

Program Announcement

for the

Department of Defense

Defense Health Program

Congressionally Directed Medical Research Programs

Joint Program Committee 8/Clinical and Rehabilitative Medicine Research Program

Psychological Health/Traumatic Brain Injury Research Program

Complex Traumatic Brain Injury Rehabilitation Research Award

Funding Opportunity Number: W81XWH-16-PHTBIRP-CTRRA

**Catalog of Federal Domestic Assistance Number: 12.420 Military Medical
Research and Development**

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-Application Submission Deadline:** 5:00 p.m. Eastern time (ET), August 17, 2016
- **Invitation to Submit an Application:** September 28, 2016
- **Application Submission Deadline:** 11:59 p.m. ET, November 30, 2016
- **End of Application Verification Period:** 5:00 p.m. ET, December 7, 2016
- **Peer Review:** February 2017
- **Programmatic Review:** April 2017

This Program Announcement/Funding Opportunity is one of two documents with instructions to prepare and submit an application for this funding opportunity. The second document, the General Application Instructions, is available for downloading from Grants.gov.

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I. FUNDING OPPORTUNITY DESCRIPTION

A. Program Description

Applications to the Fiscal Year 2016 (FY16) Psychological Health and Traumatic Brain Injury Research Program (PH/TBIRP) are being solicited for the Defense Health Agency, Research, Development, and Acquisition (DHA RDA) Directorate, by the U.S. Army Medical Research Acquisition Activity (USAMRAA). As directed by the Office of the Assistant Secretary of Defense for Health Affairs (OASD[HA]), the DHA RDA Directorate manages the Defense Health Program (DHP) Research, Development, Test, and Evaluation (RDT&E) appropriation. The U.S. Army Medical Research and Materiel Command (USAMRMC) Congressionally Directed Medical Research Programs (CDMRP) provides PH/TBIRP execution management support aligned with specific DHA RDA Directorate research program areas, including Joint Program Committee-8/Clinical and Rehabilitative Medicine Research Program Research Program (JPC-8/CRM RP). This Program Announcement/Funding Opportunity and subsequent awards will be managed by the CDMRP with strategic oversight from the JPC-8/CRM RP.

The PH/TBIRP was established by Congress in FY07 in response to the devastating impact of traumatic brain injury (TBI) and psychological health (PH) issues, including post-traumatic stress disorder, on our deployed Service members in Iraq and Afghanistan. The PH/TBIRP mission is to establish, fund, and integrate both individual and multiagency research efforts that will lead to improved prevention, detection, and treatment of PH issues and TBI. The vision of the PH/TBIRP is to prevent, mitigate, and treat the effects of traumatic stress and TBI on function, wellness, and overall quality of life for Service members as well as their caregivers and families. The DHA RDA Directorate leverages PH/TBIRP funding to complement DHP core research and development funding assigned to study PH and TBI.

The PH/TBIRP and JPC-8/CRM RP seeks innovative research that has the potential to make a significant impact on improving the health and well-being of military Service members, Veterans, and other individuals and challenges the scientific community to design innovative research that will foster new directions for, and address neglected issues in, the field of TBI research. Applications from investigators within the military Services, and applications involving multidisciplinary collaborations among academia, industry, the military Services, the U.S. Department of Veterans Affairs (VA), and other Federal Government agencies are highly encouraged.

One of six major program areas within the DHA RDA, the JPC-8/CRM RP seeks to ethically and responsibly develop long-term strategies to find, evaluate, and fund cutting-edge research in reconstruction, rehabilitation, and definitive care for injured Warfighters to improve the standard of care and outcomes, return Service members to full form and function, and ultimately restore the Warfighter to duty and improve his or her quality of life. Additional information about the JPC-8/CRM RP can be found at: <https://crmrp.amedd.army.mil/>.

B. JPC-8/CRM RP Focus Areas and FY16 PH/TBIRP Complex Traumatic Brain Injury Rehabilitation Research Award (CTRRA) Areas of Encouragement

The FY16 PH/TBIRP Complex TBI Rehabilitation Research Award (CTRRA) is intended to support observational studies and clinical trials addressing rehabilitation of patients with complex TBI. TBI is defined as being caused by (1) a direct blow or impact to the head, (2) a penetrating head injury, or (3) an exposure to external forces such as blast waves that disrupt the function of the brain. Not all blows to the head or exposure to external forces result in a TBI. The severity of TBI may range from “mild” — a brief change in mental status or consciousness — to “severe,” an extended period of unconsciousness or confusion after the injury. All applications to the FY16 PH/TBIRP CTRRA must be relevant to complex TBI, defined by a diagnosed TBI in conjunction with symptoms identified in one or more of the following JPC-8/CRM RP Focus Areas:

- The **Sensory Systems Traumatic Injury** Focus Area involves visual, auditory, and vestibular dysfunction associated with traumatic injury.
- The **Pain Management** Focus Area is concerned with chronic pain, acute pain in the context of chronic pain, and establishing safety margins for prescriptions, as well as developing strategies to help patients cope with pain.
- The **Neuromusculoskeletal Injury Rehabilitation** Focus Area deals with amputee care, spinal cord injuries, burns and contractures, and orthopaedic injuries, as well as developing guidelines for standards of care.

*In addition, research in the areas described below is **very highly encouraged**.* Patients with complex TBI demonstrate symptoms including, but not limited to, dizziness, visual dysfunction, headaches, and cognitive deficits that are refractory to treatment (i.e., slow/non-response to current treatment regimen, relapsing symptoms following treatment). The FY16 PH/TBIRP CTRRA seeks research on the affected patient populations, mechanisms of comorbidities and potential interventions in the following three Areas of Encouragement:

- **Epidemiological** studies to define differences between populations of patients with complex TBI whose symptoms are non-responsive as compared to responsive to treatment. (Observational studies only; clinical trials are not supported for this Area of Encouragement. [See the definition of a clinical trial and observational studies on page 7 of this Program Announcement/Funding Opportunity.](#))
- **Etiological** studies to identify factors that contribute to differences between patients with complex TBI who respond to treatment and those who do not, with the goal of identifying mechanisms underlying refractory symptoms. (Observational studies only; clinical trials are not supported for this Area of Encouragement. [See the definition of a clinical trial and observational studies on page 7 of this Program Announcement/Funding Opportunity.](#))
- **Interventional** studies to evaluate emerging or existing rehabilitation strategies for the treatment of patients with complex TBI compared to existing standards of care. Proposed studies evaluating interventions for patients with TBI and comorbidities that

may be refractory to treatment are of particular interest. (Both observational studies and clinical trials are allowed for this Area of Encouragement.)

Additionally, other studies of complex TBI may be considered if they address important issues relevant to the identified JPC-8/CRM RP Focus Areas in the context of TBI if sufficient justification is included in the appropriate sections of the pre-application and application.

Military Relevance: Relevance to the healthcare needs of military Service members, Veterans, and beneficiaries is a key feature of this award. Investigators are encouraged to consider the following characteristics as examples of how a project may demonstrate military relevance:

- Explanation of how the project addresses an aspect of the target disease/condition/technology that has direct relevance to military Service members, Veterans, and/or other military health system beneficiaries
- Description of how the knowledge, information, products, or technologies gained from the proposed research could be implemented in a dual-use capacity to benefit the civilian population and also address a military need
- Use of military or Veteran populations or datasets in the proposed research

Principal Investigators (PIs) are encouraged to integrate and/or align their research projects with Department of Defense (DoD) and/or VA research laboratories and programs. Collaboration with the DoD or VA investigators is also encouraged. The following websites may be useful in identifying ongoing areas of DoD research interest within the FY16 PH/TBIRP CTRRA Areas of Encouragement.

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

Center for Neuroscience and
Regenerative Medicine
<http://www.usuhs.mil/cnrm/>

Clinical and Rehabilitative Medicine
Research Program
<https://crmrp.amedd.army.mil>

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

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

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

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

Military Infectious Diseases
Research Program
<https://midrp.amedd.army.mil>

Military Operational Medicine
Research Program
<https://momrp.amedd.army.mil>

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

National Museum of Health and Medicine
<http://www.medicalmuseum.mil/index.cfm>

Naval Health Research Center
<http://www.med.navy.mil/sites/nhrc>

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

Office of Naval Research
<http://www.med.navy.mil>

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

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

U.S. Army Medical Research and
Materiel Command
<http://mrmc.amedd.army.mil/>

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

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

U.S. Naval Research Laboratory
<https://www.nrl.navy.mil/>

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

Walter Reed Army Institute of Research
<http://wrair-www.army.mil>

C. Award Information

The FY16 PH/TBIRP CTRRA is intended to support both observational studies and clinical trials addressing TBI and co-occurring clinical presentations (neuromusculoskeletal injuries, multisensory dysfunction, and pain) that are often slow/nonresponsive to treatment. The intent of the award is to advance the evidence-based practice for the treatment of TBI with JPC-8/CRMRP-relevant comorbidities by improving understanding of the composition and problems of this population and developing and evaluating treatments.

Applications for this award mechanism may propose epidemiological, etiological, and/or interventional studies (see [CTRRA Areas of Encouragement](#) on page 4).

Preclinical studies and studies using animals are not supported by this Program Announcement/Funding Opportunity.

Two different funding levels, based on the type of study proposed, are available under this Program Announcement/Funding Opportunity. *It is the responsibility of the PI to select the funding level that is most appropriate for the research proposed based on the following descriptions.*

The following, although not all-inclusive, are research projects that would be appropriate to propose under each funding level:

- **Funding Level 1:** For epidemiological and etiological studies comparing patients with complex TBI responsive versus refractory to treatments. PIs should describe a reproducible methodological approach that will identify or define factors that are associated with slow/non-response to treatment, or relapse of symptoms for patients with complex TBI. Observational studies, but not clinical trials, are permitted at this Funding Level.
- **Funding Level 2:** For interventional studies to evaluate emerging or existing treatment and rehabilitation strategies. PIs should explain how their work will inform the development, refinement, and/or revision of existing standards of care, clinical

recommendations, or guidelines. Both observational studies and clinical trials are permitted at this Funding Level.

