

I. OVERVIEW OF THE FUNDING OPPORTUNITY

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
Clinical Trial Award**

Announcement Type: Initial

Funding Opportunity Number: W81XWH-19-CTRR-CTA

**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), September 10, 2019
- **Invitation to Submit an Application:** October 9, 2019
- **Application Submission Deadline:** 11:59 p.m. ET, December 2, 2019
- **End of Application Verification Period:** 5:00 p.m. ET, December 5, 2019
- **Peer Review:** January 2020
- **Programmatic Review:** March 2020

This Program Announcement must be read in conjunction with the General Application Instructions, version 20190530. The General Application Instructions document is available for downloading from the Grants.gov funding opportunity announcement by selecting the “Package” tab, clicking “Preview,” and then selecting “Download Instructions.”

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II. DETAILED INFORMATION ABOUT THE FUNDING OPPORTUNITY

II.A. Program Description

Applications to the Fiscal Year 2019 (FY19) Psychological Health/Traumatic Brain Injury Research Program (PH/TBIRP) are being solicited for the Defense Health Agency (DHA) J9, Research and Development Directorate, by the U.S. Army Medical Research Acquisition Activity (USAMRAA) using delegated authority provided by United States Code, Title 10, Section 2358 (10 USC 2358). As directed by the Office of the Assistant Secretary of Defense for Health Affairs (OASD[HA]), the DHA manages the Defense Health Program (DHP) Research, Development, Test, and Evaluation (RDT&E) appropriation. The U.S. Army Medical Research and Development Command (USAMRDC) Congressionally Directed Medical Research Programs (CDMRP) provides execution management support for DHP research program areas, including the Joint Program Committee 8/Clinical and Rehabilitative Medicine Research Program (JPC-8/CRM RP). The execution management agent for this Program Announcement is the CDMRP.

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 (PTSD), 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 JPC-8/CRM RP seeks to implement long-term strategies to develop knowledge and materiel products to reconstruct, rehabilitate, and provide definitive care for injured Service members. The ultimate goal is to return Service members to duty and improve their quality of life. Additional information about the JPC-8/CRM RP can be found at <https://crmrp.amedd.army.mil/>.

Through the Complex TBI Rehabilitation Research (CTRR) initiative, the PH/TBIRP and JPC-8/CRM RP seek innovative rehabilitation 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 with TBI. The programs challenge the clinical and scientific communities to design innovative research that will foster new directions for, and address neglected issues in, the field of TBI rehabilitation research. Applications from investigators within the military Services, and applications involving multidisciplinary collaborations among academia, industry, the military Services, the Department of Veterans Affairs (VA), and other Federal Government agencies are highly encouraged.

II.A.1. FY19 PH/TBIRP CTRR-Clinical Trial Award (CTA) Areas of Emphasis

The FY19 PH/TBIRP CTRR-CTA is intended to support clinical trials to validate existing complex mild TBI (mTBI) rehabilitation interventions and practice patterns in Department of

Defense (DoD) and VA rehabilitation facilities (i.e., VA/DoD Clinical Practice Guideline for the Management of Concussion - Mild Traumatic Brain Injury, 2016). Partnership with Federal TBI rehabilitation researchers and clinicians is critical for the successful conduct of this research and is highly encouraged. Investigators should include diverse (but military-relevant) populations of study participants and recruit patients from heterogeneous practice settings (e.g., DoD/VA or other mixed population practices).

Trials should measure the effect of the intervention as well as measure the effectiveness of standard-of-care practices (rehabilitation and treatment strategies) in remediating post mTBI sequelae across the spectrum of known functional vulnerabilities in the area of *post-traumatic dizziness, vestibular dysfunction, imbalance or dynamic instability; visual and oculomotor dysfunction; cognitive deficits (e.g., degraded processing speed, memory, or executive functioning); central auditory processing; and autonomic dysregulation*. In particular, trials that identify determinants of successful recovery, return to duty (RTD)/work, functional restoration, and objective brain function measurement(s) following mTBI are encouraged.

Applications are encouraged to address one or more of the following FY19 PH/TBIRP CTRR-CTA Areas of Emphasis:

- **Objective outcome measures of brain impairment after mTBI using existing U.S. Food and Drug Administration (FDA)-cleared devices**
 - Develop objective measure(s) of brain function that determines severity of functional impairment
 - Correlate brain function to RTD performance
- **Optimization of treatment strategy based on patient classification to improve management of patients with mTBI as described above**
 - Determine indicators of successful recovery following mTBI
 - Validate algorithms for multi-modal treatment strategies

Projects focused on other research areas relevant to the intent of the CTRR-CTA may be submitted for consideration, provided sufficient justification is included in the application.

Applications without clinical trials should be submitted under the FY19 PH/TBIRP CTRR Clinical Research Award (Funding Opportunity Number W81XWH-19-CTRR-CRA).

II.A.2. Award History

The PH/TBIRP CTRR-CTA mechanism was first offered in FY17. Since then, 58 CTRR-CTA applications have been received, and 7 have been recommended for funding.

II.B. Award Information

The FY19 PH/TBIRP CTRR-CTA supports the rapid implementation of clinical trials with the potential to have a significant impact on the treatment or management of complex TBI. Clinical trials may be designed to evaluate promising products, pharmacologic agents (drugs or biologics), devices, clinical guidance, and/or emerging approaches and technologies. Proposed projects may range from small proof-of-concept trials (e.g., pilot, first in human, Phase 0) to demonstrate feasibility or inform the design of more advanced trials through large-scale trials to determine efficacy in relevant patient populations.

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. A complex TBI is a multi-faceted condition resulting after mTBI with comorbidities and related deficits in the areas of cognition, sensorimotor, and performance. Classification of TBI severity can be found in Table 1 of the [VA/DoD Clinical Practice Guideline for the Management of Concussion-Mild Traumatic Brain Injury](#).

The proposed research must be relevant to active duty Service members, Veterans, military beneficiaries, and/or the American public.

Funding from this award mechanism must support a clinical trial. New FY19 definition: A clinical trial is a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes. For more information, a Human Subject Resource Document is provided at <https://ebrap.org/eBRAP/public/Program.htm>.

Preclinical studies and observational clinical research studies are not supported by this Program Announcement. As stated in [Section II.H.2.c, Withdrawal](#), CTRR-CTA applications that propose preclinical studies or observational clinical research in the CTRR-CTA period of performance may be administratively withdrawn. ***Investigators seeking funding for clinical research studies should apply to the FY19 PH/TBIRP CTRR Clinical Research Award (Funding Opportunity Number W81XWH-19-CTRR-CRA).***

If the proposed clinical trial involves the use of a drug that has not been approved by the FDA for the proposed investigational use, then an Investigational New Drug (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. It is the responsibility of the applicant to provide evidence from the Institutional Review Board (IRB) of record or the FDA if an IND is not required. If an IND is required, the IND application ***must be submitted to the FDA by the CTRR-CTA application submission deadline***. The IND should be specific for the product (i.e., the product should not represent a derivative or alternate version of the investigational agent described in the IND application) and indication to be tested in the proposed clinical trial. For more information on IND applications, the FDA has provided guidance at <https://www.fda.gov/drugs/>

developmentapprovalprocess/howdrugsaredevelopedandapproved/approvalapplications/investigationalnewdrugindapplication/default.htm.

If the investigational product is a device, then an Investigational Device Exemption (IDE) application to the FDA that meets all requirements under 21 CFR 812 may be required. It is the responsibility of the applicant to provide evidence from the IRB of record or the FDA if an IDE is not required, or if the device qualifies for an abbreviated IDE. If an IDE is required, the IDE application ***must be submitted to the FDA by the CTRR-CTA application submission deadline***. The IDE should be specific for the device (i.e., should not represent a derivative or modified version of the device described in the IDE application) and indication to be tested in the proposed clinical trial.

If the clinical trial of an investigational product will be conducted at international sites, evidence that an application to the relevant national regulatory agency of the host country(ies) ***has been submitted by the CTRR-CTA application submission deadline*** is required.

Refer to [Attachment 9, Regulatory Strategy](#), for additional details on documentation of FDA applications. The Government reserves the right to withdraw funding if an IND or IDE application is necessary but has not been submitted prior to the application submission deadline, or if documentation of an active IND or IDE in effect for the proposed trial has not been obtained within 6 months of the award date.

Recruitment Milestones: The application must indicate the quarterly enrollment targets across all sites in [Attachment 5: Statement of Work \(SOW\)](#). Successful applicants will work with USAMRAA to establish milestones for human subject recruitment. Continued support for the project will be based upon satisfactory progress in meeting the established milestones.

The following are important aspects of the CTRR-CTA:

- The proposed clinical trial is expected to begin no later than 12 months after the award date, or 18 months after the award date for FDA-regulated studies.
- The proposed intervention(s) to be tested should offer significant potential impact for individuals affected by TBI.
- Inclusion of preliminary data relevant to the proposed clinical trial is required.
- The proposed clinical trial must be based on sound scientific rationale that is established through logical reasoning and critical review and analysis of the literature.
- The application should describe the planned indication for the product label, if appropriate, and include an outline of the product development plan required to support that indication.
- The application should demonstrate availability of, and access to, a suitable patient population that will support a meaningful outcome for the study. The Principal Investigator (PI) should discuss how accrual goals will be achieved and how standards of care may impact the study population.

- The application should demonstrate documented availability of and access to the drug/ compound, device, and/or other materials needed, as appropriate, for the proposed duration of the study. The quality and stability of the product should be documented and commensurate with current FDA manufacturing standards applicable to the type and phase of product being developed (i.e., Quality System Regulation, Good Manufacturing Practice [GMP] guidelines).
- The application should reflect the study team's experience interacting with the FDA, including previous FDA submissions, if applicable.
- The proposed clinical trial design should include clearly defined objectives and appropriate outcome measures, and comply with current Good Clinical Practice (GCP) guidelines.
- The application should include a clearly articulated statistical analysis plan, appropriate statistical expertise on the research team, and a power analysis reflecting sample size projections that will answer the objectives of the study.
- The application should include a clearly articulated data management plan and use of an appropriate database to safeguard and maintain the integrity of the data. If FDA-regulated, the trial must use a 21 CFR 11-compliant database and appropriate data standards. For more on data standards, see <https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/UCM511237.pdf>.
- The application should include a clearly articulated safety management plan outlining how safety pharmacovigilance will be conducted, as applicable.
- The application should include a clearly articulated clinical monitoring plan outlining how the study will be monitored for GCP compliance.
- The application should include a study coordinator(s) who will guide the clinical protocol through the local IRB of record and other Federal agency regulatory approval processes, coordinate activities from all sites participating in the trial, and coordinate participant accrual.
- The application should include a Transition Plan (including potential funding and resources) showing how the product will progress to the next clinical trial phase and/or delivery to the market after the successful completion of the FY19 PH/TBIRP CTRR-CTA.
- The application should clearly demonstrate strong institutional support and, if applicable, a commitment to serve as the FDA regulatory sponsor, ensuring all sponsor responsibilities described in 21 CFR 312, Subpart D, are fulfilled.
- Funded trials are required to post a copy of the informed consent form used to enroll subjects on a publicly available Federal website in accordance with Federal requirements described in 32 CFR 219.

