I. OVERVIEW OF THE FUNDING OPPORTUNITY

Program Announcement for the Department of Defense

Congressionally Directed Medical Research Programs

Defense Health Program Joint Program Committee 6 (JPC-6)/Combat Casualty Care Research Program (CCCRP) and Department of Affairs Office of Research & Development

Psychological Health/Traumatic Brain Injury Research Program

Long-Term Impact of Military-Relevant Brain Injury Consortium (LIMBIC) Award

Announcement Type: Initial

Funding Opportunity Number: W81XWH-18-PH/TBIRP-LIMBIC

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), October 8, 2018

- **Application Submission Deadline:** 11:59 p.m. ET, January 7, 2019

- **End of Application Verification Period:** 5:00 p.m. ET, January 11, 2019

- **Peer Review:** February 2019

- **Programmatic Review:** April 2019

This Program Announcement must be read in conjunction with the General Application Instructions, version 20180329. The General Applications 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

New for 2018: **Application submission by extramural organizations through Grants.gov requires use of the Workspace interface, which separates the application package into individual forms. Applicants must create a Workspace in Grants.gov, complete the required forms, and submit their application Workspace package.**

II.A. Program Description

Applications to the Fiscal Year 2018 (FY18) Psychological Health and 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 execution management agent for this Program Announcement is the Congressionally Directed Medical Research Programs (CDMRP). The U.S. Army Medical Research and Materiel Command (USAMRMC) Congressionally Directed Medical Research Programs (CDMRP) provides PH/TBIRP management support for DHA research program areas, including the Joint Program Committee-6/Combat Casualty Care Research Program (JPC-6/CCCRP). The execution management agent for this Program Announcement/Funding Opportunity is the CDMRP with strategic oversight from the JPC-6/CCCRP and coordination with the Department of Veterans Affairs (VA).

The PH/TBIRP was established by Congress in FY07 in response to the devastating impact of traumatic brain injury (TBI) and psychological health (PH) issues, including post-traumatic stress disorder, on deployed Service members in Iraq and Afghanistan. The PH/TBIRP mission is to establish, fund, and integrate both individual and multi-agency 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-6/CCCRP is one of six major research program areas within the DHP. The JPC-6/CCCRP is a committee of Department of Defense (DoD) and non-DoD medical and military technical experts in combat casualty care-related program areas. The JPC-6/CCCRP strives to optimize survival and recovery from combat-related or trauma-induced injury in current and future operational scenarios. This is being accomplished through the development of knowledge and materiel products for the acute and early management of combat-related or trauma-induced injury, including point-of-injury, en route, and forward surgical care. Innovations developed by JPC-6/CCCRP-supported research are applied in-theater and within the clinical facilities of the Military Health System. These solutions not only minimize the morbidity and mortality of combat-related injuries in Service members, they also are often translatable to the civilian healthcare system. The JPC-6/CCCRP Neurotrauma Portfolio (NTP) is focused on closing military-relevant gaps across a broad range of research areas to improve the prevention, diagnosis, management, and treatment of TBI and related sequelae from point-of-injury through

recovery. Ultimately, the NTP's goal is to decrease morbidity and mortality from neurotrauma, mitigate secondary brain injury across all TBI severities and all echelons of care, and advance materiel and knowledge development to expand and develop new clinical practice guidelines, care algorithms, therapies, devices, and procedures that advance the decision-making capabilities of medical personnel, enabling earlier intervention and improved outcomes.

The VA Office of Research and Development (ORD) supports health research at more than 115 VA facilities nationwide. Specially designated VA research centers conduct basic, clinical, rehabilitative, and health services research studies that support concentrated efforts by groups of scientists studying TBI, infectious diseases, substance abuse, and mental health, as well as service-connected conditions. In addition, VA research fosters dynamic collaborations with its university partners, other Federal agencies, nonprofit organizations, and private industry, thus furthering the program's impact on the health of Veterans and the nation.

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

II.B. Award Information

The PH/TBIRP Long-Term Impact of Military-Relevant Brain Injury Consortium (LIMBIC) Award is being offered for the first time in FY18. The overarching goal of this effort is to improve our understanding of the impact of mild TBI (mTBI)/concussion on Service members and Veterans. The FY18 PH/TBIRP LIMBIC Award will support a Consortium conducting a single large longitudinal study and associated sub-studies within the scope of the Program Announcement/Funding Opportunity. The knowledge gained through the proposed studies will be used to inform TBI pathways of care and illuminate specific target areas to improve acute TBI care and subsequent support systems for chronic care following mTBI.

The National Research Action Plan (NRAP) responding to Executive Order 13625, *Improving Access to Mental Health Services for Veterans, Service Members, and Military Families* (August 31, 2012), lays out a framework to ensure that Government funding agencies work together to further our knowledge and diagnostic/therapeutic capabilities with regard to post-traumatic stress disorder (PTSD), TBI, suicide, and related injuries by following longitudinal cohorts of Service members and Veterans. The DoD and VA ORD meet this directive through continued collaboration on and coordination of research efforts in the areas of TBI and PTSD. Additionally, recommendations from the DoD Blast Injury Research Program Coordinating Office's November 2015 International State of the Science Meeting *(Does Repeated Blast-Related Trauma Contribute to the Development of Chronic Traumatic Encephalopathy (CTE)?)* included pursuing longitudinal studies to evaluate links between blast-related TBI with CTE. While a number of longitudinal efforts are ongoing, the DoD and VA seek to pursue a mechanism to collaboratively streamline and continue longitudinal studies of mTBI in active duty and Veteran populations. The objective of this effort is to solicit a single Consortium of a large longitudinal study and supporting sub-studies to analyze a large TBI cohort to include Service members, Veterans, and relevant populations.

II.B.1. FY18 PH/TBIRP LIMBIC Research Elements

Applications to the FY18 PH/TBIRP LIMBIC Award must address all of the required research areas and as many secondary research areas as possible while maintaining the scientific rigor of the Consortium and project-level proposals.