Both observational studies and clinical trials, but not preclinical research studies, are allowed in the FY16 PH/TBIRP CTRRA. Observational studies and clinical trials have different submission requirements and *it is the responsibility of the PI to correctly identify the type of research proposed and to comply with the relevant submission requirements*. 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 safety, effectiveness, and/or efficacy. This outcome represents a direct effect on the human subject of that intervention or interaction. An observational study is a type of clinical study in which individuals are observed or certain outcomes are measured. No attempt is made to affect the outcome (for example, no treatment is given). These types of studies are not considered clinical trials. All projects should adhere to a core set of standards for rigorous study design and reporting to maximize the reproducibility and translational potential of research.

Research Involving Human Anatomical Substances, Human Subjects, or Human Cadavers: All DoD-funded research involving new and ongoing research with human anatomical substances, human subjects, or human cadavers must be reviewed and approved by the USAMRMC Office of Research Protections (ORP), Human Research Protection Office (HRPO) prior to research implementation. This administrative review requirement is in addition to the local Institutional Review Board (IRB) or Ethics Committee (EC) review. Local IRB/EC approval at the time of submission is *not* required. The HRPO is mandated to comply with specific laws and requirements governing all research involving human anatomical substances, human subjects, or human cadavers that is supported by the DoD. These laws and requirements will necessitate information in addition to that supplied to the IRB/EC. *Allow a minimum of 2 to 3 months for HRPO regulatory review and approval processes*. Refer to the General Application Instructions, Appendix 6, and the Human Subject Resource Document available on the eBRAP “Funding Opportunities & Forms” web page (<https://ebrap.org/eBRAP/public/Program.htm>) for additional information.

Preliminary Data: Observations that drive a research idea may be derived from laboratory discovery, population-based studies, a clinician’s first-hand knowledge of patients, or anecdotal data. Applications must include preliminary and/or published data that are relevant to complex TBI and the proposed research project.

Investigational New Drug/Investigational Device Exemption (IND/IDE): If the clinical trial involves the use of a drug that has not been approved by the U.S. Food and Drug Administration (FDA) for the proposed investigational use, then an IND application to the FDA that meets all requirements under the Code of Federal Regulations, Title 21, Part 312 (21 CFR 312) may be required and must be submitted to the FDA *prior to the application submission deadline*. If the investigational product is a device, evidence that an IDE application that meets all requirements under 21 CFR 812 has been submitted to the FDA *prior to the application submission deadline*, or that the device is exempt or qualifies for an abbreviated IDE, is required. The Government reserves the right to withdraw funding if an IND or IDE is necessary but has not been submitted

to the FDA prior to the grant submission deadline, or if documented status of the IND or IDE has not been obtained within 6 months of the award date.

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

Federal Interagency TBI Research (FITBIR) Informatics System: For studies that will enroll TBI subjects, the DoD requires that the awardees make data available to the TBI research community by depositing de-identified research data into the FITBIR Informatics System on a quarterly basis. The FITBIR Informatics System is a free resource to the TBI community designed to accelerate comparative effectiveness research on brain injury diagnosis and treatment. Data reporting to FITBIR is an opportunity for investigators to facilitate their own research and collaborate with others doing similar research. While use of the informatics system presents no direct cost to the user, a *project estimation tool* (<https://fitbir.nih.gov/jsp/contribute/fitbir-costs.jsp>) is available to help estimate indirect costs and manpower needs associated with data submission.

To contribute to FITBIR, researchers should contact the FITBIR Operations Center ahead of time to arrange for data entry support and to ensure all data have been made compatible with the system. FITBIR guidance and policies, as well as the considerable advantages of FITBIR use to the researcher, are detailed at [FITBIR: Federal Interagency Traumatic Brain Injury Research Informatics System](http://fitbir.nih.gov/) (<http://fitbir.nih.gov/>).

FITBIR allows for de-identification and storage of data (medical imaging clinical assessment, environmental and behavioral history, etc.) of various types (text, numeric, image, time series, etc.). Use of FITBIR's Global Unique Identifier (GUID) system facilitates repeated and multi-user access to data without the need to personally identify data sources. FITBIR encourages collaboration between laboratories, as well as interconnectivity with other informatics platforms. Such community-wide sharing requires common data definitions and standards.

Data elements must be reported using the National Institute of Neurological Disorders and Stroke (NINDS) TBI Common Data Elements (CDEs) or entered into the FITBIR data dictionary as new, unique data elements. For the most current version of the NINDS TBI CDEs, go to <http://www.commondataelements.ninds.nih.gov>. Assistance will be available to help the researchers map their study variables to specific CDEs and ensure the formats of the CDEs collected are compatible with the FITBIR informatics system. If the proposed research data cannot be entered in CDE format, the investigators must supply a proposal for an alternative data submission or data sharing vehicle and justification for use. Use of the TBI CDEs is required wherever possible in an effort to create standardized definitions and guidelines about the kinds of data to collect and the data collection methods that should be used in clinical research of TBI.

TBI Outcomes Reporting: PIs are highly encouraged to use the Neurobehavioral Symptom Inventory (NSI), a measure of post-TBI symptom severity, and the Patient Global Impression of Change (PGIC), a global outcome measure of patient experience of care. The NSI and PGIC

achieved unanimous concurrence by DoD and VA TBI stakeholders in September 2013 as core TBI outcome measures. More information on the NSI and PGIC is available at the respective links below:

NSI: http://dybic.dcoe.mil/sites/default/files/DVBIC_-_NSI_Information_Paper_Final.pdf

PGIC: http://dybic.dcoe.mil/sites/default/files/DVBIC_-_PGIC_Information_Paper_Final.pdf

Pain Research Outcomes Reporting: If applicable, PIs are highly encouraged to use the DoD/VA jointly developed and validated Defense and Veterans Pain Rating Scale (DVPRS) and the Pain Assessment Screening Tool and Outcomes Registry (PASTOR).

DVPRS has been integrated into clinical practice in pain specialty clinics across the Military Health System (MHS). DVPRS measures pain intensity as well as biopsychosocial and functional impact of pain (e.g., sleep, stress, mood, and activity). The scale has improved objective components to evaluate treatment effectiveness. It is adaptable to multiple clinical settings and scenarios throughout the continuum of care and research (e.g., battlefield, transport, primary care, and specialty services) and for integration into DoD/VA Electronic Health Record and registries. DVPRS is consistent with current validated pain research tools the Visual Analogue Scale, the Numerical Rating Scale, the Verbal Rating Scale, and the Faces Pain Scale-Revised.

While DVPRS is the recommended basic pain assessment tool, the MHS also has been developing PASTOR, a more comprehensive and complex capability for pain assessment and clinical decision-making. PASTOR is a 20-30 minute survey that produces a comprehensive three-page clinician report of a patient's chronic pain. PASTOR was developed in response to the National Defense Authorization Act for Fiscal Year 2010. PASTOR uses instruments developed by the National Institutes of Health, collectively known as the Patient Reported Outcomes Measurement Information System (PROMIS), to administer questions in a wide range of pain-related areas. In addition to the PROMIS instruments, PASTOR also incorporates demographics, DVPRS, an anatomical map for locating pain areas, military-specific pain-related questions, and other measures. Taking all of these items and compiling them as one large survey, PASTOR is able to create a comprehensive view of a patient's pain. This information is stored over time and allows the clinician to track a patient's progress to show improvement or decline across multiple measures. The survey is optimized to work on computers, tablets, and smartphones, which enables the patient the flexibility to respond based on his or her schedule. Patients are enrolled through a participating clinic and all PASTOR data are compiled into a three-page report, which is given to the clinician prior to their visit.

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

D. Eligibility Information

- Independent investigators at all academic levels (or equivalent) are eligible to submit an application.
- Cost sharing/matching is not an eligibility requirement.
- Eligible investigators must apply through an organization. Organizations eligible to apply include Federal agencies, national, international, for-profit, nonprofit, public, and private organizations.
- An intramural investigator is defined as a DoD military or civilian employee working within a DoD laboratory or medical treatment facility, or working in a DoD activity embedded within a civilian medical center. Submissions from intramural (DoD) organizations are allowed and encouraged for this Program Announcement/Funding Opportunity. Applicants submitting through their intramural organizations are reminded to coordinate receipt and commitment of funds through their respective resource managers. *If an investigator at an intramural organization is named as a collaborator on an application submitted through an extramural organization, the application must include a letter from the collaborator's Commander or Commanding Officer at the intramural organization that authorizes the collaborator's involvement.*
- Refer to the General Application Instructions, Appendix 1, for general eligibility information.

E. Funding

The requested funding level should be based on the type of research proposed. See [Section I.C., Award Information](#) for a description of funding levels.

Funding Level 1:

- The maximum period of performance is **3** years.
- The anticipated total costs (direct and indirect) budgeted for the entire period of performance will not exceed **\$2 million (M)**. Indirect costs are to be budgeted in accordance with the organization's negotiated rate. No budget will be approved by the Government exceeding **\$2M** total costs or using an indirect rate exceeding the organization's negotiated rate.

Funding Level 2:

- The maximum period of performance is **4** years.
- The anticipated total costs (direct and indirect) budgeted for the entire period of performance will not exceed **\$5M**. Indirect costs are to be budgeted in accordance with the organization's negotiated rate. No budget will be approved by the Government exceeding **\$5M** total costs or using an indirect rate exceeding the organization's negotiated rate.

Both Funding Levels:

- All direct and indirect costs of any subaward (subgrant or subcontract) must be included in the total direct costs of the primary award.
- The applicant may request the entire maximum funding amount for a project that may have a period of performance less than the maximum allowable period of performance for the selected funding level.

For this award mechanism, direct costs must be requested for:

- Travel costs for the PI to disseminate project results at one In-Progress Review meeting during the period of performance. For planning purposes, it should be assumed that the meeting will be a 1-day meeting held in the National Capital Area.
- Travel costs for the PI to disseminate project results at one DoD-sponsored scientific meeting (e.g., Military Health System Research Symposium) during the period of performance. These travel costs are in addition to those allowed for annual scientific/technical meetings.