- Funded studies are required to register the study in the National Institutes of Health (NIH) clinical trials registry, www.clinicaltrials.gov, prior to initiation of the study. Refer to the General Application Instructions, Appendix 1, Section C, for further details.

The anticipated total costs budgeted for the entire period of performance for an FY19 PH/TBIRP CTRR-CTA will not exceed **\$4.0 million (M)**. Refer to [Section II.D.5, Funding Restrictions](#), for detailed funding information.

The JPC-8/CRM RP expects to allot approximately \$8.0M of the FY19 PH/TBIRP appropriation to fund approximately 2 CTRR-CTA application(s). Funding of applications received is contingent upon the availability of Federal funds for this program as well as the number of applications received, the quality and merit of the applications as evaluated by scientific and programmatic review, and the requirements of the Government. Funds to be obligated on any award resulting from this funding opportunity will be available for use for a limited time period based on the fiscal year of the funds. It is anticipated that awards made from this FY19 funding opportunity will be funded with FY19 funds, which will expire for use on September 30, 2025.

Awards will be made no later than September 30, 2020. For additional information, refer to [Section II.F.1, Federal Award Notices](#).

The type of awards made under the Program Announcement will be assistance agreements (grants or cooperative agreements). The level of involvement on the part of the Department of Defense (DoD) during project performance is the key factor in determining whether to award a grant or cooperative agreement.

An assistance agreement (grant or cooperative agreement) is appropriate when the Federal Government transfers a “thing of value” to a “state, local government,” or “other recipient” to carry out a public purpose of support or stimulation authorized by a law of the United States, instead of acquiring property or service for the direct benefit and use of the U.S. Government. An assistance agreement can take the form of a grant or cooperative agreement. If “no substantial involvement” on the part of the funding agency is anticipated, a grant award will be made (31 USC 6304). Conversely, if substantial involvement on the part of the funding agency is anticipated, a cooperative agreement will be made (31 USC 6305) and the award will identify the specific substantial involvement. Substantial involvement may include collaboration, participation, or intervention in the research to be performed under the award. The award type, along with the start date, will be determined during the negotiation process.

Rigor of Experimental Design: All projects should adhere to accepted standards for rigorous study design and reporting to maximize the reproducibility and translational potential of preclinical research. Core standards are described in Landis, S.C., et al., A call for transparent reporting to optimize the predictive value of preclinical research, *Nature* 2012, 490:187-191 (www.nature.com/nature/journal/v490/n7419/full/nature11556.html). While these standards were written for preclinical studies, the basic principles of randomization, blinding, sample-size estimation, and data handling derive from well-established best practices in research and should be applied consistently across basic, translational, and clinical studies.

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 USAMRDC Office of Research Protections (ORP), Human Research Protection Office (HRPO), prior to research implementation. This administrative review requirement is in addition to the local 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.*** Additional time for regulatory reviews may be needed for clinical studies taking place in international settings. When possible, protocols should be written for research with human subjects and/or human anatomical substances that are specific to the DoD-supported effort outlined in the submitted application as a stand-alone study. Submission to HRPO of protocols involving more than the scope of work in the DoD-funded award will require HRPO review of the entire protocol (DoD and non-DoD funded). DoD human subjects protection requirements may be applied to non-DoD funded work and necessitate extensive revisions to the protocol. Applications that involve recruitment of human subjects must indicate the quarterly enrollment targets across all sites in [Attachment 5: Statement of Work \(SOW\)](#). Successful applicants will work with USAMRAA to establish milestones for human subjects recruitment. Continued support for the project will be based upon satisfactory progress in meeting the established milestones. Refer to the General Application Instructions, Appendix 1, Section B, and the Human Subject Resource Document available on the electronic Biomedical Research Application Portal (eBRAP) “Funding Opportunities & Forms” web page (<https://ebrap.org/eBRAP/public/Program.htm>) for additional information.

If the IRB determines that a trial 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 1, Section B (Research Monitor Requirement) for more information on study reporting authorities and responsibilities of the research monitor.

Multi-Institutional Clinical Trials: If the proposed clinical trial is multi-institutional, plans for the multi-institutional structure governing the research protocol(s) should be outlined in [Attachment 12: Study Personnel and Organization](#). The lead organization responsible for developing the master protocol and master consent form should be identified and should be the single point of contact for regulatory submissions and requirements. A single IRB/EC pathway is strongly recommended whenever possible. The master protocol and consent form must be reviewed by the HRPO prior to distribution to the additional sites for IRB/EC review. 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 trials.

Federal Interagency TBI Research (FITBIR) Informatics System: For studies that will enroll TBI subjects, the DoD requires that 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 FITBIR 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/>).

- Global Unique Identifier (GUID): FITBIR encourages collaboration between laboratories, as well as interconnectivity with other informatics platforms. Such community-wide sharing requires common data definitions and standards. 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 the FITBIR GUID system facilitates repeated and multi-user access to data without the need to personally identify data sources. In order to generate a GUID for a subject, the following personally identifiable information (PII) ***must be collected in the proposed research:***
 - Complete legal given (first) name of subject at birth
 - Complete legal additional name of subject at birth (if subject has a middle name)
 - Complete legal family (last) name of subject at birth
 - Day of birth
 - Month of birth
 - Year of birth
 - Name of city/municipality in which subject was born
 - Country of birth

Note that this PII is never sent to the FITBIR system. PII cannot be extracted from the GUID. Information on GUID compliance with HIPAA regulations can be found at <https://fitbir.nih.gov/content/global-unique-identifier>.

- Common Data Elements (CDEs): Data elements must be reported using the National Institute of Neurological Disorders and Stroke (NINDS) TBI CDEs or entered into the FITBIR data dictionary as new, unique data elements (UDEs). For the most current version of the NINDS TBI CDEs, see <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. 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 studies of TBI. *Use of UDEs is strongly discouraged and subject to program approval.*

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: [https://dvbic.dcoe.mil/sites/default/files/DVBIC - NSI Information Paper Final.pdf](https://dvbic.dcoe.mil/sites/default/files/DVBIC_-_NSI_Information_Paper_Final.pdf)

PGIC: [https://dvbic.dcoe.mil/sites/default/files/DVBIC - PGIC Information Paper Final.pdf](https://dvbic.dcoe.mil/sites/default/files/DVBIC_-_PGIC_Information_Paper_Final.pdf)

Principal Investigators are encouraged to integrate and/or align their research projects with DoD and/or VA research laboratories and programs.

Use of DoD or VA Resources: If the proposed research involves access to active duty military patient populations and/or DoD resources or databases, the application must describe the access at the time of submission and a plan for maintaining access as needed throughout the proposed research. Access to target active duty military patient population(s) and/or DoD resource(s) or database(s) should be confirmed by including a letter of support, signed by the lowest-ranking person with approval authority.

If the proposed research involves access to VA patient populations, VA study resources and databases, and/or VA research space and equipment, VA PIs must have a plan for obtaining and maintaining access throughout the proposed research. Access to VA patients, resources, and/or VA research space should be confirmed by including a letter of support from the VA Facility Director(s) or individual designated by the VA Facility Director(s), such as the Associate Chief of Staff for Research and Development (ACOS/R&D) or Clinical Service Chief. If appropriate, the application should identify the VA-affiliated non-profit corporation (NPC) as the applicant institution for VA PIs. If the VA NPC is not identified as the applicant institution for administering the funds, the application should include a letter from the VA ACOS/R&D confirming this arrangement and identifying the institution that will administer the funds associated with the proposed research.

Access to certain DoD or VA patient populations, resources, or databases may only be obtained by collaboration with a DoD or VA investigator who has a substantial role in the research and may not be available to a non-DoD or non-VA investigator if the resource is restricted to DoD or VA personnel. Investigators should be aware of which resources are available to them if the proposed research involves a non-DoD or non-VA investigator collaborating with the DoD and/or VA. If access cannot be confirmed at the time of application submission, the Government reserves the right to withdraw or revoke funding until the PI has demonstrated support for and access to the relevant population(s) and/or resource(s). Refer to [Section II.D.2.b.ii, Full Application Submission Components](#), for detailed information.

Principal Investigators are encouraged to integrate and/or align their research projects with DoD and/or VA research laboratories and programs. Collaboration with the DoD and/or VA is also encouraged. A list of websites that may be useful in identifying additional information about ongoing DoD and VA areas of research interest or potential opportunities for collaboration can be found in [Appendix 2](#).

The CDMRP intends that information, data, and research resources generated under awards funded by this Program Announcement 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 2, Section K.

II.C. Eligibility Information

II.C.1. Eligible Applicants

II.C.1.a. Organization: All organizations, including international organizations, are eligible to apply.

Government Agencies Within the United States: Local, state, and Federal Government agencies are eligible to the extent that applications do not overlap with their fully funded internal programs. Such agencies are required to explain how their applications do not overlap with their internal programs.

As applications for this Program Announcement may be submitted by extramural and intramural organizations, these terms are defined below.

Extramural Organization: An eligible non-DoD organization. Examples of extramural organizations include academic institutions, biotechnology companies, foundations, Federal Government organizations other than the DoD, and research institutes.

Intramural DoD Organization: A DoD laboratory, DoD military treatment facility, and/or DoD activity embedded within a civilian medical center.

Note: Applications from an intramural DoD organization or from an extramural Federal Government organization may be submitted to Grants.gov through a research foundation.

The USAMRAA makes awards to eligible organizations, not to individuals.

II.C.1.b. Principal Investigator

Independent investigators at all academic levels (or equivalent) are eligible.

An eligible PI, regardless of ethnicity, nationality, or citizenship status, must be employed by, or affiliated with, an eligible organization.

The CDMRP encourages all PIs to participate in a digital identifier initiative through Open Researcher and Contributor ID, Inc. (ORCID). Registration for a unique ORCID identifier can be done online at <https://orcid.org/>.

II.C.2. Cost Sharing

Cost sharing/matching is not an eligibility requirement.

II.C.3. Other

Organizations must be able to access **.gov** and **.mil** websites in order to fulfill the financial and technical deliverable requirements of the award and submit invoices for payment.

There are no limitations on the number of applications for which an investigator may be named as a PI.

For general information on required qualifications for award recipients, refer to the General Application Instructions, Appendix 3.

Refer to [Section II.H.2, Administrative Actions](#), for a list of administrative actions that may be taken if a pre-application or application does not meet the administrative, eligibility, or ethical requirements defined in this Program Announcement.

