Program Announcement

Department of Defense Congressionally Directed Medical Research Programs

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

Advanced Technology/Therapeutic Development Award

Funding Opportunity Number: W81XWH-09-PH/TBIRP-AT/TDA

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I. FUNDING OPPORTUNITY DESCRIPTION

A. Program Background

The Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury (DCoE) was established in 2007 under Department of Defense (DoD) Health Affairs to lead a collaborative global network to optimize Psychological Health (PH) and Traumatic Brain Injury (TBI) treatment for the DoD. The support of basic, translational, and clinical research is critical to DCoE's mission to validate, oversee, and facilitate prevention, resilience, identification, treatment, outreach, rehabilitation, and reintegration for the nation's warriors and their families. The DCoE takes a holistic approach to serving warriors, Veterans, families, caregivers, and communities, and is a source of leadership for a national network of medical, organizational, community support, academic, research, and advocacy assets.

B. Program Objectives

The objective of the current program is to promote research that will advance the prevention, detection, diagnosis, and treatment of military-relevant PH issues and TBI. Funding will be focused on innovative projects that have the potential to make a significant near-term impact on improving the function, wellness, and overall quality of life for warriors, Veterans, families, caregivers, and communities. It is anticipated that approximately $40.6M will be available to support PH/TBI research in FY09. The Government reserves the right to increase or decrease the PH/TBI funding of $40.6M to execute the program.

Proposals involving multidisciplinary collaborations among academia, industry, the military Services, the Department of Veterans Affairs, and other Federal Government agencies are highly encouraged. Though the program supports groundbreaking research, all projects must demonstrate solid judgment and rationale.

C. FY09 PH/TBI Research Program Congressionally Directed Topic Areas

This Program is focused on the spectrum of PH and TBI research from basic, applied, and clinical research, to translational research that transforms scientific discoveries into clinical applications and best practices that prevent, mitigate, and effectively treat TBI and optimize PH in the short and long term. The goal is to increase understanding of the etiology of PH problems, TBIs, and associated comorbidities – including patients with TBI and/or Post-Traumatic Stress Disorder (PTSD), depression, anxiety, and/or substance dependence/abuse – in order to develop preventive interventions and new treatments and to arrive at evidenced-based solutions.

The following paragraphs describe in greater detail examples of broad categories of interest, and include incorporating training, combat theater operations, and post-deployment evidence-based preventive and early intervention measures, practices, or procedures to reduce the likelihood that personnel in combat will develop PTSD or other stress-related conditions or sustain traumatic brain injuries. Priorities include interventions across the deployment lifecycle for warriors, Veterans, families, caregivers, and communities, particularly those at risk for mental disorders and psychosocial problems. Investigators are encouraged to take into account considerations for special populations, such as gender-specific or racial/ethnic groups as a focus. Consideration of

Active Duty, Reserve Component, National Guard and/or Veteran populations is also encouraged.

All applications for funding must specifically and clearly address <u>at least one</u> of the following topic areas and have direct relevance to the health care needs warriors, Veterans, families, caregivers, and/or communities. Proposals should focus on basic, translational, clinical, and/or preventive medicine research within PH/TBI. The intended or target population (Active Duty, Reserve Component, National Guard and/or Veterans) should be noted. Specific areas of interest are those listed below.

1. Studies aimed at improving the understanding of military-related psychological health issues in specific areas of interest.

The objective of this topic area is to improve understanding of combat-related psychological health as related to diagnosis, treatment, and prevention. Studies must be clearly aimed at developing evidence-based solutions to improve the diagnosis, treatment, and prevention of military-related stress disorders and co-morbid conditions such as drug/alcohol abuse and depression. Basic research solutions should be developed to fill gaps that may be related to improving therapeutic approaches. Preference will be given to studies that clearly demonstrate immediate impact. Specifically, topic areas include:

- Identification/validation of risk factors associated with PTSD and co-morbid conditions that can be used to develop improved metrics and tools for assessment of combat-related psychological health disorders.
- Identification of risk factors for the safety of redeployment of Service members for multiple tours.
- Identification of barriers to treatment for PH issues and TBI, especially for Service members returning to the civilian community from their Reserve and National Guard status.
- Basic research aimed at improving understanding of psychological resilience in military populations that can be used to develop and/or validate novel strategies to reduce psychological health disorders.
- Validated resilience-building interventions demonstrating improved or enhanced mental health and/or well-being.
- Studies of novel and early interventions using mono-, adjunctive, or combination therapeutic approaches for combat-related psychological health disorders.
- Basic research on the biological mechanisms that underlie human emotional reactions to combat stress and associated clinical symptoms or disorders.
- Basis of neuropsychiatric disorders associated with combat-related PTSD and TBI.