II.B.1.a. Required Research Elements

To meet the intent of the LIMBIC award mechanism, applicants must be able to:

- ***Demonstrate the ability to enroll relevant cohorts, to include military and Veteran populations, and follow them over time.***

- Describe a military-relevant cohort with a history of mTBI. Applicants are strongly encouraged to leverage as many existing research efforts, infrastructure, and sample repositories as appropriate. As such, the applications should articulate plans for merging or leveraging existing cohorts (e.g., combination of cross-sectional studies, or follow-on work from existing larger longitudinal cohorts).

- Address enrollment of active duty Service members with the understanding they will eventually transition to Veteran status.

  - For prospectively enrolling studies, the target population must include a robust distribution of Service members and Veterans at the time of original enrollment into the study. Engagement and inclusion of existing intramural DoD and VA efforts and cohorts are strongly encouraged.

  - Subjects are not necessarily limited to those with combat experience; however, the ability to capture data from Service members and Veterans with combat-related TBI is strongly encouraged.

- Collect data in accordance with established TBI Common Data Elements (CDEs) guidelines for submission to the Federal Interagency TBI Research (FITBIR; https://fitbir.nih.gov/) Information System, to include data required to generate FITBIR Global Unique Identifier (GUID). Use of Unique Data Elements (UDEs) are strongly discouraged unless the research question warrants inclusion. Acceptance of UDEs is subject to approval of the program office.

- Identify potential differences in long-term neurological outcomes from blast-related versus impact-only TBI.

- Identify pathophysiological and biomarker signatures that may be predictive of long-term outcomes and healthcare utilization (e.g., fiber tract breaks in specific brain regions).

- Describe analysis(es) from existing available biorepositories and/or biospecimens from the proposed longitudinal study to identify novel biomarkers for chronic TBI and stratify and characterize mTBI subgroups based on recovery (poor versus good outcomes) and neurodegeneration (determining susceptibility to neurodegenerative conditions).

- Conduct epidemiological analysis of existing DoD and VA databases relating to mTBI for correlations and associations of mTBI and associated comorbidities such as pain, neurodegenerative disease, psychological health status, and neurosensory deficits.

II.B.1.b. Secondary Research Elements

Incorporation of the following research elements in the application is also encouraged:

- Investigate mTBI comorbidities in the prospective study cohorts, such as:

  ○ Psychological health and suicide comorbidities in the longitudinal study cohort

  ○ Incidence of pain and opioid (or other substance) use/misuse disorders correlated to mTBI

  ○ Incidence of the major comorbidities associated with the chronic effects of neurotrauma including psychological, neurological, neuro-endocrine, cognitive and sensory deficits, movement disorders, and pain

- Identify potential differences between single versus multiple TBI history in outcomes.

- Identify potential differences between individuals with historical exposure to repetitive low-level blast (e.g., Multi-Role Anti-Armor Anti-Personnel Weapon System [MAAWS], artillery, mortars, heavy weapons, breaching, explosives) and those without.

- Evaluate chronic mTBI biomarker profile(s) over time and injury severity (e.g., therapeutic indicators for responders versus non-responders to treatment indicators).

- Evaluate novel/advanced neuroimaging techniques, with promising initial findings, to understand the relationships between mTBI and neurodegenerative disease and/or comorbidities associated with mTBI.

- Identify potential variations in long-term outcomes in deployment-related versus nondeployment-related mTBI (addressing both the different systems of care in the two environments as well as the bulk of mTBI in Service members, nondeployment-related training and sports concussions).

- Determine relationships between history of mTBI and decreased military-relevant performance metrics (e.g., promotion rates, evaluation ratings, marksmanship, physical training tests, employment, attrition rates).

- Describe the economic burden of TBI, such as:

  ○ Disability outcomes and related costs in Service members and Veterans who have sustained one or more TBIs.

  ○ Healthcare utilization for comorbidities related to a history of mTBI.

- ○ Prevalence of comorbidities that are not generally considered TBI-related (e.g., obesity, chronic obstructive pulmonary disease, cardiovascular diseases) in Service members and Veterans with a history of TBI. Determine how, if at all, this rate compares with Service members who do not have a history of TBI.

- ○ Quantify the number of lost-duty days from mTBI.

- Identify potential policy implications of study findings to include efforts/plans to integrate with appropriate organizations for knowledge transition and translation (e.g., Defense and Veterans Brain Injury Center [DVBIC], VA Polytrauma Centers, Mental Illness Research, Education and Clinical Center [MIRECC], civilian sector).

The DoD expects to incrementally fund one LIMBIC Award. DoD funding for the FY18 PH/TBIRP LIMBIC Award will not exceed **$25M, of which $5M is currently available**. Incremental funding is anticipated to be **$5M** per year for **FY19, FY20, FY21, and FY22**, if funds are appropriated. The VA anticipates contributing up to $5M annually for 5 years to VA-eligible investigators through direct funding mechanisms. Refer to Section II.D.5, Funding Restrictions, for detailed funding information. Funds obligated by the VA will only be utilized to support research at VA sites; such funding will be coordinated through the VA Office of Research and Development. All collaborators may be eligible for other DoD and VA funding (if eligible for VA funding) should additional funds become available. The maximum period of performance is 5 years.

Leveraging existing resources, including infrastructure and/or research funding, is highly encouraged.

Award selection will depend upon evaluation of the proposed Coordinating Center structure, core laboratories, scientific studies, record of productivity, evidence of VA and DoD collaboration, available capabilities, access to military and/or Veteran populations, and feasibility of the entire group to accomplish the overall award objectives.

A DoD/VA co-chaired Government Steering Committee (GSC) will provide Government-level Consortium oversight of research activities. Relevance to the healthcare needs of the Armed Forces and/or the Veteran population is a key feature of the LIMBIC Award. Therefore, applications proposing collaborations that partner extramural academic, industry, and non-DoD Federal investigators with DoD intramural investigators (especially Principal Investigators [PIs] at military treatment facilities [MTFs]) are highly encouraged.