II.D. Application and Submission Information

Submission of applications that are essentially identical or propose essentially the same research project to different funding opportunities within the same program and fiscal year is prohibited and will result in administrative withdrawal of the duplicative application(s).

Extramural Submission: An application submitted by an organization to Grants.gov.

Intramural DoD Submission: An application submitted by a DoD organization to eBRAP.

II.D.1. Address to Request Application Package

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.

Extramural Submissions:

- Pre-application content and forms must be accessed and submitted at eBRAP.org.
- Full application packages must be accessed and submitted at Grants.gov.

Intramural DoD Submissions:

- Pre-application content and forms must be accessed and submitted at eBRAP.org.
- Full application packages must be accessed and submitted at eBRAP.org.

Contact information for the CDMRP Help Desk and the Grants.gov Contact Center can be found in [Section II.G, Federal Awarding Agency Contacts](#).

II.D.2. Content and Form of the Application Submission

Submission is a two-step process requiring both *pre-application* and *full application* as indicated below. The submission process should be started early to avoid missing deadlines. There are no grace periods.

Pre-Application Submission: All pre-applications for both extramural and intramural organizations must be submitted through eBRAP.org.

Full Application Submission: Full applications must be submitted through the online portals as described below.

Extramural Organization Submissions: Full applications from extramural organizations must be submitted through a Grants.gov Workspace. Applications submitted by extramural organizations (e.g., research foundations) on behalf of intramural DoD or other Federal organizations or investigators will be considered extramural submissions. Applications from extramural organizations, including non-DoD Federal organizations, received through eBRAP will be withdrawn. See definitions in [Section II.C.1, Eligible Applicants](#).

Intramural DoD Organization Submissions: Intramural DoD organizations may submit full applications to either eBRAP or Grants.gov. Intramural DoD organizations that are unable to submit to Grants.gov should submit through eBRAP. Intramural DoD organizations with the capability to submit through Grants.gov may submit following the instructions for extramural submissions through Grants.gov or may submit to eBRAP.

For Both Extramural and Intramural Applicants: eBRAP allows an organization's representatives and PIs to view and modify the full application submissions associated with them. eBRAP will validate full application files against the specific Program Announcement 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.

The application title, eBRAP log number, and all information for the PI, Business Official(s), performing organization, and contracting organization must be consistent throughout the entire pre-application and full application submission process. Inconsistencies may delay application processing and limit or negate 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 submission deadline.

II.D.2.a. Step 1: Pre-Application Submission Content

During the pre-application process, eBRAP assigns each submission a unique log number. This unique eBRAP log number is required during the full application submission process.

To begin the pre-application process, first select whether the submitting organization is extramural or intramural, then confirm your selection or cancel. **Incorrect selection of extramural or intramural submission type will delay processing.**

If an error has been made in the selection of extramural versus intramural and the pre-application submission deadline has passed, the PI or Business Official must contact the CDMRP Help Desk at help@eBRAP.org or 301-682-5507 to request a change in designation.

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

The applicant organization and associated PI 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.

Principal Investigators with an ORCID identifier should enter that information in the appropriate field in the “My Profile” tab in the “Account Information” section of eBRAP.

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**

Submission of application information includes assignment of primary and secondary research classification codes, which may be found at <https://ebrap.org/eBRAP/public/Program.htm>. Note that the codes have recently been revised. Applicants are strongly encouraged to review and confirm the codes prior to making their selection.

- **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 Research & Related Form). The Business Official must be either 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 Research & Related Form), and click on “Add

Organizations to this Pre-application.” The organization(s) must be either 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.

[FY19 PH/TBIRP CTRR 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 II.H.2.c, Withdrawal](#), or contact the CDMRP Help Desk at help@eBRAP.org or 301-682-5507.

- **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).

- **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:

- **Alignment:** Describe how the proposed clinical trial addresses one or more FY19 PH/TBIRP CTRR-CTA Area(s) of Emphasis. If the clinical trial research area is other than an identified Area of Emphasis, state how this clinical trial meets the intent of the award mechanism.
- **Objective/Hypothesis and Rationale:** State the hypothesis to be tested or the objective to be reached. State the ideas, reasoning, and/or literature on which the proposed clinical trial is based. Briefly describe how the preliminary data and rationale support the research idea.
- **Research Strategy:** Clearly describe the clinical trial being proposed, and indicate the phase of trial and/or class of device and regulatory status as appropriate. Describe

the intervention. Concisely state the project’s objectives and specific aims. Briefly describe the study population, 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.
- **Impact and Military Benefit:** Describe how the proposed work will impact the healthcare needs of military Service members, Veterans, and other individuals recovering from complex TBI in conjunction with symptoms associated with cognitive performance, sensory function and motor performance or multimodal 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 the following:
 - 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, reference title, and reference source, including 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.
 - Key Personnel Biographical Sketches (six-page limit per individual). *All biographical sketches should be uploaded as a single combined file.* Biographical sketches 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, the JPC-8/CRM RP and the PH/TBIRP, pre-applications will be screened based on the following criteria:

- **Alignment:** How well the proposed clinical trial addresses a critical problem or question in the field of research and/ patient care of one or more FY19 PH/TBIRP CTRR-CTA Area(s) of Emphasis. If application states “a research area other than an identified Area of Emphasis,” how relevant the research area is to the intent of CTRR-CTA.

- **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 outcomes are defined and are appropriate for the proposed clinical trial. Whether the proposed study population, recruitment strategies, and methodology are appropriate for accomplishing the research aims.
- **Impact and Military Benefit:** To what degree the proposed work would impact the healthcare needs of military Service members, Veterans, and other individuals recovering from complex TBI.
- **Research Team:** How the qualifications and expertise of the PI and key personnel are appropriate to perform the proposed 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 in [Section I, Overview of the Funding Opportunity](#). Invitations to submit a full application are based on the Pre-Application Screening Criteria listed above.

II.D.2.b. Step 2: Full Application Submission Content

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

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 full application package for this Program Announcement. The full application package is submitted by the Authorized Organizational Representative through Grants.gov (<https://www.grants.gov/>) for extramural organizations or through eBRAP (<https://ebrap.org/>) for intramural organizations. See Table 1 below for more specific guidelines.

II.D.2.b.i. Full Application Guidelines

Extramural organizations must submit full applications through Grants.gov. Applicants must create a Grants.gov Workspace for submission, which allows the application components to be completed online and routed through the applicant organization for review prior to submission. Applicants may choose to download and save individual PDF forms rather than filling out webforms in Workspace. A compatible version of Adobe Reader **must** be used to view, complete, and submit an application package consisting of PDF forms. If more than one person is entering text into an application package, the *same version* of Adobe Reader software should be used by each person. Check the version number of the Adobe software on each user's computer to make sure the versions match. Using different versions of Adobe Reader may cause

submission and/or save errors – even if each version is individually compatible with Grants.gov. Refer to the General Application Instructions, Section III, and the “Apply For Grants” page of Grants.gov (<https://www.grants.gov/web/grants/applicants/apply-for-grants.html>) for further information about the Grants.gov Workspace submission process. Submissions of extramural applications through eBRAP may be withdrawn.

Table 1. Full Application Submission Guidelines

Extramural Submissions	Intramural DoD Submissions
Application Package Location	
<p>Download application package components for W81XWH-19-CTRR-CTA from Grants.gov (https://www.grants.gov) and create a Grants.gov Workspace. Workspace allows online completion of the application components and routing of the application package through the applicant organization for review prior to submission.</p>	<p>Download application package components for W81XWH-19-CTRR-CTA from eBRAP (https://ebrap.org).</p>
Full Application Package Components	
<p>SF424 Research & Related Application for Federal Assistance Form: Refer to the General Application Instructions, Section III.A.1, for detailed information.</p>	<p>Tab 1 – Summary: Provide a summary of the application information.</p> <p>Tab 2 – Application Contacts: This tab will be pre-populated by eBRAP; add Authorized Organizational Representative.</p>
<p>Descriptions of each required file can be found under Full Application Submission Components:</p> <ul style="list-style-type: none"> • Attachments • Research & Related Personal Data • Research & Related Senior/Key Person Profile (Expanded) • Research & Related Budget • Project/Performance Site Location(s) Form • Research & Related Subaward Budget Attachment(s) Form (if applicable) 	<p>Tab 3 – Full Application Files: Upload files under each Application Component in eBRAP. Descriptions of each required file can be found under Full Application Submission Components:</p> <ul style="list-style-type: none"> • Attachments • Key Personnel • Budget • Performance Sites <p>Tab 4 – Application and Budget Data: Review and edit proposed project start date, proposed end date, and budget data pre-populated from the Budget Form.</p>

Extramural Submissions	Intramural DoD Submissions
Application Package Submission	
<p>Create a Grants.gov Workspace. Add participants (investigators and Business Officials) to Workspace, complete all required forms, and check for errors before submission.</p> <p>Submit a Grants.gov Workspace Package. An application may be submitted through Workspace by clicking the “Sign and Submit” button on the “Manage Workspace” page, under the “Forms” tab. Grants.gov recommends submission of the application package at least 24-48 hours prior to the close date to allow time to correct any potential technical issues that may disrupt the application submission.</p> <p>Note: If either the Project Narrative or the budget fails eBRAP validation or if the Project Narrative or the budget 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 <i>prior to</i> the application submission deadline.</p>	<p>Submit package components to eBRAP (https://ebrap.org).</p> <p>Tab 5 – Submit/Request Approval Full Application: After all components are uploaded and prior to the full application submission deadline, enter your password in the space provided next to “Enter Your Password Here” and press the “Submit Full Application” button. eBRAP will notify your Resource Manager/Comptroller/Task Area Manager or equivalent Business Official by email.</p>
<u>Application Verification Period</u>	
<p>The full application package submitted to Grants.gov may be viewed and modified in eBRAP until the end of the application verification period. During the application verification period, the full application package may be modified <i>with the exception of the Project Narrative and Research & Related Budget Form</i>.</p>	<p>After eBRAP has processed the full application, the organizational Resource Manager/Comptroller/Task Area Manager or equivalent Business Official and PI will receive email notification of this status and will be able to view and modify application components in eBRAP. During the application verification period, the full application package may be modified <i>with the exception of the Project Narrative and Research & Related Budget Form</i>. Your Resource Manager/Comptroller/Task Area Manager or equivalent Business Official should log into eBRAP to review and to approve prior to the application verification deadline.</p>

Extramural Submissions	Intramural DoD Submissions
Further Information	
<p>Tracking a Grants.gov Workspace Package. After successfully submitting a Workspace package, a Grants.gov Tracking Number is automatically assigned to the package. The number will be listed on the “Confirmation” page that is generated after submission.</p> <p>Refer to the General Application Instructions, Section III, for further information regarding Grants.gov requirements.</p>	<p>Refer to the General Application Instructions, Section IV, for further information regarding eBRAP requirements.</p>

Both Extramural and Intramural organizations: Application viewing, modification, and verification in eBRAP are strongly recommended, but not required. ***The Project Narrative and Research & Related 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. Other application components may be changed until the end of the application verification period. Verify that subaward budget(s) and budget justification forms are present in eBRAP during the application verification period. If these components are missing, upload them to eBRAP before the end of the application verification period. After the end of the application verification period, the full application cannot be modified.