2. Studies to examine cellular regrowth and interconnection strategies and therapies in the central nervous system (brain and spinal cord).

The objective of this topic area is to increase understanding of neuroregeneration and to facilitate the translation of that understanding into improved treatment of neurological conditions and improved neurorehabilitation. Research areas of interest include:

- Investigation of basic mechanisms of cellular regrowth.
- Examination of pharmaceutical and/or other approaches to neural regrowth and injury including, blast-related cell damage and resulting effects on neurological response.

3. Research on evidence-based prevention and rehabilitation strategies for TBI, PTSD, and co-occurring conditions encompassing cognitive, motor, emotional, psychological, and sensory functioning.

The objective of this topic is to improve rehabilitative approaches to the treatment of PTSD, TBI, and co-morbid conditions. Research must employ rigorous validation criteria to assure safety and efficacy, and proper control groups and sham conditions where appropriate. Therapeutic approaches must be applicable to use in the military population. Approaches of interest include:

- "Activity-based" physical therapy
- Computer-based approaches
- Complementary or alternative medicine approaches
- Combination therapies

4. Three-dimensional models of Improvised Explosive Device (IED) blast waves to develop equipment to mitigate injury to Service members.

The objective of this topic area is to develop biomedically valid computational models of blast-related TBI that can be used to design, build, and test personal protection systems, such as combat helmets, and combat vehicle crew protection systems that prevent blast-related TBI.

Furthermore, this topic area is intended to support studies that take an end-to-end approach that combines appropriate animal injury and/or post-mortem human studies (PMHS) with computational modeling, and include model validation. Blast-related TBI mechanisms of interest include:

- Blunt force impact
- Blast overpressure
- Acceleration

- Force transference
- Combinations of the above

5. PH and/or TBI research exploring the use of advanced neuroimaging, behavioral and/or genetic information to identify biomarkers and to develop diagnostics and treatments for semi-acute, acute, and chronic injury stages, and for the possible integration of informatics and advanced computational research to better understand the intersection of PH and TBI.

The objective of this topic area is to identify reliable, biologically based, and assayable indicators of psychological health status or TBI. Special areas of interest include:

- DA-EEG assessment and MRI quantization to allow accurate assessment of TBI.
- Identification of biomarkers specific to and capable of distinguishing between PTSD, TBI, and their co-occurance. Computational approaches to integrate global transcriptomics and proteomics information to identify the biological networks that are altered following TBI.
- A fully automated, self-contained, disposable chip to diagnose TBI at the point of injury based on validated criteria for diagnosis.

If the proposed project is not relevant to a specified FY09 PH/TBI Research Program topic area, the Government reserves the right to administratively withdraw the proposal.

D. Award Description

The PH/TBI Research Program Advanced Technology/Therapeutic Development Award is intended to support the assessment of scientific and/or military field deployment feasibility for promising new products, pharmacologic agents (drugs or biologics), behavioral interventions, devices, clinical guidance, and/or emerging approaches and technologies. These awards are expected to yield potential products, approaches, or technologies for the treatment, prevention, detection, and/or diagnosis of PH issues and/or TBI. The products developed may be pharmacologic agents (drugs, biological), cognitive/behavioral interventions, devices, or clinical guidance.

Military relevance is a key feature of this award. All applications must specifically and clearly address the military relevance of the proposed research. Each PI must provide a transition plan (including funding and resources) showing how the product will progress to clinical trials and/or delivery to the military market after the successful completion of this PH/TBI Research Program award.

The overall goal of this award mechanism is to accelerate the introduction of improved therapies, treatments, devices, or technologies for PH/TBI into the clinical setting. Examples of the types of research that may be supported include, but are not limited to:

- Collection and analysis of data for developing and validating clinical guidance.
- Developing new behavioral or cognitive interventions.

- Testing new therapeutic modalities (agents, delivery systems, chemical modification of lead compounds) using established or validated novel preclinical systems.
- Comparative activity/efficacy testing to define a single lead agent from a limited library of candidates.
- Designing and implementing full-scale, pilot Good Manufacturing Practice (GMP) production of therapeutics and/or delivery systems for use in advanced preclinical and initial clinical trials.
- Developing pharmacologic agents through the elements of adsorption, distribution, metabolism, excretion, and toxicity (ADMET).
- Developing pharmacologic agents to Investigational New Drug (IND) stage for initiation of Phase I clinical trials.
- Developing prototype devices for diagnosis or treatment to Investigational Device Exemption (IDE) stage for initiation of Phase I clinical trials.
- Generation of safety and/or efficacy data (e.g., Phase I or Phase I/II clinical studies) on therapeutics and devices in clinical trials.
- Development and validation of assays and reagents required to measure biological responses and molecular endpoints.
- Developing and validating computational models.
- Optimizing diagnostic or treatment devices for field deployment.