Studies involving animal research do not meet the intent of this award mechanism.

All projects shall be limited to clinical and epidemiological research. It is expected that the Consortium may leverage the resources and populations of the LIMBIC Award in efforts outside this award. Although work supported by the LIMBIC Award may eventually lead to clinical trials of U.S. Food and Drug Administration (FDA)-regulated interventions or diagnostics, **clinical trials are not supported by this award mechanism**. A clinical trial is defined as a prospective accrual of human subjects in which an intervention (e.g., device, drug, biologic, surgical procedure, rehabilitative modality, behavioral intervention, or other) is tested on a

human subject for a measurable outcome with respect to safety, effectiveness, and/or efficacy. This outcome represents a direct effect on the human subject of that intervention or interaction.

Consortium Oversight:

The Government will have substantial involvement in the Consortium through GSC, VA, and USAMRMC staff interactions with the Consortium. A GSC comprised of Government personnel will be established and co-chaired by DoD and VA representatives. The GSC will review progress, and it will provide input on scientific, military, and Veteran relevance and on the coordination of proposed projects with other relevant initiatives. The GSC will provide approval recommendations to the USAMRAA Grants Officer and Grants Officer's Representative (GOR) regarding proposed Consortium sub-studies prior to implementation.

General Consortium Requirements:

The Coordinating Center and Study Sites must apply to this Program Announcement/Funding Opportunity through a single application. A single award will be made to the selected Coordinating Center to support the Coordinating Center's efforts as well as Consortium-associated Study Sites slated for receipt of DoD funding. The institution that hosts the Coordinating Center may also serve as a Study Site. VA Consortium Study Sites will receive intramural VA funding directly though the VA Office of Research and Development.

LIMBIC Award applications should describe a single large longitudinal cohort study and a minimum of four related sub-studies that address the required and secondary research areas. Sub-studies are subject to the approval of the GSC.

All applications must have direct relevance to the overall objectives of the Consortium, with key expert personnel also collaborating across the multiple disciplines of interest. Applications must be able to describe a Consortium framework consisting of a Coordinating Center, multiple research sites (Study Sites), and relevant integrated supporting infrastructure (e.g., named Research Cores) and collaborations. It is expected that each research study will consist of collaborating partners, namely, a VA and/or DoD Treatment Facilities and one or more strongly relevant non-Federal entities including academic institutions and industry (e.g., private clinics and rehabilitation centers). Applicants must be able to describe any established collaborations between the Coordinating Center and proposed research sites.

LIMBIC Award applications should name and describe individual core facilities at member organizations that will serve as official Consortium Integrated Research Cores, which may include but are not limited to informatics, biorepository, imaging, and statistical laboratories. Establishment of Consortium-wide core facilities will enable more consistent, high-quality, standardized data to be collected across sites for Consortium-supported studies, as well as availability of specimens for planned and future analyses.

It is anticipated that the Consortium's DoD budget will support the Coordinating Center, core laboratories/facilities, and DoD-funded research Study Sites. It is anticipated that VA sites will be supported with intramural VA funds. The Coordinating Center will be required to submit quarterly written reports that outline overall progress toward performance measures.

Programmatic consideration will be given to applications that demonstrate ongoing strong collaborations between DoD or VA sites and academic, industry, other military, and nonprofit organizations, with established ties to the proposed Coordinating Center. In some cases, studies may include civilian sites/populations; however, this must be justified with respect to the overall relevance to supporting research on Service members and Veterans.

The Coordinating Center will provide the administrative protocol development, regulatory guidelines, statistical resources, and data management/storage functions necessary to facilitate all Consortium activities. The Coordinating Center will coordinate study activities, including site participation, as well as the collection, storage, use, and analyses of data and anatomical specimens. The Principal Investigator (PI) of the Coordinating Center shall provide evidence of prior experience with the design and administration of multi-institutional research studies.

The Coordinating Center PI and other key personnel, as noted below, must present written and oral briefings to the GSC and USAMRMC and VA staff at bi-annual GSC meetings in the National Capital Area. Based on these reports and presentations, the GSC, VA, and USAMRMC staff will evaluate progress, provide feedback, and invoke modifications as needed to facilitate the success of the Consortium.

A Consortium Committee, through the Coordinating Center, is expected to maintain monthly or more frequent contact with the GOR, who will maintain full documentation of interactions. The USAMRAA Grants Officer will issue the final approval of any proposed projects or award modifications of the DoD award, as well as issue approval to release DoD funds for the initiation of approved studies.

Summary of Consortium Responsibilities:

a. **All Consortium Participants:** Procedures for the Consortium, while proposed by the Coordinating Center, will be fully developed and agreed upon by all participants working collaboratively via a process to be detailed in the LIMBIC Award application. The process shall be codified in a Standard Operating Procedure (SOP), for review by the GOR within 90 calendar days of the award date. Draft or existing SOPs are requested for the full application.

b. **Consortium Coordinating Center:** The Coordinating Center PI will serve as the Director of the Consortium and Chair of the Consortium Committee. The Consortium Coordinating Center serves as the primary liaison with the GOR and will:

- Serve as the applicant institution in response to the Program Announcement/Funding Opportunity;

- Ensure that the Consortium adheres to the planned timeline and milestones for overall study execution;

- Develop and maintain the Consortium organizational structure;

- Establish and manage Consortium-developed procedures for external scientific review, prioritization, and implementation of potential new sub-studies proposed by or through Consortium members;

- Establish and manage procedures to ensure that all sites that receive DoD funding maintain compliance with local Institutional Review Boards (IRBs) and the USAMRMC Office of Research Protections (ORP) Human Research Protection Office (HRPO) for the proper conduct of clinical studies and the protection of human subjects (as appropriate) along with any other applicable DoD policies. All VA-funded studies at VA sites involving human subjects and human biological/anatomical substances must be reviewed by a VA IRB and must adhere to all applicable VA policies. Where applicable, the Consortium should consider utilization of a single IRB to process, review, and approve research protocols that involve multiple institutions to reduce IRB burdens and delays in the conduct of multicenter studies. A single IRB will conduct reviews on behalf of all Study Sites that agree to participate in the Consortium.