Material submitted after the end of the application verification period, unless specifically requested by the Government, will not be forwarded for processing.

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

II.D.2.b.ii. Full Application Submission Components

- **Extramural Applications Only**

SF424 Research & Related Application for Federal Assistance Form: Refer to the General Application Instructions, Section III.A.1, for detailed information.

- **Extramural and Intramural Applications**

Attachments:

Each attachment to the full application components must be uploaded as an individual file in the format specified and in accordance with the formatting guidelines listed in the General Application Instructions, Appendix 4.

For all attachments, ensure that the file names are consistent with the guidance. Attachments will be rejected if the file names are longer than 50 characters or have incorrect file names

that contain characters other than the following: A-Z, a-z, 0-9, underscore, hyphen, space, and period. In addition, there are file size limits that may apply in some circumstances. Individual attachments may not exceed 20 MB, and the file size for the entire full 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 6-10 described below. Failure to submit these attachments as part of the application package will result in rejection of the entire application.

- **Attachment 1: Project Narrative (20-page limit): 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) 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.

Describe the proposed project in detail using the outline below.

- **Background:** State the relevance of the research to remediation of cognitive impairments and functional limitations after complex TBI. Explain the applicability of the proposed findings. Present the ideas and reasoning behind the proposed work. Describe previous experience and expertise of the investigators that is most pertinent to this project. ***Include preliminary and/or published data that are relevant to complex TBI and the proposed research project.***

Describe in detail the rationale for the study. Provide a literature review and describe the preliminary studies and/or preclinical data that led to the development of the proposed 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 any current clinical use of the intervention under investigation, and/or details of its study in clinical trials for other indications (as applicable). Describe the proposed study population and state its relevance to the target population. Describe the dosing of active ingredients for nutritional supplements, if applicable, to ensure the consistency. The background section should clearly support the choice of study variables and should explain the basis for the study questions and/or study hypotheses. This section should establish the relevance of the study and explain the applicability of the proposed findings.

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

- **Objectives/Specific Aims/Hypotheses:** Provide a description of the purpose and objectives of the study with detailed specific aims and/or study questions/hypotheses.

This information should agree with the primary aims and associated tasks described in the Statement of Work ([Attachment 5](#)).

- **Study Design:** Describe the type of study to be performed (e.g., treatment, prevention, diagnostic), the study phase or class (if applicable), and the study model (e.g., single group, parallel, crossover). Outline the proposed methodology in sufficient detail to show a clear course of action. Specify potential pitfalls and alternative strategies to mitigate the pitfalls.
 - Define the target population with regard to injury severity; refer to the classifications of TBI severity in Table 1 of the [VA/DoD Clinical Practice Guideline for the Management of Concussion-Mild Traumatic Brain Injury](#).
 - Identify the intervention to be tested and describe the projected results.
 - Define the primary and any secondary or interim outcome measures, outline why they were chosen, and describe how and when they will be measured. Include a description of appropriate controls. Outline the timing and procedures planned during the follow-up period.
 - As applicable, identify the data elements used, both FITBIR CDEs and any unique data elements. Describe any proposed modifications to CDEs. Justify the use of any UDEs.
 - Describe the study population and the 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).
 - Define each arm/study group of the proposed trial, if applicable. Describe the human subject-to-group assignment process (e.g., randomization, block randomization, stratified randomization, age-matched controls, alternating group, or other procedures). Explain the specific actions to accomplish the group assignment (e.g., computer assignment, use of table of random numbers).
 - Outline whether subjects, clinicians, data analysts, and/or others will be blinded during the study. Describe any other measures to be taken to reduce bias.
 - If using psychometric measures, describe their reliability and validity.
 - Describe potential problem areas and discuss alternative methods/approaches that may be employed to overcome them. Estimate the potential for subject loss to follow-up, and how such loss will be handled/mitigated.
- **Statistical and Data Analysis Plan:** Describe the statistical model and data analysis plan with respect to the study objectives. 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. 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. Ensure sufficient information is provided to allow thorough evaluation of all statistical calculations during review of the application.

- **Attachment 2: Supporting Documentation: Combine and upload as a single file named “Support.pdf”.** Start each document on a new page. If documents are scanned to PDF, the lowest resolution (100 to 150 dpi) should be used. The Supporting Documentation attachment should not include additional information such as figures, tables, graphs, photographs, diagrams, chemical structures, or drawings. These items should be included in the Project Narrative.

There are no page limits for any of these components unless otherwise noted. Include only those components described below; inclusion of items not requested or viewed as an extension of the Project Narrative 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 articles are not publicly 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:** 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, such as those from members of Congress, do not impact application review or funding decisions.
- **Letters of Collaboration (if applicable):** 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. 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.
- Letters of Commitment (if applicable): 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.
 - Intellectual Property: Information can be found in 2 CFR 200.315, "Intangible Property."
 - 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.
 - Describe the plan to make data available to the TBI research community through the FITBIR Informatics System. If an alternative data-sharing vehicle will be employed, provide a justification for its use.
 - Refer to the General Application Instructions, Appendix 2, Section K, for more information about the CDMRP expectations for making data and research resources publicly available.
 - **Use of DoD Resources (if applicable):** Provide a letter of support signed by the lowest-ranking person with approval authority confirming access to active duty military populations and/or DoD resources or databases.
 - **Use of VA Resources (if applicable):** Provide a letter of support from the VA Facility Director(s) or individual designated by the VA Facility Director(s), such as the ACOS/R&D or Clinical Service Chief confirming access to VA patients, resources, and/or VA research space. For VA PIs, if the VA NPC is not identified as the applicant institution for administering the funds, include a letter from the VA ACOS/R&D confirming this arrangement and identifying the institution that will administer the funds associated with the proposed research.
 - Quad Chart: Provide a Quad Chart for the proposed project. The format for the quad chart is available on the eBRAP "Funding Opportunities & Forms" web page at <https://ebrap.org/eBRAP/public/Program.htm>.
 - o **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 publicly. **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. Programmatic reviewers typically do not have access to the full application and rely on the technical abstract for appropriate description of the project's key aspects. Therefore, clarity and completeness within the space limits of the technical abstract are highly important.

- **Background:** State how the proposed research addresses one or more of the FY19 PH/TBIRP CTRR-CTA Areas of Emphasis. If “a research area than an identified Area of Emphasis” is stated, justify how the research area is relevant to the intent of CTRR-CTA. Present the ideas and rationale behind the proposed clinical trial.
- **Hypothesis/Objective(s):** State the hypothesis to be tested and/or objective(s) to be reached.
- **Specific Aims:** State the specific aims of the study.
- **Study Design:** Briefly describe the study design, including appropriate controls.
- **Clinical Impact/Military Benefit:** Briefly explain how the proposed project will have an impact on the health and well-being of military Service members, Veterans, and other individuals living with 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 publicly. **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.**

- Clearly describe the objectives and rationale for the proposed study and intervention 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 and benefits?
- Briefly describe how the proposed project will benefit military Service members, Veterans, and other individuals living with complex TBI.

- **Attachment 5: Statement of Work (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 CTRR-CTA mechanism, use the SOW format example titled “SOW for Clinical Research (Including Trials, Special Populations).” The SOW must be in PDF format prior to attaching.

The SOW should include a list of major tasks that support the proposed specific aims, followed by a series of subtasks outlined related to the major tasks and milestones within the period of performance. The SOW should describe only the work for which funding is being requested by this application and, as applicable, should also:

- Include the name(s) of the key personnel and contact information for each study site/subaward site.
- Indicate the number (and type, if applicable) of research subjects projected or required for each task and at each site. Indicate quarterly enrollment targets. Refer to the General Application Instructions, Appendix 1, for additional information regarding regulatory requirements.
- If human anatomical substances (including cell lines) will be used, specify whether or not identifiable information is accessible to the research team by any means.
- If applicable, indicate timelines required for regulatory approvals relevant to human subject research (e.g., IND or IDE applications) by the FDA or other Government agency.
- Briefly state the methods to be used.
- For FITBIR, eligible research should include:
 - FITBIR investigator and study registration within the first 30 days of the award
 - Sharing of draft data collection forms with FITBIR
 - Annual FITBIR data submissions
- **Attachment 6: Intervention (no page limit): Upload as “Intervention.pdf”.** The Intervention attachment should include the components listed below.
 - **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, and availability, dose, schedule, administration route, washout period, duration of the intervention, and concomitant medications allowed. Measures to ensure consistency of dosing of active ingredients for nutritional supplements should be described, if applicable. 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. A description of how the intervention compares with currently available interventions and/or standards of care should be specified. Research procedures should be clearly delineated from routine clinical procedures. Indicate who holds the intellectual property rights to the intervention, if applicable, and how the PI has obtained access to those rights for conduct of the clinical trial.

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

- **Study Procedures:** Describe the interaction with the human subject, including 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. Clearly delineate research procedures from routine clinical procedures. Discuss how compliance with current Good Laboratory Practice (GLP) guidelines, GMP, and other regulatory considerations will be established, monitored, and maintained, as applicable.
- **Clinical Monitoring Plan:** Describe how the study will be conducted by and monitored for current 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 7: Human Subject Recruitment and Safety Procedures (no page limit): Upload as “HumSubProc.pdf”.** The Human Subject Recruitment and Safety Procedures attachment should include the components listed below.
 - **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). Provide a table of anticipated enrollment counts at each study site. Demonstrate that the research team has access to the proposed study population at each site, and describe the efforts that will be made to achieve accrual goals. Furthermore, discuss past efforts in recruiting human subjects from the target population for previous clinical trials (if applicable). Address any potential barriers to accrual and plans for addressing unanticipated delays, including a mitigation plan for slow or low enrollment. Identify ongoing clinical trials that may compete for the same patient population and how they may impact enrollment progress. Provide justification related to the scientific goals of the proposed study for limiting inclusion of any group by age, race, ethnicity, or sex/gender. *For clinical*

trials proposing to include military personnel, refer to the General Application Instructions, Appendix 1, for more information.

- **Inclusion/Exclusion Criteria:** List the inclusion and exclusion criteria for the proposed clinical trial. Inclusion/exclusion criteria should take into consideration the specific risk profile of the studies to be conducted and the standard of care for that patient population. Provide detailed justification for exclusions.
 - ***Inclusion of Women and Minorities in Study.*** Consistent with the Belmont Report, “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 USAMRDC. This policy is intended to promote equity both in assuming the burdens and in receiving the benefits of human subjects research. Include an appropriate justification if women and/or minorities will be excluded from the clinical trial.

- **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.