May be requested for (not all-inclusive):

- Salary
- Research supplies and equipment
- Research-related subject costs
- Clinical research costs
- Support for multidisciplinary collaborations, including travel
- Travel costs to attend scientific/technical meetings in addition to the required meetings described above

Awards to extramural organizations will consist solely of assistance agreements (Cooperative Agreements and Grants). Awards to intramural (DoD) agencies and other Federal agencies may be managed through a direct fund transfer (e.g., the Military Interdepartmental Purchase Request [MIPR]; Funding Authorization Document [FAD] process; or DD Form 1144 Support Agreement). Direct transfer of funds from the recipient to a DoD agency is not allowed except under very limited circumstances. Refer to the General Application Instructions, Section II.C.4., for budget regulations and instructions for the Research & Related Budget. ***For Federal agencies or organizations collaborating with Federal agencies, budget restrictions apply as are noted in Section II.C.4. of the General Application Instructions.***

The JPC-8/CRM RP expects to allot approximately \$20M of the FY16 PH/TBIRP appropriation to fund approximately five Funding Level 1 and two Funding Level 2 Complex TBI Rehabilitation 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 two-step process requiring both (1) pre-application submission through the electronic Biomedical Research Application Portal (eBRAP) (<https://eBRAP.org/>) and (2) application submission through Grants.gov (<http://www.grants.gov/>). Refer to the General Application Instructions, Section II.A., for registration and submission requirements for eBRAP and Grants.gov.

The pre-application and application submission process should be started early to avoid missing deadlines. There are no grace periods. Federal applicants must be familiar with Grants.gov requirements, including the need for an active System for Award Management (SAM) registration and a Data Universal Numbering System (DUNS) number. Refer to Appendix 3 of the General Application Instructions for further information regarding Grants.gov requirements.

eBRAP is a multifunctional web-based system that allows PIs to submit their pre-applications electronically through a secure connection, to view and edit the content of their pre-applications and full applications, to receive communications from the CDMRP, and to submit documentation during award negotiations and period of performance. A key feature of eBRAP is the ability of an organization's representatives and PIs to view and modify the Grants.gov application submissions associated with them. eBRAP will validate Grants.gov application files against the specific Program Announcement/Funding Opportunity requirements and discrepancies will be noted in an email to the PI and in the Full Application Files tab in eBRAP. It is the applicant's responsibility to review all application components for accuracy as well as ensure proper ordering as specified in this Program Announcement/Funding Opportunity.

The application title, eBRAP log number, and all information for the PI, Business Official(s), performing organization, and contracting organization must be consistent for the entire pre-application and application submission process. Inconsistencies may delay application processing and limit the ability to view, modify, and verify the application in eBRAP. If any changes need to be made, the applicant should contact the CDMRP Help Desk at help@eBRAP.org or 301-682-5507 prior to the application deadline.

Application viewing, modification, and verification in eBRAP is strongly recommended, but not required. ***The Project Narrative and Budget cannot be changed after the application submission deadline.*** Prior to the full application deadline, a corrected or modified full application package may be submitted. Revisions to the Project Narrative or Budget will require a changed/corrected application to be submitted to Grants.gov prior to the application deadline. Other application components may be changed until the end of the [application verification period](#). After the end of the application verification period, the full application cannot be modified.

A. Where to Obtain the Grants.gov Application Package

To obtain the Grants.gov application package, including all required forms, perform a basic search using the Funding Opportunity Number W81XWH-16-PHTBIRP-CTRRA in Grants.gov (<http://www.grants.gov/>).

B. Pre-Application Submission Content

The pre-application process should be started early to avoid missing deadlines. There are no grace periods. During the pre-application process, each submission is assigned a unique log number by eBRAP. This unique eBRAP log number will be needed during the application process on Grants.gov.

All pre-application components must be submitted by the PI through eBRAP (<https://eBRAP.org/>).

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

The pre-application consists of the following components, which are organized in eBRAP by separate tabs (refer to the General Application Instructions, Section II.B., for additional information on pre-application submission):

- **Tab 1 – Application Information**
- **Tab 2 – Application Contacts**
 - Enter contact information for the PI. Enter the organization’s Business Official responsible for sponsored program administration (the “person to be contacted on matters involving this application” in Block 5 of the Grants.gov SF424 (R&R) Form). The Business Official must either be selected from the eBRAP list or invited in order for the pre-application to be submitted.
 - Select the performing organization (site at which the PI will perform the proposed work) and the contracting organization (organization submitting on behalf of the PI, which corresponds to Block 5 on the Grants.gov SF424 (R&R) Form), and click on “Add Organizations to this Pre-application.” The organization(s) must either be selected from the eBRAP drop-down list or invited in order for the pre-application to be submitted.
 - It is recommended that PIs identify an Alternate Submitter in the event that assistance with pre-application submission is needed.
- **Tab 3 – Collaborators and Key Personnel**
 - Enter the name, organization, and role of all collaborators and key personnel associated with the application.
 - [FY16 PH/TBIRP CTRRA Programmatic Panel](#) members should not be involved in any pre-application or application. For questions related to Panel members and pre-applications or applications, refer to [Section IV.C., Withdrawal](#), or contact the CDMRP Help Desk at help@eBRAP.org or 301-682-5507.
 - To preserve the integrity of its peer and programmatic review processes, the CDMRP discourages inclusion of any employee of its review contractors having any role in application preparation, research, or other duties for submitted

applications. For FY16, the identities of the peer review contractor and the programmatic review contractor may be found at the CDMRP website (<http://cdmrp.army.mil/about/2tierRevProcess.shtml>). Applications that include names of personnel from either of these companies will be administratively withdrawn unless plans to manage conflicts of interest (COIs) are provided and deemed appropriate by the Government. Refer to the General Application Instructions, Appendix 1, for detailed information.

- **Tab 4 – Conflicts of Interest**

- List all individuals other than collaborators and key personnel who may have a COI in the review of the application (including those with whom the PI has a personal or professional relationship). Refer to Appendix 1, Section C, of the General Application Instructions for further information regarding COIs.

- **Tab 5 – Pre-Application Files**

Note: Upload documents as individual PDF files unless otherwise noted. eBRAP will not allow a file to be uploaded if the number of pages exceeds the limit specified below.

Preproposal Narrative (three-page limit): The Preproposal Narrative page limit applies to text and non-text elements (e.g., figures, tables, graphs, photographs, diagrams, chemical structures, drawings) used to describe the project. Inclusion of URLs that provide additional information to expand the Preproposal Narrative and could confer an unfair competitive advantage is prohibited and may result in administrative withdrawal of the pre-application.

The Preproposal Narrative should include the following:

- **Rationale:** State the ideas and reasoning on which the proposed observational study or clinical trial is based. Briefly describe how the preliminary data and rationale support the research idea. State how this project meets the intent of the award mechanism.
- **Alignment:** Note specifically which of the JPC-8/CRM RP Focus Area(s) and FY16 PH/TBIRP CTRRA Area(s) of Encouragement the proposed work addresses. If the proposed work does not address one of the FY16 PH/TBIRP CTRRA Areas of Encouragement, explain how it is relevant to an important issue for the identified JPC-8/CRM RP Focus Areas in the context of TBI.
- **Hypothesis or Objective:** State the hypothesis to be tested or the objective to be reached.
- **Research Strategy:** Clearly describe the observational study or clinical trial being proposed, and indicate the phase of trial and/or class of device and regulatory status as appropriate. Describe the intervention, if applicable. Concisely state the project's objectives, specific aims, and ultimate endpoints. Briefly describe the proposed recruitment strategies and methods, how they will accomplish the project's aims, and the outcome measures that will be used.

- Research Team: Provide a description of the research team that clearly demonstrates appropriate background and expertise to accomplish the proposed work.
- Military Benefit: Describe how the proposed work would impact the healthcare needs of military Service members and/or Veterans recovering from TBI in conjunction with symptoms associated with pain, neuromusculoskeletal injury, and/or sensory dysfunction.
- Estimated total budget.

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

- References Cited (one-page limit): List the references cited (including URLs if available) in the Preproposal Narrative using a standard reference format that includes the full citation (i.e., author[s], year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).
- List of Abbreviations, Acronyms, and Symbols: Provide a list of abbreviations, acronyms, and symbols used in the Preproposal Narrative.
- PI Biographical Sketch (five-page limit). *The biographical sketch should be uploaded as a single file.* The biographical sketch should be used to demonstrate background and expertise through education, positions, publications, and previous work accomplished.

- **Tab 6 – Submit Pre-Application**

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

Pre-Application Screening

- **Pre-Application Screening Criteria**

To determine the technical merits of the pre-application and the relevance to the mission of the DHP and the JPC-8/CRM RP, pre-applications will be screened based on the following **rank-ordered** criteria:

- Alignment: How well the project addresses at least one of the JPC-8/CRM RP Focus Area(s) and at least one of the FY16 PH/TBIRP CTRRA Area(s) of Encouragement. If the proposed work does not address one of the FY16 PH/TBIRP CTRRA Areas of Encouragement, to what degree the project is relevant to an important issue for the identified JPC-8/CRM RP Focus Areas in the context of TBI.
- Military Benefit: How the proposed work would benefit the healthcare needs of military Service members and/or Veterans recovering from complex TBI.
- Objective/Hypothesis and Rationale: How well the objective/hypothesis is stated and supported through preliminary data, scientific rationale, and referenced literature.

- Research Strategy: To what degree the rationale, objectives, and specific aims support the research idea. How well the endpoints are defined and are appropriate for the proposed study. Whether the proposed recruitment strategies and methodology are appropriate for accomplishing the research aims.
- Personnel: How the qualifications and expertise of the PI and key personnel are appropriate to perform the proposed research or clinical trial.
- **Notification of Pre-Application Screening Results**
Following the pre-application screening, PIs will be notified as to whether or not they are invited to submit applications; however, they will not receive feedback (e.g., a critique of strengths and weaknesses) on their pre-application. The estimated timeframe for notification of invitation to submit an application is indicated on the [title page](#) of this Program Announcement/Funding Opportunity. Invitations to submit a full application are based on the Pre-Application Screening Criteria as published above.