Preference will be given to proposals that include preliminary and/or published data relevant to the PH/TBI topic area and the proposed project, but omission of these will not be a disqualifying factor.

Partnering PI Option: As a method to support an accelerated assessment of scientific and/or military market feasibility for promising new products, devices, and/or emerging technologies, the FY09 PH/TBI Research Program is offering a Partnering PI option for this award mechanism. Development of the research plan should involve a reciprocal flow of ideas and information with equal intellectual input from all partners into the design of a single research project. For example, a proposed project in which a partner merely supplies support services, tissue samples, or access to patients will not meet the intent of this option.

This award option is structured to accommodate up to three PIs. One member of the team will be identified as the Initiating PI, who will be responsible for the majority of the administrative tasks associated with application submission. The other members will be identified as the Partnering PI(s) and will need to complete administrative tasks associated with application submission. Separate awards will be made to each PI's institution. One Initiating and up to two Partnering PIs may be designated. Additional collaborators may be included, but they will not be designated as PIs. Multidisciplinary and multi-institutional projects are allowed. If the project is multi-institutional, PIs should include plans for communication between investigators at each institution. Additionally, participating institutions must be willing to resolve potential intellectual and material property issues, and to remove any barriers that might interfere with achieving high levels of cooperation to ensure successful completion of this award.

Submissions that include clinical research involving humans should:

- Describe clearly defined and appropriate endpoints for the proposed clinical research
- Clearly articulate the statistical analysis plan
- Discuss the potential impact of the study results for patients with the specified disease/condition
- Include a named study coordinator who will guide the clinical protocol through Institutional Review Board (IRB), Human Subjects Research Review Board (HSRRB), and other regulatory approval processes, coordinate activities from all sites participating in the trial, and coordinate participant accrual

Multi-institutional research: If the proposed research is multi-institutional, plans for communication and data transfer between the collaborating institutions, as well as how 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.

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 VA research laboratories and programs. The following websites may be useful in identifying information about ongoing DOD areas of research interest within the FY09 PH/TBI Research Program topic areas:

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/

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
www-nmcphc.med.navy.mil/main.htm

U.S. Department of Veterans Affairs, Office of Research and Development
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
www.nrl.navy.mil

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

U.S. Army Medical Research Acquisition Activity
http://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 Military Populations: Describe the military population(s) to be used for the proposed study, if applicable. Coordination of access to various military populations is described below.

1. Active Duty, National Guard, Reserve troops, and/or military patient populations (not CENTCOM Area of Responsibility)**:** Unless the PI has an already established Service member population, access to Active Duty, National Guard, or Reserve troops must be coordinated through the CDMRP. ***PIs who do not have a previously established study population should not contact unit Commanders at this time or during preparation of the proposal submission. If selected for funding, the PI will be provided guidance on how to obtain access to the appropriate population.***

2. CENTCOM Area of Responsibility military populations: Access to military populations in these areas is very limited and will be coordinated through the CDMRP as described above.

Research conducted using military populations in Iraq is conducted with oversight by the Multi-National Force-Iraq (MNF-I). PIs that are outside of this system and submit a research proposal designed to recruit patients within MNF-I must coordinate with the in-theater Deployed Combat Casualty Research Team charged with facilitating an in-theater review, and be approved by the MNF-I Command and the MNF-I designated Institutional Review Board (IRB). The same is true for research conducted in Afghanistan in the US Forces-Afghanistan (USFOR-A) Area of Responsibility. PIs who are outside of this system and submit a research proposal designed to recruit patients within USFOR-A must coordinate with the in-theatre Deployed Combat Casualty Research Team charged with facilitating an in-theatre review, and be approved by the USFOR-A Command and the USFOR-A designated IRB. If selected for funding, CDMRP will assist with guidance on how to obtain the required in-theater approvals.

Given the constraints of wartime operations, investigators without an ongoing collaboration with an appropriate military investigator should strongly consider alternatives to conducting in-theater research. DOD-supported human subjects research can only be conducted by institutions (including those in-theater) with approved Federal Assurances of Compliance from the Human Research Protection Office (HRPO). It is strongly suggested that proposals necessitating the use of this population involve civilian and non-deployed military populations as an alternative.

3. **Department of Veterans Affairs (VA) Medical Centers patient populations:** Access to patient populations from VA Medical Centers or use of information from VA data systems must be coordinated by the PI. PIs who submit a research proposal designed to recruit patients from a VA Medical Center or use information from VA data systems, and who do not have an appointment at one of the VA Medical Centers, must include a collaborator with a VA appointment. This collaborator must be willing to assume the role of PI for the VA component of the research.