- **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. FITBIR-eligible applications should include FITBIR consent language (see [Appendix 3](#) for sample consent language).***
 - 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:* In compliance with 10 USC 980 (<https://www.gpo.gov/fdsys/pkg/USCODE-2011-title10/pdf/USCODE-2011-title10-subtitleA-partII-chap49-sec980.pdf>), the application must describe a clear intent to benefit for human subjects who cannot give their own consent to participate in the proposed clinical trial. If applicable, refer to the General Application Instructions, Appendix 1, for more information.
 - *Assent.* If minors or other populations that cannot provide informed consent are included in the proposed clinical trial, a plan to obtain assent (agreement) from those with capacity to provide it, or a justification for a waiver of assent, should be provided. PIs should consult with their local IRB to identify the conditions necessary for obtaining assent.
- **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:* Some screening procedures may require a separate consent or a two-stage consent process.
- **Risks/Benefits Assessment:**
- **Effect on daily life:** Describe how participation in the study will affect the daily life of subjects (e.g., Will human subjects still be able to take their regular medications while participating in the study? Are human subjects required to stay overnight in a hospital?).
 - **Foreseeable risks:** Clearly identify all study risks, including potential safety concerns and adverse events. Study risks include any risks that the human subject is exposed to as a result of participation in the clinical trial. Consider psychological, legal, social, and economic risks as well as physical risks. If the risks are unknown, this should be stated. If applicable, any potential risk to the study personnel should be identified.

- **Risk management and emergency response:**
 - ❖ Describe how safety surveillance and reporting to the IRB 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, including 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 trial 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 1, Section B (Research Monitor Requirement), 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 subjects who will participate in the study. Articulate the importance of the knowledge to be gained as a result of the proposed research. Discuss why the potential risks to human subjects are reasonable in relation to the anticipated benefits to the human subjects and others that may be expected to result.
- **Attachment 8: Data Management (no page limit): Upload as “Data_Manage.pdf”.** The Data Management attachment should include the components listed below.
 - **Data Management:** Describe all methods used for data collection, including 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. Describe the proposed database, how it will be developed and validated, and its capability to safeguard and maintain the integrity of the data. Describe the database lock process. For FDA-regulated studies, compliance with 21 CFR 11 and appropriate data standards (such as those established by the Clinical Data Interchange Standards Consortium) are required.
- **Data reporting:** Describe how data will be reported and how it will be assured that the documentation will support a regulatory filing with the FDA, if applicable.
- **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, including results from any screening or diagnostic tests performed as part of the study.
- **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, including 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, including

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, the applicable quality standard, and any special precautions that should be taken in handling the samples. Special precautions that should be taken by the human subject before, during, or after the laboratory procedure should be clearly defined. If transport of samples is required, describe provisions for ensuring proper storage during transport.
- **Attachment 9: Regulatory Strategy (no page limit): If submitting multiple documents, start each document on a new page. Combine and upload as a single file named “Regulatory.pdf”.** Answer the following questions and provide supporting documentation as applicable.
 - State the product/intervention name.

For products/interventions that do not require regulation by the FDA or an international regulatory agency:

- Explain why the product/intervention is exempt from FDA oversight. Provide confirmation that the trial does not require regulation by the FDA in writing from the IRB of record or the FDA. If the clinical trial will be conducted at international sites, provide equivalent information relevant to the host country(ies) regulatory requirements. No further information for this attachment is required.

For products that require regulation by the FDA and/or an international regulatory agency:

- State whether the product is FDA-approved, -licensed, or -cleared, and marketed in the U.S.
- If the product is marketed in the U.S., state the product label indication. State whether the proposed research involves a change to the approved label indication for the route of administration, dosage level, and/or subject population. Indicate whether the proposed research involves a change that increases the risks associated with using the product. State whether the product is being promoted for an off-label use (where promotion involves the sale of a marketed product).
- If the product is not currently FDA-approved, -licensed, or -cleared, state the planned indication/use. Indicate whether the product would be classified as a drug, device, biologic, or combination product. Indicate whether the FDA has confirmed the proposed classification. Identify the regulatory sponsor. Include a signed sponsor commitment letter acknowledging the regulatory sponsor’s understanding of all sponsor responsibilities and commitment to oversee execution of the study.
- For the FY19 PH/TBIRP CTRR-CTA, ***if an IND or IDE is required, the application must be submitted to the FDA prior to the FY19 PH/TBIRP CTRR-CTA***

- application submission deadline.*** The IND or IDE should be specific for the investigational product (i.e., not a derivative or alternate version of the product) and indication to be tested in the proposed clinical trial. Provide the date of submission, the application number, and a copy of the FDA letter acknowledging the submission. If there are any existing cross-references in place, provide the application number(s) and associated sponsor(s). Provide an explanation of the status of the application (e.g., past the critical 30-day period, pending response to questions raised by the FDA, on clinical hold, on partial clinical hold). If the IND or IDE application has been placed on clinical hold or partial hold, explain the conditions that must be met for release of the hold. Provide a summary of any previous meetings with the FDA on development of this product. 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 available, provide a copy of the communication from the FDA indicating the IND or IDE application is active/safe to proceed.
 - If an active IND or IDE for the investigational product is in effect, but an amendment is needed to include the proposed trial, describe the type and nature of the amendment(s) and the timeline for submission. Indicate whether the amendment increases the risk of the intervention.
 - If the clinical trial will be conducted at international sites, provide equivalent information and supporting documentation relevant to the product indication/label and regulatory approval and/or filings in the host country(ies).
 - Provide the current status for manufacturing development (e.g., manufacturer’s name, GMP-compliant lots available, status of stability testing), non-clinical development (e.g., test facility name, status of pivotal GLP toxicology studies to support Phase I testing), and clinical development (e.g., clinical site name, safety profile, status of any completed or ongoing clinical trials).
 - Describe the overall regulatory strategy and product development plan that will support the planned product indication. Include a description of the numbers and types of studies proposed to reach approval, licensure, or clearance, the types of FDA meetings that will be held/planned, and the submission filing strategy. Include considerations for compliance with current GMP, GLP, and GCP guidelines.
- **Attachment 10: Transition Plan (three-page limit): Upload as “Transition.pdf”.** Describe/discuss the methods and strategies proposed to move the intervention to the next phase of development (clinical trials, commercialization, and/or delivery to the civilian or military market) after successful completion of the award. Applicants are encouraged to work with their organization’s Technology Transfer Office (or equivalent) to develop the transition plan. PIs are encouraged to explore developing relationships with industry and/or other funding agencies to facilitate moving the product into the next phase of development. The post-award transition plan should include the components listed below.

- Details of the funding strategy to transition to the next level of development and/or commercialization (e.g., specific industry partners, clinical communities of interest, specific funding opportunities to be applied for). Include a description of collaborations and other resources that will be used to provide continuity of development.
- A description of collaborations and other resources that will be used to provide continuity of development.
- A brief schedule and milestones for transitioning the intervention to the next phase of development (i.e., next-phase clinical trials, commercialization, delivery to the military or civilian market, incorporation into clinical practice, and/or approval by the FDA).
- 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.
- A risk analysis for cost, schedule, manufacturability, and sustainability, as applicable.
- **Attachment 11: Impact and Military Benefit Statement (two-page limit): Upload as “Impact.pdf”.** Describe the short- and long-term impact of this study on the field of complex TBI research, patient care, and/or quality of life, including an assessment of the likelihood that a successful outcome of the proposed research project will lead to a practical application in individuals recovering from military-relevant injuries and diseases incident to military service as well as injuries and diseases occurring in the general public. Address the impact on one or more of the FY19 PH/TBIRP CTRR-CTA Areas of Emphasis or “a research area other than an identified Area of Emphasis,” which is relevant to the intent of CTRR-CTA. Although not all-inclusive, the following are examples of ways in which research projects may have an impact, if successful:
 - The proposed research has the potential to advance the field of complex TBI research.
 - The proposed research will contribute to the development or validation of evidence-based policy or guidelines for patient evaluation and care and/or informs return-to-duty decision making.
 - The proposed research will address relevant controversies or treatment issues.
 - The proposed research addresses potential issues that might limit the impact of the findings.
 - If an active duty military, Veteran, or military family member population(s) will be used in the proposed research project, describe the population(s), the appropriateness of the population(s) for the proposed research, and the feasibility of using the population. If a non-military population will be used for the proposed research project, explain how the results will be relevant to active duty military, Veteran, or military family member population(s).

- **Attachment 12: 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.
 - **Organizational Chart:** Provide an organizational chart that identifies key members of the study team and provides an outline of the governing structure for multi-institutional studies. Identify collaborating organizations, centers, and/or departments and name each person’s position on the project. Include any separate laboratory or testing centers. Identify the data and clinical coordinating center(s) and note any involvement from Contract Research Organizations, as appropriate. Identify and provide justification for the inclusion of international sites, as appropriate. If applicable, identify the FDA regulatory sponsor and 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.
 - **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, including previous interactions with the FDA, if applicable. An external research monitor (if applicable) and study coordinator(s) should be included.
 - **Study Management Plan:** Provide a plan for ensuring the standardization of procedures among staff and across sites (if applicable). If the proposed clinical trial is multi-institutional, clearly describe the multi-institutional structure governing the research protocol(s) across all participating institutions. Provide a regulatory submission plan for the master protocol and master consent form by the lead organization; include a single IRB/EC pathway whenever possible. If applicable, describe how communication and data transfer between the collaborating institutions will occur, as well as how data, specimens, and/or imaging products obtained during the study will be handled and shared.
- **Attachment 13: Surveys, Questionnaires, and Other Data Collection Instruments, if applicable (no page limit): Upload as “Surveys.pdf”.** The Surveys, Questionnaires, and Other Data Collection Instruments attachment should include a copy of the most recent version of surveys, questionnaires, data collection forms, rating scales, interview guides, or other instruments. For each instrument, describe how the information collected is related to the objectives of the study. 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 14: Representations, if applicable (extramural submissions only): Upload as “RequiredReps.pdf”.** All extramural applicants must complete and submit the Required Representations template available on eBRAP (<https://ebrap.org/eBRAP/public/Program.htm>). For more information, see the General Application Instructions, Appendix 5, Section B, Representations.

- **Attachment 15: DoD Military Budget Form(s), if applicable: Upload as “MFBudget.pdf”.** If a military facility (Military Health System facility, research laboratory, medical 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 DoD Military 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 III.A.8, for detailed information.

- **Extramural and Intramural Applications**

To evaluate compliance with Title IX of the Education Amendments of 1972 (20 USC A§1681 et seq.), the DoD is collecting certain demographic and career information to be able to assess the success rates of women who are proposed for key roles in applications in science, technology, engineering, and/or mathematics (STEM) disciplines. To enable this assessment, each application must include the following forms completed as indicated.

Research & Related Personal Data: For extramural submissions (via Grants.gov), refer to the General Application Instructions, Section III.A.3, and for intramural submissions (via eBRAP), refer to the General Application Instructions, Section IV.A.2, for detailed information.