- Establish and manage a communications plan and a real-time communications system between the Coordinating Center and Study Sites, including the purchase of multi-site licenses, if necessary;

- Ensure appropriate agreements, such as Cooperative Research and Development Agreements (CRADAS), Material Transfer Agreements (MTAs), Consortium Committee agreements, and sub-awards, are in place within 90 calendar days of award;

- Submit all finalized Consortium SOPs and manuals to the Grants Officer and GOR within 90 calendar days of award;

- Ensure the standardized collection, storage and use of specimens, imaging products, and other data by core facilities;

- Manage Consortium-developed quality assurance and quality control mechanisms for study monitoring appropriate to the proposed work, to include (as applicable):

  ○ Registration, tracking, and reporting of participant accrual

  ○ Timely medical review, rapid reporting, communication of adverse events, and data management/coordination among all sites

  ○ Interim evaluation and consideration of measures of outcome

  ○ Metrics for performance of participating research sites

- Manage Consortium-developed comprehensive data collection and data management systems that address the needs of all Study Sites in terms of access to data, data security, and data integrity measures;

- Implement statistical execution plans/support for all Consortium studies;

- Manage costs to support the Study Sites, including provision of personnel, equipment, and materials required to conduct approved studies (as applicable);

- Facilitate a mechanism to provide DoD and VA sites with non-financial resources necessary for participation in the Consortium. Details for budgetary requests for DoD sites can be found in the General Application Instructions, Section III.A.5, Research & Related Budget (Federal Agency Plan and DoD Military Budget Forms). Details for VA budgets are listed in the Full Application requirements.

- Manage Consortium-developed intellectual and material property issues among organizations participating in the Consortium with respective VA and DoD Technology Transfer departments;

- Manage Consortium-developed procedures for the timely publication of major findings and other public dissemination of data;

- Coordinate the preparation of written and oral bi-annual briefings to the GSC and USAMRMC and VA staff at 1- to 2-day meetings to be held in the National Capital Area (activity to be included in Coordinating Center Budget); and,

- Develop, organize, and submit quarterly written progress reports, annual reports, and a final written comprehensive report to the USAMRMC and VA.

c. **Study Site PIs:**

- Participate fully in the Consortium Committee;

- During the performance period of the award, identify potential sub-studies and develop projects in accordance with the Consortium SOP for consideration by the GSC;

- Integrate with studies at other Study Sites as appropriate;

- Work with a Consortium Data Management Committee to monitor each study site for minimal recruitment rate on an ongoing basis;

- As applicable, designate a Clinical Research Coordinator, who will interact with the Clinical Research Coordinators of other Clinical Study Sites and the Consortium Clinical Research Manager at the Coordinating Center to expedite and guide clinical protocols through regulatory approval processes and to coordinate patient accrual and study activities across sites;

- Implement the Consortium's core data collection methodology and strategies;

- Comply with Consortium-developed quality assurance and quality control procedures, as appropriate, including:

  ○ Participate in an on-site monitoring program to be managed by the Coordinating Center;

  ○ Implement the Consortium-developed management plan for acquisition and aggregation of protocol-specified specimens, biological/anatomical fluids, and

relevant clinical data to the appropriate laboratories or Research Cores for testing or storage necessary for the conduct and analyses of clinical studies during the performance period of the award; and

- ○ Submit appropriate data and materials to allow for verification and review of protocol-related procedures (e.g., pathology, imaging techniques, surgical methods, and therapeutic use).

- Implement procedures established by the Coordinating Center to meet the local IRB and the USAMRMC ORP HRPO requirements for the conduct of clinical studies and the protection of human subjects as applicable. All VA-funded and -nonfunded studies at VAs involving human subjects and human biological/anatomical substances must be reviewed by a local VA IRB or, if it is multi-site, the VA Central IRB;

- Serve as a resource or core for the conduct of protocol-specified laboratory projects (including correlative studies), as applicable;

- Participate in Consortium-developed procedures for the timely publication of major findings;

- Participate in Consortium-developed procedures for resolving intellectual and material property issues among organizations participating in the Consortium;

- Participate in the preparation of written and oral bi-annual briefings to the GSC and USAMRMC and VA staff at 1- to 2-day meetings;

- Assist with the preparation of quarterly written progress reports and a final written comprehensive report; and

- Prepare for a site visit audit, if applicable.

The type of award made under the Program Announcement will consist solely of a cooperative agreement due to substantial government involvement to include GSC oversight. The level of involvement on the part of the DoD during project performance is the key factor in determining whether to award a grant or cooperative agreement.

Research Involving Human Anatomical Substances, Human Subjects, or Human Cadavers: All DoD-funded research involving new and ongoing research with human anatomical substances, human subjects, or human cadavers must be reviewed and approved by the USAMRMC ORP 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. Refer to the General Application Instructions, Appendix 1, 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.

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 should 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.

FITBIR Data Sharing: The DoD requires that awardees make TBI data generated via this award mechanism available to the research community by depositing de-identified research data into the FITBIR Informatics System on a bi-annual basis. The FITBIR Informatics System is a free resource to the research 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 to collaborate with others doing similar research. While there is no direct charge to users of the FITBIR Informatics System, a project estimation tool (https://fitbir.nih.gov/jsp/contribute/fitbir-costs.jsp) is available to help estimate costs and manpower needs that may be 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 FITBIR's 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: 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. For the most current version of the NINDS TBI CDEs, go to http://www.commondataelements.ninds.nih.gov. Assistance will be available to help the researchers map their study variables to specific CDEs and ensure the formats of the CDEs collected are compatible with the FITBIR Informatics System. 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 Unique Data Elements is strongly discouraged and subject to program approval.*

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.