Use of human subjects and human biological substances: All Department of Defense (DOD)-funded research involving human subjects and human biological substances must be reviewed and approved by the USAMRMC Office of Research Protections (ORP), HRPO, in addition to local IRBs. The HRPO is mandated to comply with specific laws and directives governing all research involving human subjects that is conducted or supported by the DOD. These laws and directives are rigorous and detailed, and will require information in addition to that supplied to the local review board. Allow a minimum of 6 months for regulatory review and approval processes for studies involving human subjects. Refer to the Application Instructions & General Information, Appendix 6, for detailed information.

E. Eligibility

Independent investigators at all academic levels (or equivalent) are eligible to submit proposals. Refer to Application Instructions & General Information, Appendix 1, for general eligibility information.

F. Funding

- The maximum period of performance is **5** years.
- The maximum allowable combined funding for the entire period of performance is **$6M** in direct costs.
- More cost-effective studies that do not request the full available funding amount are encouraged. The applicant may also request the entire maximum direct cost amount for a project that may be less than the maximum **5**-year period of performance.
- Regardless of the period of performance proposed, the applicant(s) may not exceed the maximum direct cost. In addition to the direct costs, indirect costs may be proposed in accordance with the institution's negotiated rate agreement.
- **Partnering PI Option:**
    - A separate award will be made to each PI's institution.
    - The combined total funding for the Initiating PI and the Partnering PIs may not exceed **$6M** for direct costs for up to a **5**-year performance period, plus indirect costs as appropriate.

Within the guidelines provided in the Application Instructions & General Information, funds can cover:

- Salary
- Research supplies
- Equipment
- Clinical research costs
- Travel to scientific/technical meetings
- Travel between collaborating institutions
- Other direct costs as described in Application Instructions & General Information for Detailed Budget and Justification

In addition, each PI must request travel funds to attend one Military Health Research Forum (MHRF) during the award period of performance. The MHRF is a CDMRP-sponsored meeting that is typically held every 2-3 years. In the event a MHRF is not held during the period of performance for the award, each PI should plan to attend another military relevant meeting.

The DCoE expects to allot approximately $24M of the $40.6M FY09 PH/TBI Research Program appropriation to fund approximately 2-3 AT/TDA applications, depending on the quality and number received. Funding of applications received in response to this Program Announcement/Funding Opportunity is contingent on the availability of Federal funds for this program.

G. Award Administration

The results of the research funded under this solicitation are of extreme importance to the DOD and we will be implementing a rigorous program management plan. Proposals submitted for this solicitation should clearly state expected deliverables, timelines, and metrics to gauge success or failure of the research plan. Quarterly technical progress reports that outline research status, accomplishments, and adherence to stated goals and timelines may be required.

A change in PI or institution will not be allowed for proposals that include clinical research except under extenuating circumstances, which will be evaluated on a case-by-case basis and at the discretion of the Grants Officer, provided that the intent of the award mechanism is met.

Refer to the Application Instructions & General Information, Appendix 5, for general award administration information.

II. TIMELINE FOR SUBMISSION AND REVIEW

Submission is a two-step process consisting of (1) pre-application submission and (2) application submission. ***Pre-application submission is a required first step.***

Pre-application Submission Deadline:	**August 14, 2009, 5:00 p.m. Eastern time (ET)**
Invitation to Submit Full Proposals Sent:	**September 2009**
Application Submission Deadline:	**October 28, 2009, 11:59 p.m. ET**
Scientific Peer Review:	**December 2009**
Programmatic Review:	**February 2010**

Awards will be made approximately 4 to 6 months after receiving a funding notification letter, but no later than September 30, 2010.

III. SUBMISSION PROCESS

Submission is a two-step process consisting of (1) a pre-application submission through the CDMRP eReceipt system (https://cdmrp.org/) and (2) an application submission through Grants.gov (http://www.grants.gov/). ***A letter of invitation is mandatory for submission of an application. Applications will be invited based on pre-application screening.***

Partnering PI Option:

This award is structured to accommodate up to three PIs under the Partnering PI Option. One PI will be identified as the Initiating PI, who will be responsible for the majority of the administrative tasks associated with proposal submission. The other PI(s) will be identified as Partnering PI(s). Initiating and Partnering PIs each have different submission requirements; however, both PIs should contribute to the preparation of the proposal. ***The Initiating PI must complete the pre-application process and submit contact information for the Partnering PI(s).***

PIs and organizations identified in the application submitted through Grants.gov should be the same as those identified in the pre-application. If there is a change in PI or organization after submission of the pre-application, the PI must contact the eReceipt help desk at help@cdmrp.org or 301-682-5507.

The Government reserves the right to reject duplicative applications submitted to different award mechanisms within the same program or to other CDMRP programs.