Research & Related Senior/Key Person Profile (Expanded): For extramural submissions (via Grants.gov), refer to the General Application Instructions, Section III.A.4, and for intramural submissions (via eBRAP), refer to the General Application Instructions, Section IV.A.3, for detailed information.

- PI Biographical Sketch (six-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 NIH Biographical Sketch may also be used. All biographical sketches should be submitted in uneditable PDF format.
- PI Previous/Current/Pending Support (no page limit): Upload as “Support_LastName.pdf”.
- Key Personnel Biographical Sketches (six-page limit each): Upload as “Biosketch_LastName.pdf”.
- Key Personnel Previous/Current/Pending Support (no page limit): Upload as “Support_LastName.pdf”.

Research & Related Budget: For extramural submissions (via Grants.gov), refer to the General Application Instructions, Section III.A.5, and for intramural submissions (via eBRAP), refer to the General Application Instructions, Section IV.A.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.

Project/Performance Site Location(s) Form: For extramural submissions (via Grants.gov), refer to the General Application Instructions, Section III.A.6, and for intramural submissions (via eBRAP), refer to the General Application Instructions, Section IV.A.5, for detailed information.

- **Extramural Applications Only**

Research & Related Subaward Budget Attachment(s) Form (if applicable): Refer to the General Application Instructions, Section III.A.7, for detailed information.

- **Extramural Subaward:** Complete the Research & Related Subaward Budget Form through Grants.gov. (Refer to the General Application Instructions, Section III.A.7, for detailed information.) Verify subaward budget(s) and budget justification forms are present in eBRAP during the application verification period. If these components are missing, upload them to eBRAP before the end of the application verification period.
- **Intramural DoD Collaborator(s):** Complete the DoD Military Budget Form and upload to Grants.gov attachment form as Attachment 15. (Refer to the General Application Instructions, Section IV.A.4, for detailed information.) Intramural DoD Collaborator(s) costs per year should be included on the Grants.gov Research and Related Budget Form under subaward costs.

II.D.3. Dun and Bradstreet Data Universal Numbering System (DUNS) Number and System for Award Management (SAM)

Applicant organizations and all sub-recipient 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. Verify the status of the applicant’s organization’s Entity registration in SAM well in advance of the application submission deadline. Allow several weeks to complete the entire SAM registration process. If an applicant has not fully complied with the requirements at the time the Federal awarding agency is ready to make a Federal award, the Federal awarding agency may determine that the applicant is not qualified to receive a Federal award and use that determination as a basis for making a Federal award to another applicant. Refer to the General Application Instructions, Section III, for further information regarding Grants.gov requirements.

II.D.4. Submission Dates and Times

All submission dates and times are indicated in [Section I, Overview of the Funding Opportunity](#). Pre-application and application submissions are required. The pre-application and application submission process should be started early to avoid missing deadlines. There are no grace periods. Failure to meet either of these deadlines will result in submission rejection.

Applicant Verification of Full Application Submission in eBRAP

Following retrieval and processing of the full application, eBRAP will notify the organizational representatives and PI by email to log into eBRAP to review, modify, and verify the full application submission. eBRAP will validate retrieved files against the specific Program Announcement 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. ***If either the Project Narrative or the budget fails eBRAP validation or needs to be modified, an updated full application package must be submitted prior to the application submission deadline.*** The Project Narrative and Budget Form cannot be changed after the application submission deadline.

Extramural Submission: The full application package submitted to Grants.gov may be viewed and modified in eBRAP until the end of the application verification period. During the application verification period, the full application package, ***with the exception of the Project Narrative and Budget Form,*** may be modified.

Intramural DoD Submission: After eBRAP has processed the full application, the organizational Resource Manager/Comptroller/Task Area Manager or equivalent Business Official and PI(s) will receive email notification of the status and will be able to view and modify application components in eBRAP. During the application verification period, the full application package, ***with the exception of the Project Narrative and Budget Form,*** may be modified. The Resource Manager/Comptroller/Task Area Manager or equivalent Business Official should log into eBRAP to review and to approve the application package prior to the application verification deadline.

For All Submissions: Verify that subaward budget(s) with budget justification are present in eBRAP during the application verification period. If these components are missing, upload them to eBRAP before the end of the application verification period.

II.D.5. Funding Restrictions

The maximum period of performance is **3** years.

The anticipated total costs budgeted for the entire period of performance will not exceed **\$4.0M**. If indirect cost rates have been negotiated, indirect costs are to be budgeted in accordance with the organization’s negotiated rate. No budget will be approved by the Government exceeding **\$4.0M** total costs or using an indirect cost rate exceeding the organization’s negotiated rate.

All direct and indirect costs of any subaward or contract 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 **3** years.

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

- Travel costs for the PI(s) to present project information or disseminate project results at one DoD PH/TBIRP CTRR In-Progress Review meeting during the period of performance. For planning purposes, it should be assumed that the meeting will be held in the National Capital Area. These travel costs are in addition to those allowed for annual scientific/technical meetings.
- Travel costs for the PI(s) to present project information or 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.

For this award mechanism, direct costs may be requested for (not all-inclusive):

- Salary
- Research supplies
- Equipment
- Research-related subject costs
- Support for multidisciplinary collaborations, including travel
- Travel between collaborating organizations
- Travel costs for one investigator to travel to one scientific/technical meeting per year in addition to the required meeting described above to present project information or outcomes from the FY19 PH/TBIRP CTRR-CTA

Awards made to extramural organizations will consist solely of assistance agreements (grants and cooperative agreements). For extramural awards with an intragovernmental component, direct transfer of funds from an extramural award recipient to a DoD or other Federal agency is not allowed except under very limited circumstances. Funding to intramural DoD and other Federal agencies will be managed through a direct fund transfer. Intramural applicants are responsible for coordinating through their agency's procedures the use of contractual or assistance funding awards or other appropriate agreements to support extramural collaborators.

Refer to the General Application Instructions, Section III.A.5, 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 the General Application Instructions, Section III.A.5.***

Funds to be obligated on any award resulting from this funding opportunity will be available for use for a limited time period based on the fiscal year of the funds. The time is considered when establishing the award's period of performance. It is anticipated that awards made from this

FY19 funding opportunity will be funded with FY19 funds, which will expire for use on September 30, 2025.

II.D.6. Other Submission Requirements

Refer to the General Application Instructions, Appendix 4, for detailed formatting guidelines.

II.E. Application Review Information

II.E.1. Criteria

II.E.1.a. Peer Review

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

- **Clinical Impact**
 - How relevant the anticipated outcomes of the proposed clinical trial are to individuals affected by complex TBI.
 - How well the proposed research project addresses one or more of the FY19 PH/TBIRP CTRR-CTA Areas of Emphasis or is otherwise relevant to the intent of CTRR-CTA.
 - How well the sample population represents the targeted patient population that might benefit from the proposed intervention.
 - How the potential outcomes of the proposed clinical trial will provide/improve short-term benefits for individuals.
 - How significantly the long-term benefits for implementation of the intervention may impact patient care and/or quality of life.
- **Research Strategy**
 - How well the scientific rationale for clinically testing the intervention is supported by the preliminary data, critical review and analysis of the literature, and/or laboratory/preclinical evidence.
 - How well the study aims, hypotheses and/or objective(s), experimental design, methods, data collection procedures, and analyses are designed to answer clearly the clinical objective.
 - How well the inclusion and randomization criteria meet the needs of the proposed clinical trial.
 - How well the exclusion criteria are justified.

- How well plans to collect specimens and conduct laboratory evaluations are addressed, if applicable.
- To what degree the data collection instruments (e.g., surveys, questionnaires), if applicable, are appropriate to the proposed study.
- How well potential challenges and alternative strategies are discussed.
- **Intervention**
 - Whether there is evidence of support, indicating availability of the intervention from its source, for the duration of the proposed clinical trial (if applicable).
 - To what degree the intervention addresses the clinical need(s) described.
 - How the intervention compares with currently available interventions and/or standards of care.
 - To what degree the PI has provided preclinical and/or clinical evidence to support the safety of the intervention.
 - How well research procedures are clearly delineated from routine clinical procedures.
 - Whether measures are described to ensure the consistency of dosing of active ingredients for nutritional supplements (if applicable).
- **Regulatory Strategy and Transition Plan**
 - How the regulatory strategy and development plan to support the product indication or product label change, if applicable, are appropriate and well-described.
 - Whether the application includes documentation that the study is exempt from FDA or other international agency regulation, or that the IND or IDE application (and/or international equivalent) has been submitted to the FDA and/or relevant international regulatory agency, as appropriate.
 - How well the documentation provided supports the feasibility of acquiring an active IND or IDE (and/or international equivalent) covering the proposed trial, if applicable.
 - For investigator-sponsored regulatory exemptions (e.g., IND, IDE, or other international equivalent), whether there is evidence of appropriate institutional support, including capabilities to ensure monitoring as required by the FDA or relevant international regulatory agency.
 - Whether plans to comply with current GMP, GLP, and GCP guidelines are appropriate.
 - Whether the identified next level of development, implementation, and/or commercialization is realistic.

- Whether the funding strategy described to bring the intervention to the next level of development (e.g., specific industry partners, specific funding opportunities to be applied for) is reasonable and achievable.
 - Whether the proposed collaborations and other resources for providing continuity of development are established and/or achievable.
 - 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.
 - Whether the risk analysis for cost, schedule, manufacturability, and sustainability is realistic and reasonable.
 - How well the application identifies intellectual property ownership, demonstrates the appropriate access to all intellectual property rights necessary for development and commercialization, describes an appropriate intellectual and material property plan among participating organizations (if applicable), and addresses any impact of intellectual property issues on product or technology development and subsequent Government access to products or technologies supported by this Program Announcement.
- **Recruitment, Accrual, and Feasibility**
 - How well the PI addresses the availability of human subjects for the clinical trial and the prospect of their participation.
 - Whether the PI has demonstrated access to the proposed human subject population.
 - The degree to which the recruitment, informed consent, screening, and retention processes for human subjects will meet the needs of the proposed clinical trial.
 - How well the application identifies possible delays (e.g., slow accrual, attrition) and presents adequate contingency plans to resolve them.
 - To what extent the proposed 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?).
- **Statistical Plan**
 - To what degree the statistical model and data analysis plan are suitable for the planned study.
 - How the statistical plan, including sample size projections and power analysis, is adequate for the study and all proposed correlative studies.