Awards will be made no later than September 30, 2019. For additional information refer to Section II.F.1, Federal Award Notices.

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, Government, 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 organization may be submitted 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 http://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.

VA Research funds may only be awarded if the PI and any co-PI have employment status and activities that demonstrate a primary professional commitment to VA. The eligibility of each prospective PI (and co-PI) must be established prior to the funding of a research proposal. To demonstrate primary professional commitment to VA, the PI (and co-PI) must meet all of the following requirements:

VA Employment Status: A current VA paid appointment of at least 25 hours per week (5/8ths) is required before a research project can be funded. VA employment status of each PI (and co-PI, if applicable) must be indicated on the proposal for funding. The signatures of the PI (and co-PI) and the ACOS/R&D constitute verification and acceptance of the 5/8ths minimum requirement. *NOTE: Investigators who receive VA research support, as VA employees, are subject to the Government's ethics laws and rules.*

Physical Presence at VA: VA research must be conducted, principally, in a VA facility or VA-leased space. The PI (and co-PI) must have designated research space within a VA facility or VA-leased space. The specific research performance site address must be indicated on the application for funding and verified by the required signatures. Any requests for an exception to the requirement for physical presence in VA space or VA-leased space must be submitted in accordance with procedures described in *Veterans Health Administration (VHA) Handbook 1200.16*.

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

Extramural Submission is defined as an application submitted by an organization to Grants.gov.

Intramural DoD Submission is defined as an application submitted by a DoD organization to electronic Biomedical Research Application Portal (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 and 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 (https://eBRAP.org/).

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

Submitting Extramural Organizations: 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.

Submitting Intramural DoD Organizations: 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: A key feature of eBRAP is the ability of 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, each submission is assigned a unique log number by eBRAP. 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 applicant through eBRAP (https://eBRAP.org/). Because the invitation to submit an application is based on the contents of the pre-application, applicants should not change the title or research objectives after the pre-application is submitted.

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

A change in PI or organization after submission of the pre-application may be allowed after review of a submitted written appeal (contact the CDMRP Help Desk at help@eBRAP.org or 301-682-5507) and at the discretion of the USAMRAA Grants Officer.

PIs 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 (R&R) 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 (R&R) 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.

  FY18 PH/TBIRP LIMBIC GSC members will serve as the Programmatic Panel and 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.

  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 pre-application or application preparation, research, or other duties for submitted pre-applications or applications. For FY18, the identities of the peer review contractor and the programmatic review contractor may be found at the CDMRP website (http://cdmrp.army.mil/about/2tierRevProcess). Pre-applications or applications that include names of personnel from either of these companies will be administratively withdrawn unless plans to manage conflicts of interest (COIs) are provided and deemed appropriate by the Grants Officer. Refer to the General Application Instructions, Appendix 3, for detailed information.

- **Tab 4 – Conflicts of Interest**

  List all individuals other than collaborators and key personnel who may have a COI in the review of the application (including those with whom the PI has a personal or professional relationship). Refer to the General Application Instructions, Appendix 3, Section C, for further information regarding COIs.

- **Tab 5 – Pre-Application Files**

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

  ○ **Preproposal Narrative (8-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:

○ **Road Map and Goals:** Identify the critical research questions required to address the overarching goal of the LIMBIC Award, and describe the research question(s) and outcomes that are responsive to that goal. In addition to the overarching goal, briefly describe the overall aims of Consortium research. Describe how the proposed Consortium Road Map advances the knowledge of TBI and related comorbidities and may contribute to translational advances to improve care for individuals with chronic TBI.

○ **Consortium Structure:** Outline the organizations that will participate in the Consortium. Briefly discuss the qualifications of key personnel in the administration and their roles and ability to oversee studies. Describe potential core facilities and shared resources.

○ **Management Approach and Processes, to include:**

– Brief description of management processes to be implemented (to include the approach as to how to maximize available resources)

– Brief description of the process to manage performance of participating sites including strategies to mitigate lapse in performance and processes to terminate non-performing sites

○ **Research Plan:** Briefly describe a longitudinal study and at least four related sub-studies that address the required research areas and any secondary research areas of the Program Announcement/Funding Opportunity. Describe the reasoning on which each of the studies is based, the target patient population(s), and the outcomes to be measured.

– Discussion of maturity and feasibility of the research project or sub-projects and the overall research approach, including approval and technical process to move steps forward

– Schedule (in Gantt or similar format) for each major proposed research aim that addresses the overarching goal of the Program Announcement, showing major tasks and key milestones/timelines, with responsible organization and people, key decision points, and key communication points (within Consortium and between the VA, the DoD, and, if applicable, the FDA)

○ **Relevance:** Describe how the Consortium will have an impact on the lives of Service member and Veteran populations affected by mTBI and common chronic comorbidities, their family members, and the general public.

- **Leveraging Resources:** Describe the offeror's ability to leverage non-Consortium resources (research or funding, or both). Describe existing access to relevant TBI patient populations, data, and other resources.

- **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:

  – Quad Charts **(one for the main study and one for each related sub-study):** The document must be submitted by the pre-application submission deadline. The Quad Chart is a PowerPoint file that must be downloaded from the CDMRP eBRAP System and saved using Adobe Acrobat Reader as a PDF file. The Quad Chart template must be filled out as instructed and uploaded as a single combined file.

  – List of Abbreviations, Acronyms, and Symbols: Provide a list of abbreviations, acronyms, and symbols used in the Preproposal Narrative.