A. Step 1 – Pre-Application Components and Submission

Pre-application submission is the required first step. The pre-application consists of the components discussed below. All pre-application components must be submitted electronically through the CDMRP eReceipt system by ***5:00 p.m. ET on the deadline date***. Refer to the Application Instructions & General Information for detailed information.

- Proposal Information

- Proposal Contacts
- Collaborators and Conflicts of Interest (COI)
- **Preproposal Narrative**: The Preproposal Narrative has a ***three-page limit*** inclusive of figures, tables, graphs, photographs, diagrams, chemical structures, pictures, pictorials, cartoons, and other information needed to judge the preproposal. The preproposal narrative should address the following:
    - **Research Idea:** State the ideas and reasoning on which proposed work is based.
    - **Research Strategy:** Concisely state the project's objectives and specific aims.
    - **Alignment with Topic Area:** Explain how the proposed work addresses one or more of the FY09 PH/TBI topic areas.
    - **Impact on Military Populations:** State explicitly how the proposed work will have an impact on the prevention, detection, diagnosis, and/or treatment of military-relevant PH issues and/or TBI. 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:

- References: One-page limit.
- Biographical Sketches: Include biographical sketches for the PI and other key collaborators.

Partnering PI Option: The Initiating PI must complete the pre-application components listed above and must enter the contact information for each Partnering PI in the "Partnering PI" section.

Pre-Application Screening: Pre-applications will be screened by the PH/TBI Research Program Integration Panel (IP), composed of scientists, clinicians, and consumer advocates. The pre-application screening criteria are as follows:

- **Research Idea:** How the study addresses an important problem related to PH/TBI.
- **Research Strategy:** How the specific aims support the research idea.
- **Alignment with Topic Area:** How the proposed study addresses at least one of the FY09 PH/TBI topic areas.
- **Impact on Military Populations:** If successful, how the study will improve the prevention, detection, diagnosis, and/or treatment of military-relevant PH issues and/or TBI. How the proposed study may benefit warriors, Veterans, families, caregivers, and/or communities.

B. Step 2 – Application Components and Submission

Application submissions will not be accepted unless the PI has been invited. Do not submit an application unless a letter of invitation has been received. Applications must be submitted

electronically by the Authorized Organizational Representative (AOR) through Grants.gov (www.grants.gov).

Each application submission must include the completed application package of forms and attachments identified in www.grants.gov for this US Army Medical Research Acquisition Activity (USAMRAA) Program Announcement/Funding Opportunity. In addition to the specific instructions below, please refer to the Application Instructions & General Information for detailed requirements of each component.

For the Partnering PI Option, the CDMRP requires separate Grants.gov application package submissions for Initiating and Partnering PI(s). The CDMRP eReceipt system assigns a unique and separate log number to each PI (Initiating and Partnering) that must be used when submitting the Grants.gov application package. To obtain his/her unique log number, before submitting their application to Grants.gov, each Partnering PI must associate him- or herself with the Initiating PI's application by accepting the link sent by the CDMRP eReceipt system. ***Each PI also must submit an identical copy of a jointly created SOW.***

If an application is invited, the Initiating PI will receive a letter of invitation via email by the CDMRP eReceipt system. The letter will provide the information necessary to begin the application submission through Grants.gov. The Partnering PI(s) will subsequently be notified separately by email. Please note that all of the Partnering PI(s) 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.

Failure by the Initiating PI or any Partnering PI to submit his or her required application components will result in administrative rejection of all applications associated with the proposed research project.

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

The PI or Initiating PI must submit all Grants.gov application package components as listed in items 1-4 below.

The package includes:

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

2. **Attachments Form**

   - **Attachment 1: Project Narrative (25-page limit)**

     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:** State the hypothesis to be tested or the objective to be

reached.

- **Specific Aims:** Concisely explain the project's specific aims to be funded by this application. If the proposed work is part of a larger study, present only tasks that the Department of Defense award would fund.
- **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 biological 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 research:

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

- **Study Design**
- **Intervention, Drug, or Device**
- **Statistical Plan (as appropriate to phase of study)**
- **Ethics and/or Regulatory Issues**

- **Attachment 2: Supporting Documentation**
  - References Cited
  - Acronyms and Symbol Definitions
  - Facilities & Other Resources
  - Description of Existing Equipment
  - Publications and/or Patent Abstracts (five-document limit)
  - Letters of Institutional Support (two-page limit per letter)

    If the PI is a practicing clinician, the institution must clearly demonstrate a commitment to the clinician's research.
  - Letters of Collaboration (if applicable, two-page limit per letter)
  - Intellectual and Material Property Plan (if applicable)
- **Attachment 3: Technical Abstract (one-page limit)**
- **Attachment 4: Public Abstract (one-page limit)**
- **Attachment 5: Statement of Work (SOW; three-page limit)**
- **Attachment 6: Detailed Budget and Justification**
- **Attachment 7: Impact on Military Populations Statement (two-page limit)**

Describe the potential impact of this study on the field of research and/or patient care in the PH/TBI topic area addressed. Include an assessment of the likelihood that a successful outcome to the research project will lead to a practical application in patients. Demonstrate how the proposed study is responsive to the healthcare needs and quality of life of warriors, Veterans, families, caregivers, and/or communities. Show how the proposed study complements ongoing DoD areas of research interest in the FY09 PH/TBI topic area(s) addressed.