- 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.
- **Personnel and Communication**
 - Whether the composition of the study team (e.g., study coordinator, statistician) is appropriate.
 - Whether the study team's background and expertise are appropriate for accomplishing the proposed work (e.g., statistical expertise, expertise in the disease, and clinical studies).
 - How the levels of effort of the study team members are appropriate for successful conduct of the proposed trial.
 - How well the logistical aspects of the proposed clinical trial (e.g., communication plan, data transfer and management, standardization of procedures) meet the needs of the proposed clinical trial.
 - For multi-site clinical trials, how well the lead site responsibilities and human research protections regulatory coordination are defined and planned for.
- **Ethical Considerations**
 - Whether the population selected to participate in the trial stands to benefit from the knowledge gained.
 - If applicable, how well the inclusion of international sites is justified.
 - 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.
 - Whether a research monitor with expertise consistent with the nature of the potential risk(s) is identified, if applicable.
 - How well the evidence shows that the procedures are consistent with sound research design and, when appropriate, that these procedures are already in use for diagnostic or treatment purposes.
 - To what degree privacy and confidentiality issues are appropriately considered.
 - To what degree the process for seeking informed consent is appropriate and whether safeguards are in place for vulnerable populations.

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

- **Environment**

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

- **Budget**

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

- **Application Presentation**

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

II.E.1.b. 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:

- Ratings and evaluations of the peer reviewers
- Relevance to the mission of the DHP, JPC-8/CRM RP, and PH/TBIRP, as evidenced by the following:
 - Adherence to the intent of the award mechanism
 - Program portfolio composition
 - Relative impact and military relevance

II.E.2. 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**, the evaluation of applications against established criteria to determine technical merit, where each application is assessed for its own merit, independent of other applications. The second tier is **programmatic review**, a comparison-based process in which applications with high scientific and technical merit are further evaluated for programmatic relevance. Final recommendations for funding are made to the Commanding

General, USAMRDC, on behalf of the DHA and the OASD(HA). *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 II.E.1.b, Programmatic Review](#).* Additional information about the two-tier process used by the CDMRP can be found at <https://cdmrp.army.mil/about/2tierRevProcess>.

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 and approval 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 and approval 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 18 USC 1905.

II.E.3. Integrity and Performance Information

Prior to making an assistance agreement award where the Federal share is expected to exceed the simplified acquisition threshold, as defined in 2 CFR 200.88, over the period of performance, the Federal awarding agency is required to review and consider any information about the applicant that is available in the Federal Awardee Performance and Integrity Information System (FAPIIS).

An applicant organization may review FAPIIS, accessible through SAM, and submit comments to FAPIIS on any information about the organization that a Federal awarding agency previously entered and is currently available in FAPIIS.

The Federal awarding agency will consider any comments by the applicant, in addition to other information in the designated integrity and performance system, in making a judgment about the applicant's integrity, business ethics, and record of performance under Federal awards when determining a recipient's qualification prior to award, according to the qualification standards of the Department of Defense Grant and Agreement Regulations (DoDGARs), Section 22.415.

II.E.4. Anticipated Announcement and Federal Award Dates

All application review dates and times are indicated in [Section I, Overview of the Funding Opportunity](#).

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.

II.F. Federal Award Administration Information

II.F.1. Federal Award Notices

Awards supported with FY19 funds are anticipated to be made no later than September 30, 2020. Refer to the General Application Instructions, Appendix 2, for additional award administration information.

After email notification of application review results through eBRAP, and if selected for funding, a representative from the USAMRAA will contact the Business Official authorized to negotiate on behalf of the PI's organization.

Only an appointed USAMRAA Grants Officer may obligate the Government to the expenditure of funds. No commitment on the part of the Government should be inferred from discussions with any other individual. **The award document signed by the Grants Officer is the official authorizing document.**

Federal Government Organizations: Funding made to Federal Government organizations (to include intramural DoD organizations) will be executed through the Military Interdepartmental Purchase Request (MIPR) or Funding Authorization Document (FAD) process. Transfer of funds is contingent upon appropriate safety and administrative approvals. Intramural applicants and collaborators are reminded to coordinate receipt and commitment of funds through their respective Resource Manager/Task Area Manager/Comptroller or equivalent Business Official.

After email notification of application review results through eBRAP, and if selected for funding, a representative from the CDMRP will contact the Business Official authorized to negotiate on behalf of the PI's organization.

II.F.1.a. PI Changes and Award Transfers

The organizational transfer of an award supporting a clinical trial is strongly discouraged and in most cases will not be allowed. Approval of a transfer request will be on a case-by-case basis 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.

Unless otherwise restricted, changes in PI will be allowed at the discretion of the Grants Officer, provided the intent of the award mechanism is met.

Refer to the General Application Instructions, Appendix 2, Section B, for general information on organization or PI changes.

II.F.2. Administrative and National Policy Requirements

Applicable requirements in the DoDGARs found in 32 CFR, Chapter 1, Subchapter C, and 2 CFR, Chapter XI, apply to grants and cooperative agreements resulting from this Program Announcement.

Refer to the General Application Instructions, Appendix 2, for general information regarding administrative requirements.

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

Refer to the full text of the latest [DoD R&D General Terms and Conditions](#), the [USAMRAA General Research Terms and Conditions with Institutions of Higher Education, Hospitals, and Non-Profit Organizations: Addendum to the DoD R&D General Terms and Conditions](#), and the [USAMRAA General Research Terms and Conditions with For-Profit Organizations](#) for further information.

II.F.3. Reporting

Refer to the General Application Instructions, Appendix 2, Section A, for general information on reporting requirements. *If there are technical reporting requirement delinquencies for any existing USAMRAA-sponsored awards at the applicant organization, no new awards will be issued to the applicant organization until all delinquent reports have been submitted.*

Annual progress reports as well as a final progress report will be required.

Quarterly technical progress reports and quad charts will be required.

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

Awards resulting from this Program Announcement will incorporate additional reporting requirements related to recipient integrity and performance matters. Recipient organizations that have Federal contract, grant, and cooperative agreement awards with a cumulative total value greater than \$10,000,000 are required to provide information to FAPIIS about certain civil, criminal, and administrative proceedings that reached final disposition within the most recent 5-year period and that were connected with performance of a Federal award. Recipients are required to disclose, semiannually, information about criminal, civil, and administrative proceedings as specified in the applicable Representations (see General Application Instructions, Appendix 5, Section B).

II.G. Federal Awarding Agency Contacts

II.G.1. CDMRP Help Desk

Questions related to Program Announcement content or submission requirements as well as questions related to the pre-application or intramural application submission 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

II.G.2. Grants.gov Contact Center

Questions related to extramural 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 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.

II.H. Other Information

II.H.1. Program Announcement and General Application Instructions Versions

Questions related to this Program Announcement should refer to the Program name, the Program Announcement name, and the Program Announcement version code 20190530a. The Program Announcement numeric version code will match the General Applications Instructions version code 20190530.

II.H.2. Administrative Actions

After receipt of pre-applications or applications, the following administrative actions may occur.

II.H.2.a. Rejection

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

- 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.
- Intervention ([Attachment 6](#)) is missing.

- Human Subject Recruitment and Safety Procedures ([Attachment 7](#)) is missing.
- Data Management ([Attachment 8](#)) is missing.
- Regulatory Strategy ([Attachment 9](#)) is missing.
- Transition Plan ([Attachment 10](#)) is missing.

II.H.2.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.

II.H.2.c. Withdrawal

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

- An FY19 PH/TBIRP CTRR 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 FY19 PH/TBIRP CTRR Programmatic Panel members can be found at https://cdmrp.army.mil/phtbi/panels/panels19_ctr.*
- The application fails to conform to this Program Announcement description.
- 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 FY19, the identities of the peer review contractor and the programmatic review contractor may be found at the CDMRP website (<https://cdmrp.army.mil/about/2tierRevProcess>). Applications that include names of personnel from either of these companies may be administratively withdrawn.
- Personnel from applicant or collaborating organizations are found to have contacted persons involved in the review or approval process to gain protected evaluation information or to influence the evaluation process.
- Applications from extramural organizations, including non-DoD Federal agencies, received through eBRAP may be withdrawn.

- Applications submitted by an intramural DoD organization may be withdrawn if the intramural organization cannot coordinate the use of contractual, assistance, or other appropriate agreements to provide funds to extramural collaborators.
- The proposed research is not a clinical trial.
- The invited application does not propose the same research project described in the pre-application.
- For studies requiring an IND or IDE, documentation of IND/IDE submission and/or active status is not provided.
- The proposed project includes preclinical research.

II.H.2.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.

II.H.3. Application Submission Checklist

Application Components	Action	Completed
SF424 Research & Related Application for Federal Assistance (Extramural submissions only)	Complete form as instructed	
Summary (Tab 1) and Application Contacts (Tab 2) (Intramural submissions only)	Complete these tabs as instructed	
Attachments	Project Narrative: Upload as Attachment 1 with file name "ProjectNarrative.pdf"	
	Supporting Documentation: Upload as Attachment 2 with file name "Support.pdf"	
	Technical Abstract: Upload as Attachment 3 with file name "TechAbs.pdf"	
	Lay Abstract: Upload as Attachment 4 with file name "LayAbs.pdf"	
	Statement of Work: Upload as Attachment 5 with file name "SOW.pdf"	
	Intervention: Upload as Attachment 6 with file name "Intervention.pdf"	
	Human Subject Recruitment and Safety Procedures: Upload as Attachment 7 with file name "HumSubProc.pdf"	
	Data Management: Upload as Attachment 8 with file name "Data_Manage.pdf"	
	Regulatory Strategy: Upload as Attachment 9 with the file name "Regulatory.pdf"	
	Transition Plan: Upload as Attachment 10 with file name "Transition.pdf"	
	Impact and Military Benefit Statement: Upload as Attachment 11 with file name "Impact.pdf"	
	Study Personnel and Organization: Upload as Attachment 12 with file name "Personnel.pdf"	
	Surveys, Questionnaires, and Other Data Collection Instruments: Upload as Attachment 13 with file name "Surveys.pdf"	
	Representations (extramural submissions only): Upload as Attachment 14 with file name "RequiredReps.pdf" if applicable	
DoD Military Budget Form(s): Upload as Attachment 15 with file name "MFBudget.pdf" if applicable		

Application Components	Action	Completed
Research & Related Personal Data	Complete form as instructed	
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	
Research & Related Budget (Extramural submissions only)	Complete as instructed. Attach Budget Justification (BudgetJustification.pdf) to the appropriate field	
Budget (Intramural submissions only)	Complete the DoD Military Budget Form and justification	
Project/Performance Site Location(s) Form	Complete form as instructed	
Research & Related Subaward Budget Attachment(s) Form, if applicable	Complete form as instructed	