C. Full Application Submission Content

The application process should be started early on Grants.gov to avoid missing deadlines. There are no grace periods. Verify the status of the applicant’s organization’s Entity registration in the SAM well in advance of the application submission deadline. Allow 3 to 4 weeks to complete the entire SAM registration process. Refer to the General Application Instructions, Section II, for additional information.

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

All contributors and administrators to the application must use matching compatible versions of Adobe software when editing and preparing application components. The use of different software versions will result in corruption of the submitted file. See Section II.C. of the General Application Instructions for details on compatible Adobe software.

The CDMRP cannot make allowances/exceptions to its policies for submission problems encountered by the applicant organization using system-to-system interfaces with Grants.gov.

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

Note: The Project Narrative and Budget Form cannot be changed after the application submission deadline.

If either the Project Narrative or the budget fails eBRAP validation or if the Project Narrative or Budget Form needs to be modified, an updated Grants.gov application package must be submitted via Grants.gov as a “Changed/Corrected Application” with the previous Grants.gov Tracking ID ***prior to the application submission deadline.***

The Grants.gov application package must be submitted using the unique eBRAP log number to avoid delays in application processing.

Grants.gov application package components: For the FY16 PH/TBIRP Complex TBI Rehabilitation 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. SF424 (R&R) Application for Federal Assistance Form: Refer to the General Application Instructions, Section II.C., for detailed information.

2. Attachments Form

Each attachment to the Grants.gov application forms must be uploaded as an individual PDF file in accordance with the formatting guidelines listed in Appendix 2 of the General Application Instructions. For all attachments, ensure that the file names are consistent with the guidance. Grants.gov will reject attachments with file names longer than 50 characters or incorrect file names that contain characters other than the following: A-Z, a-z, 0-9, underscore, hyphen, space, and period. In addition, Grants.gov has file size limits that may apply in some circumstances. Individual attachments may not exceed 20 MB and the file size for the entire Grants.gov application package may not exceed 200 MB.

The Project Narrative is NOT the formal clinical trial protocol. Instead, all essential elements of the proposed clinical trial necessary for scientific review must be included as directed in Attachment 1 (the Project Narrative) and Attachments 6–9 described below, if applicable. Failure to submit these attachments as part of the application package will result in rejection of the entire application.

- **Attachment 1: Project Narrative: Upload as “ProjectNarrative.pdf.”** The page limit of the Project Narrative applies to text and non-text elements (e.g., figures, tables, graphs, photographs, diagrams, chemical structures, drawings, etc.) used to describe the project. Inclusion of URLs that provide additional information to expand the Project Narrative and could confer an unfair competitive advantage is prohibited and may result in administrative withdrawal of the application.
 - **Page Limit:** Page limits for the project narrative are correlated with the application’s funding level:
 - **Funding Level 1:** 12-page limit
 - **Funding Level 2:** 20-page limit

Describe the proposed project in detail using the outline below.

- **Background:** Describe in detail the rationale for the study or trial. Provide a literature review and describe the preliminary studies and/or preclinical data that led to the development of the proposed observational study or clinical trial. Provide a summary of other relevant ongoing, planned, or completed clinical trials and describe how the proposed study differs. Include a discussion of current clinical use of the proposed intervention and/or details of its study in

clinical trials for other indications (as applicable). Clearly articulate how prior work in the field supports the proposed study.

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

- **Objectives/Specific Aims/Hypotheses:** Provide a description of the purpose and objectives of the study or trial with detailed specific aims and/or study questions/hypotheses.
- **Research Strategy:** Describe the type of study (e.g., correlative or epidemiological) or trial to be performed (e.g., prospective, randomized, controlled) and outline the proposed methodology in sufficient detail to show a clear course of action. Describe potential challenges and alternative strategies where appropriate.
 - Identify the intervention to be tested, if applicable, and describe the projected outcomes.
 - Define the study variables, outline why they were chosen, and describe how they will be measured. Include a description of appropriate controls and the endpoints to be tested.
 - For all clinical trials and for observational studies as applicable:
 - Describe the study population and inclusion and exclusion criteria that will be used.
 - Describe the methods that will be used to recruit a sample of human subjects from the accessible population (e.g., convenience, simple random, stratified random).
 - Describe the human subject-to-group assignment process (e.g., randomization, block randomization, stratified randomization, age-matched controls, alternating group, or other procedures), if applicable. Explain the specific actions to accomplish the group assignment (e.g., computer assignment, use of table of random numbers).
 - If using psychometric measures, describe their reliability and validity.
- **Statistical Plan and Data Analysis:** Describe the statistical model and data analysis plan with respect to the study or trial objectives. If applicable, specify the approximate number of human subjects to be enrolled. If multiple study sites are involved, state the approximate number to be enrolled at each site. Include a complete power analysis to demonstrate that the sample size is appropriate to meet the objectives of the study or trial. If a subpopulation of a recruited sample population will be used for analysis, complete a statistical analysis to ensure appropriate power can be achieved within the subpopulation study or trial.

- **Impact:** Describe the anticipated outcomes for the proposed research and their impact on TBI research and patient care. Although not all-inclusive, the following are examples of ways in which research projects may have an impact, if successful:
 - Describe how the research has the potential to advance the field of TBI research.
 - If applicable, describe how the intervention has the potential to change the standard of care.
 - If applicable, describe how the research contributes to the development or validation of evidence-based policy or guidelines for patient evaluation and care.
 - Describe any relevant controversies or treatment issues that will be addressed by the proposed observational study or clinical trial.
 - Describe potential issues that might limit the impact of the proposed observational study or clinical trial.
 - If applicable, describe how the intervention represents an improvement over currently available interventions and/or standards of care.
- **Attachment 2: Supporting Documentation. Start each document on a new page. Combine and upload as a single file named “Support.pdf.”** If documents are scanned to pdf, the lowest resolution (100 to 150 dpi) should be used. *There are no page limits for any of these components unless otherwise noted. Include only those components described below; inclusion of items not requested will result in the removal of those items or may result in administrative withdrawal of the application.*
 - References Cited: List the references cited (including URLs, if available) in the Project Narrative using a standard reference format that includes the full citation (i.e., author[s], year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).
 - List of Abbreviations, Acronyms, and Symbols: Provide a list of abbreviations, acronyms, and symbols.
 - Facilities, Existing Equipment, and Other Resources: Describe the facilities and equipment available for performance of the proposed project and any additional facilities or equipment proposed for acquisition at no cost to the award. Indicate whether or not Government-furnished facilities or equipment are proposed for use. If so, reference should be made to the original or present Government award under which the facilities or equipment items are now accountable. There is no form for this information.
 - Publications and/or Patents: Include a list of relevant publication URLs and/or patent abstracts. If publications are not publically available, then copies of up to five published manuscripts may be included in Attachment 2. Extra items will not be reviewed.

- Letters of Organizational Support (recommended two-page limit per letter): Provide a letter (or letters, if applicable), signed by the Department Chair or appropriate organization official, confirming the laboratory space, equipment, and other resources available for the project. Letters of support not requested in the Program Announcement/Funding Opportunity, such as those from members of Congress, do not impact application review or funding decisions.
- 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. For applications that include an intramural collaborator, include a letter from the collaborator's Commander or Commanding Officer at the intramural organization that authorizes the collaborator's involvement.
- Letters of Commitment (if applicable) (two-page limit per letter): If the proposed study involves use of a commercially produced investigational drug, device, or biologic, provide a letter of commitment from the commercial entity indicating availability of the product for the duration of the study, support for the proposed phase of research, and support for the indication to be tested.
- Approval for Access to Military and VA Populations or Resources (if applicable, one-page limit per site): A letter of support, signed by the lowest-ranking person with approval authority, should be included for studies involving active duty military, Veterans, or military family members; military-controlled study materials; databases; and/or restricted facilities (e.g., biological or chemical containment facilities).
- Intellectual Property
 - Intangible property acquired, created or developed under this award will be subject to all rights and responsibilities established at 2 CFR 200.315. Should the applicant intend to use, in the performance of this program, pre-existing, legally protected and perfected intangible property and for which no Federal funds had been used in the development of said property, the applicant must:
 - Clearly identify all such property;
 - Identify the cost to the Federal government for use or license of such property, if applicable; or
 - Provide a statement that no property meeting this definition will be used on this project.
 - 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. PIs may be required to report data to the FITBIR informatics system (<http://fitbir.nih.gov/>). For projects involving clinical trials, PIs may be

required to register their clinical trials on Clinicaltrials.gov (<https://clinicaltrials.gov/>). Refer to the General Application Instructions, Appendix 4, Section K, for more information about the CDMRP expectations for making data and research resources publically available.

- Current Quad Chart: Complete and upload the Quad Chart template available from the eBRAP “Funding Opportunities and Forms” web page (<https://ebrap.org/eBRAP/public/Program.htm>).

- **Attachment 3: Technical Abstract (one-page limit): Upload as “TechAbs.pdf.”** The technical abstract is used by all reviewers. Abstracts of all funded research projects will be posted publically. **Do not include proprietary or confidential information.** Use only characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed.

Technical abstracts should be written using the outline below. Abstracts of all funded research projects will be posted on the CDMRP website (<http://cdmrp.army.mil>); therefore, proprietary or confidential information should not be included.

- **Background:** Present the ideas and rationale behind the proposed observational study or clinical trial.
 - **Relevance:** State the relevance of the project to at least one of the JPC-8/CRM RP Focus Areas and at least one of the FY16 PH/TBIRP CTRRA Areas of Encouragement. If the proposed work does not address one of the FY16 PH/TBIRP CTRRA Areas of Encouragement, explain how it is relevant to an important issue for the identified JPC-8/CRM RP Focus Areas in the context of complex TBI.
 - **Objective/Hypothesis:** State the objective/hypothesis to be tested. Provide evidence that supports the objective/hypothesis.
 - **Specific Aims:** State the specific aims of the study.
 - **Study Design:** Briefly describe the study design including appropriate controls.
 - **Impact:** Briefly describe how the proposed project will have an impact on TBI research and patient care.
 - **Military Benefit:** Briefly describe how the proposed project would benefit military Service members and/or Veterans recovering from complex TBI.
- **Attachment 4: Lay Abstract (one-page limit): Upload as “LayAbs.pdf.”** The lay abstract is used by all reviewers. Abstracts of all funded research projects will be posted publically. **Do not include proprietary or confidential information.** Use only characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed.