- **Attachment 8: Transition Plan (one-page limit)**

Provide information on the methods and strategies proposed to move the product, device, and/or emerging technology to the next clinical trial phase and/or military field deployment after the successful completion of the PH/TBI Research Program award. The plan should include details of potential funding sources, collaborations, other resources that will be used to provide this continuity of development, a potential timeline for field deployment, the involvement of appropriate intellectual property, licensing and/or business professionals, and plans for the further development and successful transition of the product.

- **Attachment 9: Request for Information on Study Population (if applicable, four-page limit)**
- **Attachment 10: Informed Consent (if applicable, no page limit)**

Specifically describe the plan for obtaining informed consent from volunteers. Provide the Informed Consent Form.

- 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.
- If applicable, address issues relevant to the mental capacity of the potential volunteer (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 volunteer age).
- Address how privacy and time for decision making will be provided and whether or not the potential volunteer will be allowed to discuss the study with anyone before making a decision.
- As consent is an ongoing process, 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.
- If volunteers who cannot give their own consent to participate will be included in the study, there must be a plan for the consent of the individual's Legally Authorized Representative (LAR) to be obtained prior to the volunteer's participation in the study. State law defines who may act as the LAR. The Institutional Review Board (IRB) of record should be consulted for guidance regarding who can serve as LAR for research at the study site.

- If illiterate volunteers are anticipated, the consent process to be followed for illiterate volunteers should be outlined in the protocol. The consent form should be verbally read/explained to the volunteer in the presence of a witness. The volunteers must sign or make a mark (such as a thumbprint) to indicate agreement to participate, and the witness must sign to attest that the content of the written consent form was accurately conveyed to the volunteer.
- If it is anticipated that volunteers who do not speak the primary language of the host country will be enrolled in a trial, all documentation provided to volunteers (consent form, information sheets, etc.) should be translated with a copy provided to the HRPO for review at a later date. A plan for ensuring that volunteers' questions will be addressed during the consent process and throughout the trial should be included.

NOTE: When consent will be obtained in a language other than English, documentation that the foreign language version of the consent form is an accurate translation of the English version of the consent form must be provided to the HRPO at a later date. Documentation from a qualified translator certifying the translation must be provided along with the English and foreign language version of the consent forms. The documentation of translation should include the following statement: "I certify that this is an accurate and true translation." The signature, name, address, phone number, and, if available, fax number of the translator should also be included.

- If a waiver of all or parts of the consent process is being sought, or a waiver of documentation of consent is desired, include justification of why the waiver should be considered. This justification should include how the protocol meets the criteria set forth in 32 CFR 219 (Title 32 of the Code of Federal Register, Section 219). If consent to use existing samples or data in a future study was provided as part of another study protocol, this should be clearly explained. If the institution is a covered entity, justification for Health Insurance Portability and Accountability Act (HIPAA) waiver requests should also be provided.

Assent. When minors are included in a study, a plan to obtain assent (agreement) from those with capacity to provide it, or a justification for a waiver of assent should be provided. Age-appropriate assent forms should be developed for use with minors when assent is obtained. Capacity to provide assent should also be considered for other populations that cannot provide informed consent, and assent should be obtained whenever possible.

- **Attachment 11: Federal Agency Financial Plan (if applicable)**
- **Attachments 12–15: Subaward Detailed Budget and Justification (if applicable)**

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

- PI Biographical Sketch (four-page limit)
- PI Current/Pending Support
- Key Personnel Biographical Sketches (four-page limit each)

- Include the Partnering PI(s), if applying for the Partnering PI Option

- Key Personnel Current/Pending Support
  - Include the Partnering PI(s), if applying for the Partnering PI Option

4. **Research & Related Project/Performance Site Location(s) Form**

Application Submission Components for each Partnering PI under the Partnering PI Option:

The application submission process for each Partnering PI uses an abbreviated application package of forms and attachments from Grants.gov. Each Partnering PI will be contacted via email by the CDMRP eReceipt system and provided with information necessary to begin application submission through Grants.gov. 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.