APPENDIX 1: ACRONYM LIST

ACOS/R&D	Associate Chief of Staff for Research and Development
CDEs	Common Data Elements
CDMRP	Congressionally Directed Medical Research Programs
CFR	Code of Federal Regulations
COI	Conflict of Interest
CRM RP	Clinical and Rehabilitative Medicine Research Program
CTRR-CTA	Complex TBI Rehabilitation Research – Clinical Trial Award
DHA	Defense Health Agency
DHP	Defense Health Program
DoD	Department of Defense
DoDGARs	Department of Defense Grant and Agreement Regulations
DUNS	Data Universal Numbering System
eBRAP	Electronic Biomedical Research Application Portal
EC	Ethics Committee
ET	Eastern Time
FAD	Funding Authorization Document
FAPIIS	Federal Awardee Performance and Integrity Information System
FDA	U.S. Food and Drug Administration
FITBIR	Federal Interagency Traumatic Brain Injury Research
FY	Fiscal Year
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
GUID	Global Unique Identifier
HRPO	Human Research Protection Office
ICH E6	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use)
IDE	Investigational Device Exemption
IND	Investigational New Drug
IRB	Institutional Review Board
JPC-8	Joint Program Committee 8
LAR	Legally Authorized Representative
M	Million
MIPR	Military Interdepartmental Purchase Request
mTBI	Mild Traumatic Brain Injury

NIH	National Institutes of Health
NINDS	National Institute of Neurological Disorders and Stroke
NPC	Non-Profit Corporation
NSI	Neurobehavioral Symptom Inventory
OASD(HA)	Office of the Assistant Secretary of Defense for Health Affairs
OMB	Office of Management and Budget
ORCID	Open Researcher and Contributor ID, Inc.
ORP	Office of Research Protections
PGIC	Patient Global Impression of Change
PH	Psychological Health
PH/TBIRP	Psychological Health/Traumatic Brain Injury Research Program
PI	Principal Investigator
PTSD	Post-Traumatic Stress Disorder
RDT&E	Research, Development, Test, and Evaluation
RTD	Return to Duty
SAM	System for Award Management
SOW	Statement of Work
STEM	Science, Technology, Engineering, and/or Mathematics
TBI	Traumatic Brain Injury
UDEs	Unique Data Elements
USAMRAA	U.S. Army Medical Research Acquisition Activity
USAMRDC	U.S. Army Medical Research and Development Command
USC	United States Code
VA	Department of Veterans Affairs

APPENDIX 2: DOD AND VA WEBSITES

Principal Investigators are encouraged to integrate and/or align their research projects with DoD and/or VA research laboratories and programs. Collaboration with DoD and/or VA investigators is also encouraged. Below is a list of websites that may be useful in identifying additional information about DoD and VA areas of research interest, ongoing research or potential opportunities for collaboration.

Air Force Office of Scientific Research
<https://www.wpafb.af.mil>

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

Armed Forces Radiobiology Research Institute
<https://www.usuhs.edu/afri>

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

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

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

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

Defense Health Agency
<https://health.mil/dha>

Defense Technical Information Center
<https://discover.dtic.mil>

Defense Threat Reduction Agency
<https://www.dtra.mil>

Military Health System Research Symposium
<https://mhsrs.amedd.army.mil>

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

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

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

Naval Medical Research and Development
<https://www.med.navy.mil/sites/nmrc>

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

Navy Bureau of Medicine
<https://www.med.navy.mil>

Office of Naval Research
<https://www.onr.navy.mil>

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

Telemedicine and Advanced Technology Research Center
<https://www.tatrc.org>

Uniformed Services University of the Health Sciences
<https://www.usuhs.edu/research>

U.S. Air Force 59th Medical Wing
<https://www.59mdw.af.mil>

U.S. Army Aeromedical Research Laboratory
<https://www.usaarl.army.mil>

U.S. Army Institute of Surgical Research
<https://www.usaisr.amedd.army.mil>

U.S. Army Research Institute of
Environmental Medicine
<https://www.usariem.army.mil>

U.S. Army Medical Research Institute of
Infectious Diseases
<https://www.usamriid.army.mil>

U.S. Army Medical Research and
Development Command
<https://mrdc.amedd.army.mil/>

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

U.S. Army Combat Capabilities
Development Command
<https://www.army.mil/ccdc>

U.S. Army Sharp, Ready & Resilient
Directorate
<http://readyandresilient.army.mil>

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

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

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

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

APPENDIX 3: SAMPLE FITBIR CONSENT LANGUAGE

Data from this study may be submitted to the Federal Interagency Traumatic Brain Injury (FITBIR) informatics system. FITBIR is a computer system run by the National Institutes of Health that allows researchers studying traumatic brain injury to collect and share information with each other. With an easier way to share, researchers hope to learn new and important things about traumatic brain injury more quickly than before. During and after the study, the researchers will send information about you or your child's health and behavior and in some cases, you or your child's genetic information, to FITBIR. However, before they send it to FITBIR, they will remove information such as name, date of birth, and city of birth, and replace that information with a code number. Other researchers nationwide can then file an application to obtain access to your study data for research purposes. Experts who know how to protect health and science information will look at every request carefully to minimize risks to your privacy. You or your child may not benefit directly from allowing your information to be shared with FITBIR. The information provided to FITBIR might help researchers around the world treat future children and adults with traumatic brain injury so that they have better outcomes. FITBIR will report on its website about the different studies that researchers are conducting using FITBIR data; however, FITBIR will not be able to contact you or your child individually about specific studies. You may decide now or later that you do not want to share you or your child's information using FITBIR. If so, contact the researchers who conducted this study, and they will tell FITBIR, which can stop sharing the research information. However, FITBIR cannot take back information that was shared before you changed your mind. If you would like more information about FITBIR, this is available on-line at <http://fitbir.nih.gov> Language to be used to describe certificates of confidentiality (3 versions): 1. Language for new studies that will be consenting subjects for the first time or for ongoing studies that will be re-consenting subjects because they are applying for a Certificate of Confidentiality (COC) for the study To help protect you and/or your child's privacy the investigators of this study [have applied for]/[have obtained] a Certificate of Confidentiality from the National Institutes of Health, part of the U.S. Department of Health and Human Services (DHHS), an agency of the U.S. Government. With this Certificate, we, the investigators, cannot be forced (e.g., by court subpoena) to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. Be aware that disclosure of you and/or your child's identity may be found necessary, however, upon request of DHHS for the purpose of audit or evaluation. You should also understand that a Confidentiality Certificate does not prevent you or a member of your family from voluntarily releasing information about your child, yourself, or your involvement in this research. Note, however, that if an insurer or employer learns about you and/or your child's participation, and obtains your consent to receive research information, then the investigator may not use the Certificate of Confidentiality to withhold this information. This means that you and your family must also actively protect your own privacy. We are also asking your consent to provide research data and related findings to the Federal Interagency Traumatic Brain Injury Research (FITBIR) informatics system. FITBIR is a biomedical informatics system and data repository, created by the Department of Defense and the National Institutes of Health to assist biomedical researchers working to develop a better understanding of traumatic brain injury and/or to develop more effective methods to diagnose, treat and prevent traumatic brain injuries. Data entered into FITBIR will be kept confidential, with FITBIR being designed for access by qualified researchers only. Data provided to FITBIR as part of you and/or your child's participation in this research study will be de-identified—i.e., you and/or your child's name will

be separated from the data. However, since this institution and others submitting data to FITBIR will retain individually identifying information related to the data they provide, NIH has issued a legislatively authorized “Certificate of Confidentiality” that will help FITBIR and participating institutions avoid being forced to disclose information that may identify you as a FITBIR participant in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. Finally, you should understand that we, the investigators, are not prevented from taking steps, including reporting to authorities, to prevent serious harm to you, your child, or others. With respect to you and/or your child’s participation in FITBIR, we do not plan to make voluntary disclosures except if there were severe threats to the public health or safety.

2. Language for studies that already have a Certificate and will be re-consenting subjects about FITBIR With your consent, this study will collect and provide research data and related findings to the Federal Interagency Traumatic Brain Injury Research (FITBIR) informatics system. FITBIR is a biomedical informatics system and data repository created by the Department of Defense and National Institutes of Health—part of the U.S. Department of Health and Human Services (DHHS), an agency of the U.S. Government—to assist biomedical researchers working to develop a better understanding of traumatic brain injury and/or to develop more effective methods to diagnose, treat and prevent traumatic brain injury. Data entered into FITBIR will be kept confidential, with FITBIR being designed for access by researchers only. Data provided to FITBIR as part of you and/or your child’s participation in this research study will be de-identified—i.e., you and/or your child’s name will be separated from the data. However, since this institution and others submitting data to FITBIR will retain individually identifying information related to the data they provide, NIH has issued a legislatively authorized “Certificate of Confidentiality” to help FITBIR and participating institutions avoid being forced (e.g., by court subpoena) to disclose information that may identify you as an FITBIR participant in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. Be aware that disclosure of you and/or your child’s identity may be found necessary, however, upon request of DHHS for the purpose of audit or evaluation. As you know, we have obtained a Certificate of Confidentiality from NIH that enables us to keep the individually identifiable information that you provide as a research subject private. With this Certificate, we, the investigators cannot be forced to disclose research information collected in this study that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. This protection will continue to protect you and/or your child’s privacy even though we are providing de-identified data to FITBIR. You should also understand that a Confidentiality Certificate does not prevent you or a member of your family from voluntarily releasing information about your child, yourself, or your involvement in this research. Note, however, that if an insurer or employer learns about you and/or your child’s participation, and obtains your consent to receive research information, then the investigator may not use the Certificate of Confidentiality to withhold this information. This means that you and your family must also actively protect your own privacy. Finally, as we explained when we told you about this privacy protection before, we, the investigators, are not prevented from taking steps, including reporting to authorities, to prevent serious harm to you and/or your child or others based on information they learn during this study. With respect to you and/or your child’s participation in FITBIR, we do not plan to make voluntary disclosures except if there were severe threats to the public health or safety.

3. Language for studies without a Certificate of their own With your consent, this study will collect and provide research data and related findings to the Federal Interagency Traumatic Brain Injury Research (FITBIR) informatics system. FITBIR is a biomedical informatics system and data repository created by the Department of Defense and the National Institutes of Health—part of the U.S. Department of Health and Human Services

(DHHS), an agency of the U.S. Government—to assist biomedical researchers working to develop a better understanding of traumatic brain injury and/or to develop more effective methods to diagnose, treat and prevent traumatic brain injury. Data entered into FITBIR will be kept confidential, with FITBIR being designed for access by researchers only. Data provided to FITBIR as part of you or your child’s participation in this research study will be de-identified—i.e., you and/or your child’s name will be separated from the data. However, since this institution and others submitting data to FITBIR will still retain individually identifying information related to the data provided, the NIH has issued a legislatively authorized “Certificate of Confidentiality” to help FITBIR and participating institutions avoid being forced (e.g., by court subpoena) to disclose information that may identify you as an FITBIR participant in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. Finally, you should understand that we, the investigators, are also permitted to make voluntary disclosures with respect to information that is submitted to FITBIR, but do not plan to do so except in the event of severe threats to public health or safety. If, as part of your participation in this research study itself, we learn about serious harm to you, your child or someone else, we would take steps to prevent that harm including notifying appropriate authorities like the police or child welfare.