Lay abstracts should be written using the outline below. Do not duplicate the technical abstract. Abstracts of all funded research projects will be posted on the

CDMRP website (<http://cdmrp.army.mil>); therefore, proprietary or confidential information should *not* be included.

- Clearly describe the objectives and rationale for the proposed study in a manner readily understood by readers without a background in science or medicine.
- Describe the ultimate applicability and impact 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?
 - Briefly describe how the proposed project will benefit Service members, Veterans, and/or their family members.
- **Attachment 5: Statement of Work (SOW) (three-page limit): Upload as “SOW.pdf.”** The suggested SOW format and examples specific to different types of research projects are available on the eBRAP “Funding Opportunities & Forms” web page (<https://ebrap.org/eBRAP/public/Program.htm>). For the FY16 PH/TBIRP CTRRA mechanism, use the SOW format example titled “SOW Generic Format” or “SOW for Clinical Research (Including Trials, Special Populations).” The SOW must be in PDF format prior to attaching. Refer to the General Application Instructions, Section II.C.2., for detailed guidance on creating the SOW.
- **Attachment 6: Human Sample Acquisition and Safety Procedures, if applicable (no page limit). Upload as “HumSamProc.pdf.”** The Human Sample Acquisition and Safety Procedures attachments 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(s) (population from whom the samples, data, or other resources will be recruited/drawn). Describe how anticipated findings in the proposed population(s) are relevant to military population(s). Discuss past efforts in recruiting human subjects from the target population for previous studies, (if applicable). Address potential barriers to accrual (including attrition of patients who have been enrolled) and plans for addressing any delays. Include justification of any age, race, ethnicity, or sex limitations provided. *For studies proposing to include military personnel as volunteers, refer to the General Application Instructions, Appendix 6, for more information.*
 - b. **Inclusion/Exclusion Criteria:** List the inclusion and exclusion criteria evaluation of samples for the proposed research. Inclusion/exclusion criteria should take into consideration the specific risk profile of the studies to be conducted and the standard of care for that patient population. Provide detailed justification for exclusions.

Inclusion of Women and Minorities in Study. Consistent with the Belmont Report, “Ethical Principles and Guidelines for the Protection of Human Subjects,” and congressional legislation, special attention is given to inclusion

of women and/or minorities in studies funded or supported by the DoD. 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 samples from women and/or minorities will be excluded from the proposed research.

- c. Screening Procedures:** List and describe any evaluations (e.g., laboratory procedures, history, or physical examination) that are required to determine eligibility/suitability for study inclusion and the diagnostic criteria for entry. Some screening procedures may require a separate consent or waivers of consent. Informed consent or appropriate waivers of consent must be obtained prior to initiation of any procedures for the purpose of determining eligibility.
- d. Description of the Informed Consent Process:** In certain cases, Federal regulations allow the IRB to approve a consent procedure that does not include, or that alters, some or all of the elements of informed consent, or to waive the requirement to obtain any informed consent. Most complete waivers of consent involve studies in which there are minimal risks to subjects. Specifically describe the plan for obtaining informed consent or appropriate waivers of informed consent for clinical samples from human subjects.
 - Identify who is responsible for explaining the study, answering questions, and obtaining informed consent or appropriate informed consent waivers. Include a plan for ensuring that human subjects' questions will be addressed during the consent process and throughout the study.
 - Describe the biological origin of the samples to be tested (e.g., primary fibroblast cells from adults with and without disease).
 - The narrative should also describe the sample source(s), such as purchased human samples obtained from a clinical repository, or previously collected as part of a research effort. If samples will be or have been collected as part of a research activity, the application should state whether donors provided consent for use of their samples in future research consistent with this proposed effort.
 - Describe the plan, if appropriate, for obtaining waivers of informed consent or the informed consent of the individual's Legally Authorized Representative (LAR) to be obtained prior to the human subject's participation in the study.
 - Waiver of Informed Consent, described in Federal regulation 45 CFR 46.116(d) Federal regulations at 45 CFR 46.116(d), establishes four criteria for waiving consent or altering the elements of consent in minimal risk studies. All four criteria must be addressed.
 - Waiver of Documentation of Consent, described in Federal regulation 45 CFR 46.117(c), allows the IRB to waive the requirement for obtaining signed consent if it finds that either:
 - The only record linking the subject and the research would be the consent document and the principal risk would be potential harm

resulting from a breach of confidentiality (these criteria cannot be used for FDA-regulated studies), or

- The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context. This paragraph only also applies to FDA-regulated studies per 21 CFR 56.109(c)(1).
- 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). If applicable, refer to the General Application Instructions, Appendix 6, for more information.

e. Risks/Benefits Assessment:

- **Foreseeable risks:** Clearly identify all study risks. Study risks include any risks that the human subject is subjected to (including retroactively, as identified by the ORP and IRB) as a result of participation in the research. 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.
- **Potential benefits:** Describe known and potential benefits of the study to the human subject, a specific community, or society.
- **Quality Control:** Quality control (QC) is a material or mechanism that, when used with or as part of a test system, monitors the analytical performance of that test system. It may monitor the entire test system or only one aspect of it. Note that the FDA regulates the *material or mechanism as a medical device*; it does not monitor how a QC component is used within a laboratory (i.e., how often other QC types should be run or whether the QC replaces other, more traditional external types of QC).

See [Attachment 9, Data Management](#) for general laboratory procedures. Here, describe the QC to be employed for the study and/or device and, as appropriate, include:

- Procedures that will be employed to monitor QC (i.e., how often other QC types should be run or whether the QC replaces other, more traditional external types of QC),
- Review of sample labeling for accuracy,
- Determination/inclusion of manufacture protocols and protocols to ensure stability.

- **Attachment 7: 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(s) (population from whom the sample will be recruited/drawn). Describe how the proposed sample population findings will directly relate to Service members and Veterans with complex TBI. 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 studies (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. *For applications proposing to include military personnel, refer to the General Application Instructions, Appendix 6, for more information.*
 - b. **Inclusion/Exclusion Criteria:** List the inclusion and exclusion criteria for the proposed research. Inclusion/exclusion criteria should take into consideration the specific risk profile of the studies to be conducted and the standard of care for that patient population. Provide detailed justification for exclusions.

Inclusion of Women and Minorities in Study. Consistent with the Belmont Report, “Ethical Principles and Guidelines for the Protection of Human Subjects,” and Congressional legislation, special attention is given to inclusion of women and/or minorities in studies funded or supported by the USAMRMC. This policy is intended to promote equity both in assuming the burdens and in receiving the benefits of human subjects research. Include an appropriate justification if women and/or minorities will be excluded from the proposed research.
 - c. **Description of the Recruitment Process:** Explain methods for identification of potential human subjects (e.g., medical record review, obtaining sampling lists, healthcare 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.
 - If human subjects will be compensated for participation in the study, include a detailed description of and justification for the compensation plan.
 - Describe the recruitment and advertisement materials. The recruitment materials should not be coercive or offer undue inducements and should accurately reflect the study.
 - d. **Description of the Informed Consent Process:** Specifically describe the plan for obtaining informed consent from human subjects.
 - *For the proposed study, provide a draft, in English, of the Informed Consent Form.*

- Identify who is responsible for explaining the study, answering questions, and obtaining informed consent. Include a plan for ensuring that human subjects' questions will be addressed during the consent process and throughout the trial.
 - Include information regarding the timing and location of the consent process.
 - Address issues relevant to the mental capacity of the potential human subject (e.g., altered capacity due to administration of any mind-altering substances such as tranquilizers, conscious sedation or anesthesia, brain injury, stress/life situations, or human subject age), if applicable.
 - Address how privacy and time for decision making will be provided and whether or not the potential human subject will be allowed to discuss the study with anyone before making a decision.
 - Consider the need for obtaining ongoing consent or for re-assessing capacity over the course of a long-term study and describe any relevant procedures to assure continued consent.
 - Describe the plan for the consent of the individual's Legally Authorized Representative (LAR) to be obtained prior to the human subject's participation in the study. State law defines who may act as the LAR. The local IRB of record should be consulted for guidance regarding who can serve as LAR for research at the study site. Note: The PI must describe a clear intent to benefit for human subjects who cannot give their own consent to participate in the proposed research to be in compliance with Title 10 United States Code Section 980 (10 USC 980) (<http://www.gpo.gov/fdsys/pkg/USCODE-2011-title10/pdf/USCODE-2011-title10-subtitleA-partII-chap49-sec980.pdf>). If applicable, refer to the General Application Instructions, Appendix 6, for more information.
 - **Assent.** If minors or other populations that cannot provide informed consent are included in the proposed research, 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. Note that some screening procedures may require a separate consent or a two-stage consent process. Informed consent must be obtained prior to initiation of any procedures for the purpose of determining eligibility.
- f. Risks/Benefits Assessment:**
- **Foreseeable risks:** Clearly identify all study risks, including potential safety concerns and adverse events. Study risks include any risks that the human subject is subjected to as a result of participation in the proposed research. Consider psychological, legal, social, and economic risks as well

as physical risks. If the risks are unknown, this should be stated. If applicable, any potential risk to the study personnel should be identified.