Each Partnering PI package includes only the following from the list above:

1. **SF-424 (R&R) Application for Federal Assistance Form**
2. **Attachments Form**
   - **Attachment 5: Statement of Work (SOW): Three-page limit**

     The Initiating and Partnering PIs must each submit an identical, jointly created SOW.
   - **Attachment 6: Detailed Budget and Justification**
   - **Attachment 11: Federal Agency Financial Plan (If applicable)**
   - **Attachments 12–15: Subaward Detailed Budget and Justification (if applicable)**
3. **Research & Related Project/Performance Site Location(s) Form**

IV. INFORMATION FOR APPLICATION REVIEW

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 submissions to each other and recommends proposals for funding based on scientific merit, overall goals of the program, military relevance, and specific intent of the award mechanism. Additional information about the two-tier review process used by the CDMRP may be found at http://cdmrp.army.mil/fundingprocess

The peer review and programmatic review processes are conducted confidentially to maintain the integrity of the merit-based selection process. Each tier 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. Institutional personnel and PIs are prohibited from contacting persons involved in the application 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 institution's application. Violations by panelists or PIs that compromise the confidentiality of the peer review and programmatic review processes may also result in suspension or debarment of their employing institutions 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).

The Government reserves the right to review all proposals based on one or more of the required attachments or supporting documentation (e.g., Impact on Military Populations Statement, Transition Statement, etc.).

B. Review Criteria

1. Peer Review:

Applications that <u>do not include</u> Clinical Interventions or Research will be evaluated according to the following criteria, which are listed in decreasing order of importance.

- **Impact**
  - How the proposed work addresses at least one of the FY09 PH/TBI topic areas.
  - The potential contribution of the proposed study to research and/or patient care in the topic area 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 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.
- **Transition Plan**
  - How the transition plan describes field deployment of the product, device, and/or emerging technology.

- Whether there is evidence that the PI has or can secure additional funding, or whether the PI clearly described potential options to secure the additional funding needed to bring the product, device, and/or emerging technology to clinical trial phase.
- How the proposed resources to bring the product to delivery support the likelihood of success.
- How appropriate intellectual property, licensing, and/or business professionals have been included or engaged.
- How well the plans are described for further development of the product, and how well the plan completes development of the product to ensure a successful transition.

- **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.
  - **Partnering PI Option (if applicable)**
    - Evidence that the Initiating PI and all Partnering PIs contributed substantially to the development and implementation of the research plan.
    - How the background and expertise of the Initiating PI and Partnering PI(s) demonstrate their ability to accomplish the proposed work.

Applications that <u>include</u> Clinical Interventions or Research will be evaluated according to the following criteria, which are listed in decreasing order of importance.

- **Impact**
  - How the proposed work addresses at least one of the FY09 PH/TBI topic areas.
  - The potential contribution of the proposed study to research and/or patient care in the topic area 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 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.

- **Study Design**
  - How the scientific rationale and preliminary data, including critical review and analysis of the literature, and laboratory and preclinical evidence support the proposed clinical intervention and its feasibility.
  - How the aims, hypotheses or objectives, experimental design, methods, data collection procedures, and analyses are developed.
  - How the logistical aspects of the proposed clinical research (e.g., communication plan, data transfer and management, and standardization of procedures) meet the needs of the proposed clinical research.
  - How the recruitment, informed consent, and screening processes for volunteers will be conducted to meet the needs of the proposed clinical research.
  - How the inclusion, exclusion, and randomization criteria meet the needs of the proposed clinical research.
- **Intervention, Drug, or Device**
  - How the intervention, drug, or device to be tested is appropriate for the proposed clinical research.
  - How the availability and purity of the substance to be used in the clinical research is appropriate for the proposed clinical research.
  - Whether there is documentation that an IND/IDE application has been submitted (if appropriate).
- **Statistical Plan (as appropriate to phase of study)**
  - How the statistical plan, including sample size projections and power analysis, is adequate for the study and all proposed correlative studies.
  - How the data analysis plan is consistent with the study objectives.
- **Ethics and/or Regulatory Issues**
  - How the ethical considerations, information privacy, and assessment of risks and benefits of participation in the clinical research will be addressed.
  - Evidence that an appropriate plan for dealing with adverse events, which should include named agencies or offices to be notified in this event, and point of contact information has been prepared.
  - How plans for data disposition during and after the clinical research are appropriate for the proposed clinical research.
  - How the procedures for protocol modifications during the course of the clinical research have been addressed.
  - How the plans for data and safety monitoring are appropriate for the proposed clinical research.