  – Key Personnel Biographical Sketches (five-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. VA investigators should highlight their VA affiliation/appointment

- **Tab 6 – Submit Pre-Application**

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

Pre-Application Screening

- **Pre-Application Screening Criteria**

  To determine the technical merits of the pre-application and the relevance to the mission of the DHP and the PH/TBIRP, pre-applications will be screened based on the following criteria:

  - **Road Map:** How well the proposed Road Map outlines research questions and outcomes that address the overarching goal of the LIMBIC award mechanism.

  - **Consortium Structure and Management Approach:** How well the outlined Consortium structure will provide efficient infrastructure designed to support the study coordination and core facilities required to conduct multi-institutional studies of varying scope and size. Whether the background and expertise of the administrative and research teams are appropriate with respect to their ability to oversee studies.

  - **Relevance:** The degree to which the proposed research, if successful, will have a significant impact on mTBI/concussion and common chronic comorbidities experienced by Service members and Veterans.

- ○ **Research Plan:** How well the proposed studies will meet the overarching goal and required research areas of the LIMBIC award mechanism in a reasonable representative scope and size. The degree to which the proposed studies address important questions collaboratively.

- ○ **Leveraged Resources:** How well the applicant utilizes existing resources, to include existing populations and/or samples, to support the Consortium's initiatives.

- **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 the PI has received notification of invitation.

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 (http://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 the 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	
Download application package components for W81XWH-18-PHTBIRP-LIMBIC from Grants.gov (http://www.grants.gov) and create a Grants.gov Workspace. The Workspace allows online completion of the application components and routing of the application package through the applicant organization for review prior to submission.	Download application package components for W81XWH-18-PHTBIRP-LIMBIC from eBRAP (https://ebrap.org).
Full Application Package Components	
SF424 (R&R) Application for Federal Assistance Form: Refer to the General Application Instructions, Section III.A.1, for detailed information.	**Tab 1 – Summary:** Provide a summary of the application information. **Tab 2 – Application Contacts:** This tab will be pre-populated by eBRAP; add Authorized Organizational Representative.
Descriptions of each required file can be found under Full Application Submission Components: • Attachments • Research & Related Personal Data • Research & Related Senior/Key Person Profile (Expanded) • Research & Related Budget • Project/Performance Site Location(s) Form • R&R Subaward Budget Attachment(s) Form (if applicable)	**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: • Attachments • Key Personnel • Budget • Performance Sites **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.
Application Package Submission	
Create a Grants.gov Workspace. Add participants (investigators and Business Officials) to the Workspace, complete all required forms, and check for errors before submission. **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	**Submit package components to eBRAP (https://ebrap.org).** **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.

Extramural Submissions	Intramural DoD Submissions
correct any potential technical issues that may disrupt the application submission. 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 prior to the application submission deadline.	
Application Verification Period	
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.	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, *with the exception of the Project Narrative and Budget Form,* may be modified. 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.
Further Information	
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. Refer to the General Application Instructions, Section III, for further information regarding Grants.gov requirements.	Refer to the General Application Instructions, Section IV, for further information regarding eBRAP requirements.

Application viewing, modification, and verification in eBRAP are strongly recommended, but not required. *The Project Narrative and Budget cannot be changed after the application submission deadline.* Prior to the full application deadline, a corrected or modified full application package may be submitted. 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 (R&R) 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.

  ○ **Attachment 1: Project Narrative (70-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.

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

  – **Consortium Road Map:** Identify the critical research questions required to address the overarching goal of the LIMBIC Award and describe the research question(s) appropriate for generating outcomes responsive to the overarching goal. Provide a brief description of the overall goals of the proposed research. Describe how the Consortium Road Map advances the knowledge of TBI and related comorbidities and

may contribute to translational advances to improve care for individuals with chronic TBI.

– **Consortium Structure, Expertise, Resources, and Previous Collaborations**

- Outline the structure of the proposed Consortium and identify key personnel, to include a graphical representation of the Consortium work breakdown structure.

- Describe the previous experience of the PI and other key personnel within the Coordinating Center with the design and administration of relevant multi-institutional studies. Provide any supporting documentation in the Research & Related Senior/Key Person Profile (Expanded) section of the application.

- Describe the previous experience of key personnel at each proposed Study Site with the development and conduct of relevant studies. Provide any supporting documentation in the Research & Related Senior/Key Person Profile (Expanded) section of the application.

- Describe the appropriate patient populations for any site conducting human subjects recruitment (i.e., Clinical Site) and provide evidence of the ability to enroll adequate patient numbers into Consortium-sponsored studies. Provide an estimate of case enrollment/patient load and the track record of research in this area for each Clinical Site and each Site PI.

- Describe the resources and facilities available within each Study Site for execution of relevant research projects.

- Describe organizational commitment for the Coordinating Center and each participating Study Site for the use of facilities and resources in the conduct of Consortium operations. Provide any supporting documentation in the relevant sections of the Attachments.

- Describe any plans to leverage existing or translational funding programs and infrastructure for the proposed Consortium. Provide any supporting documentation (e.g., as Letters of Organizational Support, Letters of Collaboration, and letters of support) in Attachment 2: Supporting Documentation.

- Describe how the Consortium application builds upon and streamlines existing collaborations.

- Describe ongoing and previous collaborations between Study Site entities and/or the Coordinating Center related to the overarching goal and required research areas of the LIMBIC Award.

– **Plan of Operations**

- **Government Coordination:** Describe plans to communicate and partner with any named DoD Sites, VA, or other Government research sites (Government sites). Explain how the Site PIs will provide input on all Consortium procedures and studies to a level commensurate with all other Study Sites. Outline a plan for providing resources to Government sites and establishing the research capabilities needed at the Government sites for full Consortium participation.

- **Management of Fiscal Resources:** Describe the organization required for the proper distribution of Consortium funds and other related resources. Outline processes for ensuring maximum efficiency of available funding.

- **Study Identification:** Outline a plan for the proposed project, design, and prioritization of potential future Consortium sub-studies for presentation to the GSC (including peer review process) following initial study implementation. Include a mechanism for determining Study Site participation.