- **Risk management and emergency response:**
 - Describe how safety surveillance and reporting to the IRB, USAMRMC, and FDA (if applicable) will be managed and conducted.
 - Describe all safety measures to minimize and/or eliminate risks to human subjects and study personnel or to manage unpreventable risks. Include safeguards and planned responses such as dose reduction or stopping criteria based on toxicity grading scales or other predetermined alert values.
 - Discuss the overall plan for provision of emergency care or treatment for an adverse event for study-related injuries, to include who will be responsible for the cost of such care.
 - Address any special precautions to be taken by the human subjects before, during, and after the study (e.g., medication washout periods, dietary restrictions, hydration, fasting, pregnancy prevention).
 - Describe any special care (e.g., wound dressing assistance, transportation due to side effects of study intervention impairing ability to drive) or equipment (e.g., thermometers, telemedicine equipment) needed for human subjects enrolled in the study.
 - If the IRB determines that a study presents greater than minimal risk to human subjects, the DoD requires an independent research monitor with expertise consistent with the nature of risk(s) identified within the research protocol. If applicable, refer to the General Application Instructions, Appendix 6, for more information on study reporting authorities and responsibilities of the research monitor.
- **Potential benefits:** Describe known and potential benefits of the study to the human subject, a specific community, or society.
- **Attachment 8: Intervention, if applicable (no page limit): Upload as “Intervention.pdf.”** The Intervention attachment should include the components listed below.
 - a. **Description of the Intervention:** Identify the intervention to be tested and describe the particular outcomes. As applicable, the description of the intervention should include the following components: complete name and composition, storage and handling information, source, dose, schedule, administration route, washout period, duration of the intervention, and concomitant medications allowed. Description of devices should include general concept of design, detailed operational instructions, any potential risks to users, and intended benefits. Other types of interventions should be fully described.

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

- b. Study Procedures:** Describe the interaction with the human subject to include the study intervention that he/she will experience. Provide sufficient detail in chronological order for a person uninvolved in the study to understand what the human subject will experience. Provide a schedule (e.g., flowchart or diagram) of study evaluations and follow-up procedures. PIs are highly encouraged to include at least 6 months of follow-up evaluation following a proposed intervention. Discuss how compliance with Good Laboratory Practices (GLP), Good Manufacturing Practices (GMP), and other regulatory considerations will be established, monitored, and maintained, as applicable.
 - c. Clinical Monitoring Plan:** Describe how the study will be conducted by and monitored for ICH E6 (International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use) GCP compliance, by an independent clinical trial monitor (or clinical research associate). The monitoring plan should describe the types of monitoring visits to be conducted, the intervals (based on level of risk), how corrective actions will be reported to the Sponsor and PI, and how they will be corrected and prevented by the clinical trial site/PI.
- **Attachment 9: Data Management (no page limit): Upload as “Data_Manage.pdf.”** The Data Management attachment should include the components listed below.
 - a. Data Management:** Describe all methods used for data collection to include the following:
 - **Identifiers:** Describe the unique identifiers or specific code system to be used to identify human subjects, if applicable.
 - **Confidentiality:**
 - Explain measures taken to protect the privacy of human subjects and maintain confidentiality of study data. Strategies to protect the privacy and confidentiality of study records, particularly those containing identifying information, should be addressed.
 - Address who will have access to study records, data, and specimens, including an acknowledgment that representatives of the DoD are eligible to review study records.
 - Address requirements for reporting sensitive information to state or local authorities.
 - **Data capture, verification, and disposition:** Describe how data will be captured and verified. Describe where data (both electronic and hard copy) will be stored, who will keep the data, how the data will be stored, the process for locking the database at study completion, and the length of time data will be stored. Refer to standards described for FITBIR access, common data elements, and data entry. Describe the proposed database,

how it will be developed and validated, and its capability to safeguard and maintain the integrity of the data. For FDA-regulated studies, compliance with 21 CFR 11 is required.

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

b. Laboratory Evaluations:

- **Specimens to be collected, schedule, and amount:** All specimens that will be collected for study purposes must be clearly stated. The collection schedule and amount of material collected must also be clearly described.
 - **Evaluations to be made:** Describe all evaluations that will be made for study purposes. Explain how the results of laboratory evaluations will be used to meet the objectives of the study (or to monitor safety of human subjects).
 - **Storage:** Describe specimen storage, to include location of storage, how long specimens will be stored, any special conditions required, labeling, and specimen 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 10: Study Personnel and Organization (no page limit): Start each document on a new page. Combine into one document and upload as “Personnel.pdf.”** The Study Personnel and Organization attachment should include the components listed below.
 - a. Organizational Chart:** Provide an organizational chart identifying key members of the study team including institution/center/department and name each person’s position on the project. If applicable, include any external consultants or other experts who will assist with FDA applications. While there is no specified format for this information, a table(s) or diagram is recommended. Note: This item may be made available for programmatic review.
 - b. Study Personnel Description:** Briefly describe the roles of the individuals listed in the organizational chart on the project. Describe relevant experience and qualifications that demonstrate appropriate expertise for the given role. An external research monitor (if applicable) and study coordinator(s) should be included.

- c. **Study Management Plan:** Provide a plan for ensuring the standardization of procedures among staff and across sites (if applicable). 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. Provide a plan for real-time communication among collaborating institutions (if applicable).
- **Attachment 11: 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 (e.g., [FITBIR requirements](#), [DVPRS and PASTOR data collection tools](#)). For each instrument, describe how the information collected is related to the objectives of the study. Describe how and when the instrument(s) will be administered. Describe how the instrument(s) will be adapted to the subject population, if applicable.
- **Attachment 12: Impact and Military Relevance Statement (two-page limit). Upload as “Impact.pdf.”**
 - Identify the volunteer population(s) that will participate in the proposed research, describe how they represent the target population that would benefit from the research, and describe the potential impact of the proposed research on the outcomes of individuals with complex TBI.
 - Describe the short-term impact: Detail the anticipated outcomes that will be directly attributed to the results of the proposed research.
 - Describe the long-term impact: Explain the long-range vision for implementation of the anticipated research outcomes in the clinic or field, and describe the anticipated long-term benefits for the targeted population.
 - Explain the relevance of the proposed research to Service member and/or Veteran populations with complex TBI.
 - Describe any relevant controversies, treatment issues or other issues in TBI patient care that will be addressed by the proposed research.
 - Describe any potential issues that might limit the impact of the proposed research.
 - If applicable, describe how the proposed intervention represents an improvement over currently available interventions and/or standards of care.
- **Attachment 13: Transition Plan (two-page limit): Upload as “Transition.pdf.”** A key feature of the intent of this award mechanism is the transition of information to the next stage of development or implementation. Applications must include a Transition Plan that clearly describes how this will be accomplished. Describe/discuss the methods and strategies proposed to move the anticipated research outcomes to the next phase of development or implementation (e.g., next phase

clinical trials, commercialization, and/or delivery to the civilian or military market) after successful completion of the award. The post-award transition plan should include the components listed below.

- The planned indication for the product label, if appropriate, and an outline of the development plan required to support that indication.
 - Details of the funding strategy to transition the anticipated research outcomes to the next phase of development, implementation, and/or commercialization (e.g., partners, internal/external funding opportunities to be applied for).
 - For Knowledge Products, a description of collaborations and other resources that will be used to provide continuity of development including proposed development or modification of clinical practice guidelines and recommendations, provider training materials, patient brochures, and other clinical support tools, scientific journal publications, models, simulations, and applications. A “Knowledge Product” is a non-materiel product that addresses an identified need, topic area, or capability gap, is based on current evidence and research, aims to transition into medical practice, training, tools, or to support materiel solutions (systems to develop, acquire, provide, and sustain medical solutions and capabilities), and educates or impacts behavior throughout the continuum of care, including primary prevention of negative outcomes.
 - A brief schedule and milestones for transitioning the anticipated research outcomes to the next phase of development (next-phase clinical trials, commercialization, delivery to the military or civilian market, incorporation into clinical practice, and/or approval by the FDA). Include identification of the FDA regulatory strategy (if appropriate). Identify existing or potential commercial partner(s) for transitioning materiel solutions (if appropriate).
 - Ownership rights/access to the intellectual property necessary for the development and/or commercialization of products or technologies supported with this award and the Government’s ability to access such products or technologies in the future.
 - If applicable, a risk analysis for cost, schedule, manufacturability, and sustainability.
- **Attachment 14: IND/IDE Documentation, if applicable:** If submitting multiple documents, start each document on a new page. **Combine and upload as a single file named “IND-IDE.pdf.”** The IND/IDE Documentation Form located on the eBRAP website may *not* be used in place of this information.
 - Complete the IND/IDE Documentation Form, which is available for download on the Full Announcement page for this Program Announcement/Funding Opportunity on Grants.gov.
 - State whether the proposed intervention requires regulation by the FDA. If FDA regulation is required, describe the planned indication for the proposed product and whether an IND/IDE is necessary.

- If an IND or IDE has already been obtained for the investigational drug or device pertaining to the indication to be studied, provide evidence in the form of formal communication (e.g., letterhead correspondence) from the FDA.
- If an IND or IDE application has been submitted, provide an explanation of the status of the IND or IDE application (e.g., past the critical 30-day period, pending response to questions raised by the Agency, on clinical hold) within 6 months of award. Provide a summary of previous meetings with the FDA on development of this product, if appropriate. A copy of the Agency meeting minutes should be included if available. Provide copies of communications from the FDA relevant to the most recent status of the IND or IDE application.
- If an IND or IDE is not required for the proposed study, or if it qualifies for an abbreviated IDE, provide evidence in the form of formal communication (e.g., letterhead correspondence) from the FDA or the IRB of record to that effect. Devices qualifying for an abbreviated IDE must comply with the abbreviated IDE requirements but do not require the submission of an IDE application to the FDA.
- **Attachment 15: Collaborating DoD Military Facility Budget Form(s), if applicable: Upload as “MFBudget.pdf.”** If a Military Facility (MHS facility, research laboratory, treatment facility, dental treatment facility, or a DoD activity embedded with a civilian medical center) will be a collaborator in performance of the project, complete the Collaborating DoD Military Facility Budget Form, available for download on the eBRAP “Funding Opportunities & Forms” web page (<https://ebrap.org/eBRAP/public/Program.htm>), including a budget justification, for each Military Facility as instructed. The costs per year should be included on the Grants.gov Research and Related Budget form under subaward costs. Refer to the General Application Instructions, Section II.C.7., for detailed information.