- **Transition Plan**
    - How the transition plan describes field deployment of the product, device, and/or emerging technology.
    - Whether there is evidence that the PI has or can secure additional funding, or whether the PI clearly described potential options to secure the additional funding needed to bring the product, device, and/or emerging technology to clinical trial phase.
    - How the proposed resources to bring the product to delivery support the likelihood of success.
    - How appropriate intellectual property, licensing, and/or business professionals have been included or engaged.
    - How well the plans are described for further development of the product, and how well the plan completes development of the product to ensure a successful transition.
- **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.
    - **Partnering PI Option (if applicable)**
        - Evidence that the Initiating PI and all Partnering PIs contributed substantially to the development and implementation of the research plan.
        - How the background and expertise of the Initiating PI and Partnering PI(s) demonstrate their ability to accomplish the proposed work.

For all applications, the following criteria will not be individually scored, but may impact the overall evaluation of the application:

- **Environment**
    - The appropriateness of the scientific environment for the proposed research.
    - How the research requirements are supported adequately by the availability of and accessibility to facilities and resources (including collaborative arrangements).
    - The quality and extent of institutional support.
- **Budget**
    - Whether the budget is appropriate for the proposed research and within the limitations of the award mechanism.
- **Application Presentation**
    - How the writing and components of the application influenced the review.

2. Programmatic Review: The following criteria are used by programmatic reviewers to make funding recommendations that maintain the program's broad portfolio:

- Responsiveness to at least one of the FY09 PH/TBI topic areas,
- Military relevance,
- Ratings and evaluations of the peer reviewers,
- Programmatic relevance,
- Program portfolio balance,
- Relative impact, and
- Adherence to the intent of the award mechanism.

Scientifically sound proposals that best fulfill the above criteria and most effectively address the unique focus and goals of the program will be identified by the by Integration Panel (IP) members and recommended for funding to the Director, Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury. The highest scoring applications from the first tier of review are not automatically recommended for funding. All applications are carefully considered to ensure that the funds available are allocated to those proposals that best fulfill the goals and objectives of the program.

V. ADMINISTRATIVE ACTIONS

After receipt of pre-applications from 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.
- 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 all applications associated with the proposed research project:

- Initiating or Partnering PI(s) application is missing.
- Project Narrative exceeds page limit.
- Project Narrative is missing.
- Initiating or Partnering PI(s) budget is missing.

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

B. Modifications

- Pages exceeding the specified limits will be removed for all documents other than the Project Narrative.
- Documents not requested will be removed.
- ***NEW for FY09:*** Following the application deadline, the applicant may be contacted by email from CDMRP with a request to provide certain missing supporting documents (excluding those listed directly above in Section A, Rejection). The missing documents must be provided by 5:00 p.m. Eastern time on the second full business day following the date the email was sent. Otherwise, the application will be peer reviewed without the missing documents.

C. Withdrawal

The following may result in administrative withdrawal of the application:

- The proposed research is not relevant to any of the FY09 PH/TBI topic areas.
- FY09 IP member(s) 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 FY09 IP members may be found at http://cdmrp.army.mil/phtbi/panel09
- Submission of the same research project to different award mechanisms within the same program or to other CDMRP programs.
- The application does not conform to this funding opportunity description to an extent that precludes appropriate scientific peer and programmatic review.
- Direct costs as shown on the detailed budget form exceed the maximum allowed by the award mechanism.
- Inclusion of URLs, with the exception of links to published references.

D. Withhold

Applications that appear to involve research misconduct will be administratively withheld from further consideration pending institutional investigation. The institution 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.

VI. CONTACT INFORMATION

A. Program Announcement/Funding Opportunity, application format, or required documentation: To view all funding opportunities offered by the CDMRP, perform a Grants.gov basic search using the CFDA Number 12.420. Submit questions as early as possible. Response times will vary depending upon the volume of inquiries. Every effort will be made to answer questions within 5 working days.

Phone: 301-619-7079
Fax: 301-619-7792
Email: cdmrp.pa@amedd.army.mil

B. eReceipt system: Questions related to pre-application components through the CDMRP eReceipt system should be directed to the eReceipt help desk, which is available Monday through Friday from 8:00 a.m. to 5:00 p.m. ET.

Phone: 301-682-5507
Website: https://cdmrp.org
Email: help@cdmrp.org

C. Grants.gov contacts: Questions related to application submission through the Grants.gov (http://www.grants.gov/) portal should be directed to the Grants.gov help desk, which is available Monday through Friday, 7:00 a.m. to 9:00 p.m. ET. Deadlines for application submission are 11:59 p.m. ET on the deadline date. Please note that the CDMRP help desk is unable to answer questions about Grants.gov submissions.

Phone: 800-518-4726
Email: support@grants.gov

Grants.gov will notify PIs of changes made to this Program Announcement/Funding Opportunity and/or application package ONLY if the PI subscribes to the mailing list by clicking on the "send me change notification emails" link on the Opportunity Synopsis page for this announcement. If the PI does not subscribe and the application package is updated or changed, the original version of the application package may not be accepted.