- **Study Management and Monitoring:** Describe plans for real-time communication among all organizations participating in the Consortium (including the rapid dissemination of adverse events). Include a named Consortium Research Manager(s), who will interact with other individual site clinical coordinators to guide clinical protocols through the regulatory approval processes, coordinate participant accrual, and coordinate study activities across sites. Outline procedures for quality assurance, quality control, safety, and study monitoring. Describe procedures related to mitigation strategies and redirection of resources as necessary in response to Study Site activation and/or closure.

- **Core Facilities:** Outline essential cores and other facilities to be shared that will be necessary for facilitation of Consortium success. Discuss how the core facilities will be utilized and integrated across all Study Sites.

- **Clinical Protocol Development and Human Subjects Protection:** Describe plans for coordinating the development of clinical protocols and associated clinical documents that include HRPO/VA IRB-prescribed content (as applicable). Outline a plan for the external peer review of all Consortium clinical protocols and the coordination of IRB submissions and approvals. Describe the development of a plan for addressing human subjects protection requirements as outlined by HRPO/VA IRB. The link to the USAMRMC ORP HRPO website is https://mrmc.amedd.army.mil/index.cfm?pageid=research_protections.hrpo. Outline plans for developing procedures to ensure compliance with FDA requirements for investigational agents, as appropriate. Information on VA policies on human research can be found at https://www.research.va.gov/resources/policies/human_research.cfm. The link to the VA Central IRB is http://www.research.va.gov/vacentralirb/.

- **Data Management:** Outline a strategy for the development and implementation of a Consortium-wide data management plan, including (1) descriptions of the overall approach to data collection and management, (2) a statistical plan that includes methods to monitor quality and consistency of data collection and methods to measure outcomes, (3) a plan for real-time data transfer, (4) data security measures, and (5) a description of how to use/apply findings for future studies.

- **Specimen Handling and Distribution:** Describe plans for the development of standardized methods for the handling, distribution, analysis, banking, and security of any specimens and/or imaging products generated from Consortium-sponsored studies.

- **Information Technology (IT) Resources:** Since the Consortium will rely heavily on IT, provide the name of the individual who will be responsible for database and information infrastructure. Describe relevant personnel and organizational experience with implementing multi-institutional real-time communications. Describe the level of compliance for IT infrastructure with respect to the Federal Information Security Management Act of 2002 (FISMA) for management of any human subjects data originating from DoD or VA populations.

- **Publication and Data Dissemination:** Describe plans for ensuring rapid publication and other public dissemination of data while maintaining participant privacy. Ensure that all data sharing requirements have been considered and addressed. Data sharing includes dissemination of research results at research conferences as well as submission of TBI research data to the FITBIR Informatics System. The Consortium, as a whole, should plan to attend a large scientific research conference/symposium and present research findings twice in the performance of the LIMBIC Award.

- **Fiscal and Legal Administration:** Describe the fiscal and any applicable legal organization necessary for the proper distribution of funds and resources between Study Sites for performance of studies.

- **Research Plan:** The Research Plan must describe a longitudinal study and at least four related sub-studies that collectively address the required and secondary research areas of the award mechanism. For the longitudinal study and each individual sub-study, include the following:

  - **Background:** Present the ideas and reasoning behind the proposed work. Cite relevant literature and any available preliminary data. Describe previous experience most pertinent to this project.

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

- **Research Strategy:** Describe the study design, methods, and analyses, including appropriate controls, in sufficient detail for analysis. Address potential problem areas and present alternative methods and approaches. If human subjects or human anatomical samples will be used, include a detailed plan for the recruitment of subjects or the acquisition of samples. Describe the statistical plan, if appropriate, for the research proposed.

For submissions that include clinical research, the following are also required:

- Study Design: Describe the type of study to be performed and outline the proposed methodology in sufficient detail to show a clear course of action:

  - Define the study variables and describe how they will be measured. Include a description of appropriate controls and the endpoints to be tested.

  - Describe the methods that will be used to recruit a sample of human subjects from the accessible population (e.g., convenience, simple random, stratified random).

  - Describe the human subject-to-group assignment process (e.g., randomization, block randomization, stratified randomization, age-matched controls, alternating group, or other procedures), if applicable. Explain the specific actions to accomplish the group assignment (e.g., computer assignment, use of table of random numbers).

  - Describe the reliability and validity of psychometric measures, if applicable.

- **Statistical and Data Analysis Plan:** Include a complete power analysis to demonstrate that the sample size is appropriate to meet the objectives of the study. Specify the approximate number of human subjects that will be enrolled.

  - As applicable, state the approximate number to be enrolled at each Study Site. Describe the data analysis plan in a manner that is consistent with the study objectives.

- **Military and VA Benefit:** Describe how the Consortium's proposed studies build on the research goals in order to maximally benefit Service members and Veterans. Describe how the studies will have impact on improving the TBI pathways of care and overall health for individuals with long-term TBI.

- **Study Personnel:** Describe the background and expertise of investigators. Briefly describe their roles on the project.

○ **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 publications 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 (2-page limit per letter): Provide a letter (or letters, if applicable), signed by the Department Chair or appropriate organization official, confirming the laboratory space, equipment, and other resources available for the project. Letters of support not requested in the Program Announcement, such as those from members of Congress, do not impact application review or funding decisions.

– Letters of Collaboration (if applicable) (1-page limit per letter): Provide a signed letter from each collaborating individual or organization that will demonstrate that the PI has the support or resources necessary for the proposed work. 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.

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

– Intellectual Property: Information can be found in Code of Federal Regulations, Title 2, Part 200.315 (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. Describe existing CRADAs, MTAs, and Consortium Committee agreements. CRADAs, MTAs, and Programmatic Panel agreements must be in place within 90 days of the award start date.