3. Research & Related Senior/Key Person Profile (Expanded): Refer to the General Application Instructions, Section II.C.4., for detailed information.

- PI Biographical Sketch (five-page limit): Upload as “Biosketch_LastName.pdf.” The suggested biographical sketch format is available on the “Funding Opportunities & Forms” web page (<https://ebrap.org/eBRAP/public/Program.htm>) in eBRAP. The National Institutes of Health Biographical Sketch may also be used. All biographical sketches should be submitted in the portable document format (pdf) that is not editable.

Biographical Sketches should be used to demonstrate background and expertise through education, positions, publications, and previous work accomplished.
- PI Previous/Current/Pending Support (no page limit): Upload as “Support_LastName.pdf.”
- Key Personnel Biographical Sketches (five-page limit each): Upload as “Biosketch_LastName.pdf.”
- Key Personnel Previous/Current/Pending Support (no page limit): Upload as “Support_LastName.pdf.”

4. **Research & Related Budget:** Refer to the General Application Instructions, Section II.C.4., for detailed information.
 - Budget Justification (no page limit): Upload as “BudgetJustification.pdf.” The budget justification for the entire period of performance must be uploaded to the Research & Related Budget after completion of the budget for Period 1.
5. **Project/Performance Site Location(s) Form:** Refer to the General Application Instructions, Section II.C.5., for detailed information.
6. **R & R Subaward Budget Attachment(s) Form (if applicable):** Refer to the General Application Instructions, Section II.C.6., for detailed information.

Collaborating DoD Military Facilities Form: A Military Facility collaborating in the performance of the project should be treated as a subaward for budget purposes. However, do not complete the Grants.gov R & R Subaward Budget Attachment Form; instead, complete the Collaborating DoD Military Facility Budget Form (use Attachment 15, Collaborating DoD Military Facility Budget Form) to show all direct and indirect costs. The costs per year should be included on the Grants.gov Research and Related Budget form under subaward costs. Refer to the General Application Instructions, Section II.C.7., for detailed information.

D. Applicant Verification of Grants.gov Submission in eBRAP

Prior to the end of the application verification period, PIs and organizational representatives can review and modify in eBRAP certain components of an application submitted to Grants.gov. Following retrieval and processing of the Grants.gov application, eBRAP will notify the organizational representatives and PI by email to log into eBRAP to review, modify, and verify the Grants.gov application submission. eBRAP will validate retrieved files against the specific Program Announcement/Funding Opportunity requirements and discrepancies will be noted in both the email and in the Full Application Files tab in eBRAP. eBRAP does not confirm the accuracy of file content. It is the applicant’s responsibility to review all application components and ensure proper ordering as specified in the Program Announcement/Funding Opportunity. *If either the Project Narrative or the budget fails eBRAP validation or needs to be modified, an updated Grants.gov application package must be submitted via Grants.gov as a “Changed/Corrected Application” with the previous Grants.gov Tracking ID prior to the application submission deadline.* The Project Narrative and Budget Form cannot be changed after the application submission deadline.

E. Submission Dates and Times

All submission dates and times are indicated on the [title page](#) of this Program Announcement/Funding Opportunity. Pre-application and application submissions are required. Failure to meet either of these deadlines will result in submission rejection.

F. Other Submission Requirements

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

All extramural applications must be submitted through Grants.gov. Applicant organizations and all subrecipient organizations must have a DUNS number to submit applications to Grants.gov. The applicant organization must also be registered in the Entity Management functional area of the SAM with an “Active” status to submit applications through the Grants.gov portal. Refer to the General Application Instructions, Section II.A., for information on Grants.gov registration requirements.

III. APPLICATION REVIEW INFORMATION

A. Application Review and Selection Process

All applications are evaluated by scientists, clinicians, and consumers in a two-tier review process. The first tier is peer review of applications against established criteria for determining technical merit. Each application is evaluated for its own merit, independent of other applications. The second tier is a programmatic review that makes recommendations for funding to the DHA RDA Directorate and the OASD(HA), based on technical merit, the relevance to the mission of the DHP and JPC-8/CRM RP, the specific intent of the award mechanism, and to other specified evaluation criteria in the Program Announcement/Funding Opportunity. Programmatic review is a comparison-based process in which applications with scientific and technical merit compete in a common pool. *The highest-scoring applications from the first tier of review are not automatically recommended for funding. Funding recommendations depend on various factors as described in [Section III.B.2., Programmatic Review](#).* Additional information about the two-tier process used by the CDMRP can be found at <http://cdmrp.army.mil/about/fundingprocess.shtml>.

All CDMRP review processes are conducted confidentially to maintain the integrity of the merit-based selection process. Panel members sign a statement that application and evaluation information will not be disclosed outside the panel. Violations of confidentiality can result in the dissolving of a panel(s) and other corrective actions. In addition, personnel at the applicant or collaborating organizations are prohibited from contacting persons involved in the review process to gain protected evaluation information or to influence the evaluation process. Violations of these prohibitions will result in the administrative withdrawal of the organization’s application. Violations by panel members or applicants that compromise the confidentiality of the review process may also result in suspension or debarment from Federal awards. Furthermore, the unauthorized disclosure of confidential information of one party to another third party is a crime in accordance with Title 18 United States Code 1905.

Extramural and Intramural applications will be reviewed by the same panels and evaluated with the same criteria.

B. Application Review Process

- 1. Peer Review:** To determine technical merit, all applications will be evaluated according to the following scored criteria, which are listed in decreasing order of importance:

- **Research Strategy**
 - How well the scientific rationale for the proposed study or trial design is supported by the preliminary data, critical review and analysis of the literature, and/or laboratory/preclinical evidence.
 - How well the study aims, hypotheses or objectives, experimental design, methods, data collection procedures, and analyses are designed to accomplish the clinical objective.
 - If applicable, how well the inclusion and randomization criteria are justified and meet the needs of the proposed research.
 - If applicable, how well plans to collect or obtain specimens and plans for their storage are addressed. How well plans for conduct laboratory evaluations are addressed.
 - If applicable, how well plans to collect and store clinical data are addressed.
 - If applicable, to what degree the data collection instruments (e.g., surveys, questionnaires) are appropriate to the proposed study.
 - How well the PI acknowledges potential problems and addresses alternative approaches.
 - Whether the research can be completed within the proposed period of performance.
 - How well the PI has outlined an appropriate plan for management and sharing of research data.
- **Impact**
 - How relevant the anticipated outcomes of the proposed observational study or clinical trial are to individuals with complex TBI.
 - How well the proposed research addresses one or more of the JPC-8/CRM RP Focus Areas.
 - How well the proposed research addresses one or more of the FY16 PH/TBIRP CTRRA Areas of Encouragement or justifies relevance to an important issue for the identified JPC-8/CRM RP Focus Areas in the context of TBI.
 - How well the sample population represents the targeted patient population that might benefit from the proposed intervention, if applicable.
 - How the potential outcomes of the proposed observational study or clinical trial will provide/improve short-term benefits for individuals with complex TBI.
 - How significantly the anticipated research outcomes may impact TBI research or patient care in the long-term.
- **Personnel and Communication**
 - Whether the composition of the study team (e.g., study coordinator, statistician) is appropriate.

- To what degree the study team’s background and expertise are appropriate to accomplish the proposed work (e.g., statistical expertise, expertise in complex TBI, and clinical research).
- How the levels of effort of the study team members are appropriate for successful conduct of the proposed study or trial.
- If applicable, how well the logistical aspects of the proposed observational study or clinical trial (e.g., communication plan, data transfer and management, standardization of procedures) meet the needs of the proposed observational study or clinical trial.
- **Transition Plan**
 - Whether the identified next phase of development, implementation, and/or commercialization is realistic.
 - Whether the funding strategy, schedule, and milestones described to bring the anticipated research outcomes to the next phase of development, implementation, or commercialization (e.g., specific industry partners, specific funding opportunities to be applied for) are reasonable and realistic.
 - How the development plans to support a product label change are appropriate and well described, if applicable.
 - If applicable, whether the proposed collaborations and other resources for providing continuity of development, including proposed development or modification of clinical practice guidelines and recommendations, provider training materials, patient brochures, and other clinical support tools, scientific journal publications, models, simulations, and applications are established and/or achievable.
 - If applicable, whether the schedule and milestones for bringing the intervention to the next level of development (next-phase clinical trials, transition to industry, delivery to the market, incorporation into standard practice, and/or approval by the FDA) are achievable.
 - If applicable, whether the risk analysis for cost, schedule, manufacturability, and sustainability is realistic and reasonable.
 - How well the application identifies intellectual property ownership, describes an appropriate intellectual and material property plan among all participating organizations (if applicable), and addresses potential intellectual property issues on product development and subsequent Government access to products or technologies supported by this Program Announcement/Funding Opportunity.
- **Recruitment, Accrual, and Feasibility**
 - How well the PI addresses the availability of human subjects for the study and the prospect of their participation.
 - How well the PI addresses the availability of samples for the study.

- Whether the PI has demonstrated access to the proposed human subjects population or human samples necessary for the proposed research.
- The degree to which the recruitment, informed consent, screening, and retention processes for human subjects will meet the needs of the proposed observational study or clinical trial, as applicable.
- How well the application identifies possible delays (e.g., slow accrual, attrition) and presents adequate contingency plans to resolve them.
- If applicable, to what extent the proposed observational study or clinical trial might affect the daily lives of the individual human subjects participating in the study (e.g., Will human subjects still be able to take their regular medications while participating in the clinical trial? Are human subjects required to stay overnight in a hospital?).
- **Intervention (required for clinical trials)**
 - Whether there is evidence of support, indicating availability of the intervention from its source, for the duration of the proposed clinical trial.
 - To what degree the intervention addresses the clinical need(s) described.
 - How the intervention compares with currently available interventions and/or standards of care, if applicable.
 - To what degree the PI has provided sufficient evidence to support the safety of the proposed intervention.
 - Whether a member of the study team holds the IND/IDE for the indication proposed or whether the timeline proposed for obtaining the IND/IDE is appropriate (if applicable).
 - For investigator-sponsored INDs, whether there is evidence of appropriate institutional support, including capabilities to ensure monitoring as required by the FDA.
 - Whether plans to comply with GMP, GLP, and GCP guidelines are appropriate.
 - Whether measures are described to ensure the consistency of dosing of active ingredients for nutritional supplements (if applicable).
- **Statistical Plan**
 - To what degree the statistical model and data analysis plan are suitable for the planned study or trial.
 - How the statistical plan, including sample size projections and power analysis, is adequate for the study or trial and all proposed correlative studies.
 - If applicable, whether the statistical plan compensates for the use of a subpopulation of a recruited sample population to ensure appropriate power can be achieved within the subpopulation study.

