organization will receive notification of the funding recommendation. PIs will receive a scientific peer review summary statement on the strengths and weaknesses of the application.

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

The following will result in administrative rejection of the application:

- Project Narrative exceeds page limit.
- Project Narrative is missing.
- Budget is missing.
- Pre-application was not submitted.
- Submission of an application for which a letter of invitation was not received.
- All associated applications (Initiating and Partnering PI) are not submitted by the deadline.

B. Modification

- Pages exceeding the specified limits will be removed prior to review for all documents other than the Project Narrative and Preproposal Narrative.
- Documents not requested will be removed.
- Following the application deadline, you may be contacted by CDMRP via email with a request to provide certain missing supporting documents (excluding those listed 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.

C. Withdrawal

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

- Applicant Response to Scientific Peer Review Summary Statement was not submitted prior to specified deadline (if applicable).
- FY11 PH/TBI Research Program CCC JPC-6, MOM JPC-5, and CRM JPC-8 member is 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 FY11 PH/TBI Research Program CCC JPC-6, MOM JPC-5, and CRM JPC-8 members may be found at http://cdmrp.army.mil/phtbi/panels/panels11.
- Submission of the same research project to different funding opportunities within the same program and fiscal year.
- The pre-application or application does not conform to this Program Announcement/ Funding Opportunity description to an extent that precludes appropriate review.
- Direct costs as shown on the Research and Related Budget form exceed the maximum allowed by this Program Announcement/Funding Opportunity.
- Inclusion of URLs with the exception of links to published references.
- Page size is larger than 8.5 inches x 11.0 inches (approximately 21.59 cm x 27.94 cm).
- Human Subject Recruitment and Safety Procedures attachment (Attachment 6) is missing (for clinical trial applications).
- Intervention attachment (Attachment 7) is missing (for clinical trial applications).
- Data Management attachment (Attachment 8) is missing.
- IDE/IND has not been submitted and/or cleared/approved (if applicable).
- 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 institutional investigation. The institution will be required to provide the findings of the investigation to the US Army Medical Research Acquisition Activity (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, 2012. 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 C, for general information regarding administrative and national policy requirements.

C. Reporting

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

Quarterly technical progress reports will be required.

D. Award Transfers

Refer to the General Application Instructions, Appendix 4, Section E, for general information on organization or PI changes.

The transfer of an award to another institution is strongly discouraged. A transfer will not be allowed for any institution that includes a study site/clinical trial at its location. Approval of a transfer request from an institution that does not include a study site at its location will be at the discretion of the USAMRAA Contracting/Grants Officer.

VI. AGENCY CONTACTS

A. CDMRP Help Desk

Questions related to Program Announcement/Funding Opportunity content or submission requirements and 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	Initiating PI Completed	Partnering PI 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 Public Abstract (PublicAbs.pdf) as Attachment 4.		
	Upload Statement of Work (SOW.pdf) as Attachment 5.		
	Upload Human Subject Recruitment and Safety Procedures (HumSubProc.pdf), if applicable, as Attachment 6.		
	Upload Intervention (Intervention.pdf) as Attachment 7.		
	Upload Data Management (Data_Manage.pdf) as Attachment 8.		
	Upload Study Personnel and Organization (Personnel.pdf) as Attachment 9.		
	Upload Surveys, Questionnaires, and Other Data Collection Instruments (Surveys.pdf), if applicable, as Attachment 10.		
	Upload Impact Statement (Impact.pdf) as Attachment 11.		
	Upload Transition Plan (Transition.pdf) as Attachment 12.		
	Upload Military Benefit Statement (MilBen.pdf) as Attachment 13.		
	Upload Letters Confirming Access to Target Military or VA Patient Population(s) (Access.pdf) as Attachment 14.		
	Upload Current Quad Chart (Quad.pdf) as Attachment 15.		

Grants.gov Application Components	Action	Initiating PI Completed	Partnering PI Completed
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 form 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.		