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

- **Ethical Considerations**

- If applicable, how the level of risk to human subjects is minimized and how the safety monitoring and reporting plan is appropriate for the level of risk.
- If applicable, whether a research monitor with expertise consistent with the nature of the potential risk(s) is identified.
- How well the evidence shows that the procedures are consistent with sound research design and, when appropriate, whether these procedures are already in use for diagnostic or treatment purposes.
- To what degree privacy issues are appropriately considered.
- If applicable, to what degree the process for seeking informed consent is appropriate and whether safeguards are in place for vulnerable populations.

- **Budget**

- Whether the total maximum costs are equal to or less than the allowable total maximum costs as published in the Program Announcement/Funding Opportunity.
- Whether the budget is appropriate for the proposed research.

- **Environment**

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

- **Application Presentation**

- To what extent the writing, clarity, and presentation of the application components influence the review.

2. **Programmatic Review:** To make funding recommendations and select the application(s) that, individually or collectively, will best achieve the program objectives, the following criteria are used by programmatic reviewers:

- a. **Ratings and evaluations of the peer reviewers**

- b. **Relevance to the mission of the DHP and JPC-8/CRM RP, as evidenced by the following:**

- Adherence to the intent of the award mechanism
- Program portfolio composition
- Military relevance
- Relative impact

- Programmatic relevance in relation to JPC-8/CRM RP Focus Areas and FY16 PH/TBIRP CTRRA Areas of Encouragement

C. Recipient Qualification

For general information on required qualifications for award recipients, refer to the General Application Instructions, Appendix 1.

D. Application Review Dates

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

E. Notification of Application Review Results

Each PI and organization will receive email notification of posting of the funding recommendation in eBRAP. Each PI will receive a peer review summary statement on the strengths and weaknesses of the application.

IV. ADMINISTRATIVE ACTIONS

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

A. Rejection

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

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

The following will result in administrative rejection of the application:

- Submission of an application for which a letter of invitation was not received.
- Project Narrative exceeds page limit.
- Project Narrative is missing.
- Budget is missing.
- For observational studies with human subjects, Human Sample Acquisition and Safety Procedures (Attachment 6) is missing.
- For clinical trials, Human Subject Recruitment and Safety Procedures (Attachment 7) is missing.
- For clinical trials, Intervention (Attachment 8) is missing.
- Data Management (Attachment 9) is missing.

B. Modification

- Pages exceeding the specific limits will be removed prior to review for all documents other than the Preproposal Narrative and Project Narrative.
- Documents not requested will be removed.

C. Withdrawal

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

- An FY16 JPC-8/CRM RP PH/TBIRP CTRRA Programmatic Panel member is named as being involved in the research proposed or is found to have assisted in the pre-application or application processes including, but not limited to, concept design, application development, budget preparation, and the development of any supporting documentation. *A list of the FY16 JPC-8/CRM RP PH/TBIRP CTRRA Programmatic Panel members can be found at http://cdmrp.army.mil/phtbi/panels/panels16_crmr.shtml.*
- The application fails to conform to this Program Announcement/Funding Opportunity description to the extent that appropriate review cannot be conducted.
- Inclusion of URLs, with the exception of links in References Cited and Publication and/or Patent Abstract sections.
- Page size is larger than 8.5 inches x 11.0 inches (approximately 21.59 cm x 27.94 cm).
- To preserve the integrity of its peer and programmatic review processes, the CDMRP discourages inclusion of any employee of its review contractors having any role in the preparation, research or other duties for submitted applications. For FY16, the identities of the peer review contractor and the programmatic review contractor may be found at the CDMRP website (<http://cdmrp.army.mil/about/2tierRevProcess.shtml>). Applications that include names of personnel from either of these companies will be administratively withdrawn unless plans to manage COIs are provided and deemed appropriate by the Government. Refer to the General Application Instructions, Appendix 1, for detailed information.
- Personnel from applicant or collaborating organizations are found to have contacted persons involved in the review process to gain protected evaluation information or to influence the evaluation process.
- The invited application does not propose the same research project described in the pre-application.
- The proposed research is not an observational study or clinical trial.
- The proposed project includes preclinical research.
- For studies requiring an IND or IDE, documentation of IND/IDE submission and/or approval is not provided.

D. Withhold

Applications that appear to involve research misconduct will be administratively withheld from further consideration pending organizational investigation. The organization will be required to provide the findings of the investigation to the USAMRAA Grants Officer for a determination of the final disposition of the application.

V. AWARD ADMINISTRATION INFORMATION

A. Award Notice

Awards will be made no later than September 30, 2017. Refer to the General Application Instructions, Appendix 4, for additional award administration information.

Any assistance instrument awarded under this Program Announcement/Funding Opportunity will be governed by the award terms and conditions, which conform to DoD's implementation of the Office of Management and Budget (OMB) circulars applicable to financial assistance. Terms and conditions of new awards made after December 26, 2014 may include revisions to reflect DoD implementation of new OMB guidance in the Code of Federal Regulations, Title 2, Part 200, "Uniform Administrative Requirements, Cost Principles, and Audit Requirements for Federal Awards" (2 CFR part 200).

B. Administrative Requirements

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

C. National Policy Requirements

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

D. Reporting

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

Quarterly technical progress reports and quad charts will be required.

In addition to written progress reports, in-person presentations may be requested.

E. Award Transfers

An organizational transfer of an award is discouraged and will be evaluated on a case-by-case basis and only allowed at the discretion of the Grants Officer. An organizational transfer of an award will not be allowed in the last year of the (original) period of performance or any extension thereof.

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

VI. VERSION CODES AND AGENCY CONTACTS

A. Program Announcement/Funding Opportunity and General Application Instructions Version

Questions related to this Program Announcement/Funding Opportunity should refer to the Program name, the Program Announcement/Funding Opportunity name, and the Program Announcement/Funding Opportunity version code 20160210i. The numeric sequence of the Program Announcement/Funding Opportunity version code will match the General Applications Instructions version code 20160210.

B. CDMRP Help Desk

Questions related to Program Announcement/Funding Opportunity content or submission requirements as well as questions related to the submission of the pre-application through eBRAP should be directed to the CDMRP Help Desk, which is available Monday through Friday from 8:00 a.m. to 5:00 p.m. ET. Response times may vary depending upon the volume of inquiries.

Phone: 301-682-5507

Email: help@eBRAP.org

C. Grants.gov Contact Center

Questions related to application submission through Grants.gov portal should be directed to the Grants.gov Contact Center, which is available 24 hours a day, 7 days a week (closed on U.S. Federal holidays). Note that the CDMRP Help Desk is unable to provide technical assistance with Grants.gov submission.

Phone: 800-518-4726; International 1-606-545-5035

Email: support@grants.gov

Sign up on Grants.gov for “send me change notification emails” by following the link on the Synopsis page for the Program Announcement/Funding Opportunity or by responding to the prompt provided by Grants.gov when first downloading the Grants.gov application package. If the Grants.gov 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	Upload Order	Action	Completed
SF-424 (R&R) Application for Federal Assistance		Complete form as instructed.	
Attachments Form	1	Project Narrative: Upload as Attachment 1 with file name "ProjectNarrative.pdf."	
	2	Supporting Documentation: Upload as Attachment 2 with file name "Support.pdf."	
	3	Technical Abstract: Upload as Attachment 3 with file name "TechAbs.pdf."	
	4	Lay Abstract: Upload as Attachment 4 with file name "LayAbs.pdf."	
	5	Statement of Work: Upload as Attachment 5 with file name "SOW.pdf."	
	6	Human Sample Acquisition and Safety Procedures: Upload as Attachment 6 with file name "HumSamProc.pdf," if applicable.	
	7	Human Subject Recruitment and Safety Procedures: Upload as Attachment 7 with file name "HumSubProc.pdf," if applicable.	
	8	Intervention: Upload as Attachment 8 with file name "Intervention.pdf," if applicable.	
	9	Data Management: Upload as Attachment 9 with file name "Data_Manage.pdf."	
	10	Study Personnel and Organization: Upload as Attachment 10 with file name "Personnel.pdf."	
	11	Surveys, Questionnaires, and Other Data Collection Instruments: Upload as Attachment 11 with file name "Surveys.pdf," if applicable.	
	12	Impact and Military Relevance Statement: Upload as Attachment 12 with file name "Impact.pdf."	
	13	Transition Plan: Upload as Attachment 13 with file name "Transition.pdf."	
	14	IND/IDE Documentation: Upload as Attachment 14 with file name "IND-IDE.pdf," if applicable.	
	15	Collaborating DoD Military Facility Budget Form(s): Upload Attachment 15 with file name "MFBudget.pdf," if applicable.	
Research & Related Senior/Key Person Profile (Expanded)		Attach PI Biographical Sketch (Biosketch_LastName.pdf) to the appropriate field.	
		Attach PI Previous/Current/Pending Support (Support_LastName.pdf) to the appropriate field.	
		Attach Biographical Sketch (Biosketch_LastName.pdf) for each senior/key person to the appropriate field.	
		Attach Previous/Current/Pending (Support_LastName.pdf) for each senior/key person to the appropriate field.	

Grants.gov Application Components	Upload Order	Action	Completed
Research & Related Budget		Complete as instructed. Attach Budget Justification (BudgetJustification.pdf) to the appropriate field.	
Project/Performance Site Location(s) Form		Complete form as instructed.	
R & R Subaward Budget Attachment(s) Form		Complete form as instructed.	