  ▪ Include a named coordinator responsible for managing and resolving material and intellectual property issues among Consortium organizations.

– Use of DoD Resources (if applicable): For each DoD resource, provide a letter of support signed by the lowest-ranking person with approval authority confirming access to active duty military patient 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. Funding for VA Resources will primarily be supported by VA funds for this Program Announcement/Funding Opportunity. If a VA NPC must be utilized and is not 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.

○ **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.

  – **Background:** Describe the general management and organizational structure of the Consortium. Outline the management and expertise of Consortium personnel at the Coordinating Center and Study Sites.

  – **Objectives:** Describe the Consortium's overall research goals and objectives.

  – **Research Plan:** Briefly describe the studies the Consortium plans to pursue during the performance period. State how the proposed projects address the LIMBIC Award objectives and the required and secondary research elements.

  – **Military/VA Benefit:** Briefly describe how the expected results will have a significant impact on mTBI/concussion and common chronic comorbidities experienced by Service members and Veterans. Briefly state how the work of this Consortium may benefit the American public.

- ○ **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 in a manner readily understood by readers without a background in science or medicine. Minimize use of acronyms and abbreviations, where appropriate. Do not duplicate the technical abstract

  – Clearly describe the rationale, objective, and aims of the proposed research.

  – Describe the ultimate applicability of the Consortium's research. What types of patients will it help and how will it help them?

  – What are the potential applications, benefits, and risks?

  – What is the projected time it may take to achieve a relevant outcome?

  – What are the likely contributions of this study to advancing the field of research?

- ○ **Attachment 5: Statement of Work (SOW) (five-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 LIMBIC Award, 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 (animal or human) and/or human anatomical samples projected or required for each task and at each site. Refer to the General Application Instructions, Appendix 1, for additional information regarding regulatory requirements.

  – For studies with prospective accrual of human subjects, indicate quarterly enrollment for the overall effort and for each site recruiting human subjects. If sub-studies are recruiting subjects, clearly articulate quarterly recruitment and if the recruitment is a subset of the overall longitudinal study.

  – Identify cell line(s) and commercial or organizational source(s) to be used.

- – If applicable, indicate timelines required for regulatory approvals relevant to human subjects research (e.g., Investigational New Drug and Investigational Device Exemption applications) by the FDA or other Government agency.

- – Identify all proposed sites, including VA and DoD. For VA sites, clearly identify the site PI that is able to serve as the VA lead for VA funding for that particular site.

For awards that will be prospectively enrolling human subjects, add the following tasks and milestones to the SOW:

- – Register for a FITBIR account and register the study within the first 30 days of award.

- – Within the first 30 days of the award, provide the human subjects' data collection forms to the CDMRP point of contact.

- – Conduct bi-annual uploads to FITBIR coinciding with the year following the start of human subjects enrollment (e.g., if enrollment begins in year 1 quarter 2, FITBIR submission starts in year 2 quarter 2). Submission deadlines will be coordinated during award negotiations.

- – Include quarterly enrollment for the overall effort and for each site recruiting human subjects. If sub-studies are recruiting subjects, clearly articulate quarterly recruitment and if the recruitment is a subset of the overall longitudinal study.

- ○ **Attachment 6: Data and Research Resources Sharing and Management (required; no page limit):** Upload as "Data_Manage.pdf". The Data and Research Resources Sharing and Management attachment should include the components listed below.

  - – **Data Sharing**: Describe how data and resources generated during the performance of the project will be shared with the research community. *TBI and PH data must be collected in accordance with established CDEs as much as is practicable and submitted to FITBIR*.

    - ▪ Describe current or planned access to and interactions with the FITBIR Informatics System.

    - ▪ Describe the planned CDEs, any UDEs, and alignment to FITBIR data elements and forms. If the proposed research cannot be entered in CDE format, the applicant must explain why an existing CDE does not apply or is not appropriate for the study(ies) proposed under this Consortium.

    - ▪ For any UDEs, the applicant must supply an appropriate proposal, with full justification, for alternative data submission or data sharing vehicles. 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.

- **Data Management:** Describe all methods to be used for data collection to include the following:

  - Briefly describe the resources and expertise in each participating Study Site for effective data management and maintenance of data security/confidentiality.

- **Identifiers:** Describe the unique identifiers or specific code system to be used to identify human subjects, if applicable.

  - Address collection and management of data collected to generate GUIDs required for FITBIR.

- **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 USAMRMC are eligible to review study records.

  - Address requirements for reporting sensitive information to state or local authorities.

- **Disposition of Data:** Describe where data (both electronic and hard copy) will be stored, who will keep the data, how the data will be stored, and the length of time data will be stored. For electronic systems, address FISMA compliance and categorization of systems.

- **Data reporting:** Describe how data, other than that submitted to FITBIR, 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, to include 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, to include location of storage, how long specimens will be stored, any special conditions required, labeling, and disposition. Outline the plan to store specimens for future use to include considerations for informed consent and providing human subjects with an opportunity to decline participation in the study.

- **Labs performing evaluations and special precautions:** Identify the laboratory performing each evaluation, as well as any special precautions that should be taken in handling the samples. Special precautions that should be taken by the human subject before, during, or after the laboratory procedure should be clearly defined. If transport of samples is required, describe provisions for ensuring proper storage during transport.

○ **Attachment 7: Military and Veteran Benefit Statement (one-page limit):** Upload as "MilBen.pdf".

– Describe how the Consortium is responsive to the healthcare needs of Service members, Veterans, their families and caregivers, and/or individuals who are experiencing effects of chronic mTBI. State how the proposed work may be used to improve or change TBI pathways of care. State how the proposed work is applicable and beneficial to the general public.

– Show how the proposed study complements ongoing DoD and VA research, if applicable.

– If Service member (active duty, National Guard, and/or Reserve) and/or Veteran population(s) will be used in the proposed research project, describe the population(s), the appropriateness of the population(s) for the proposed study, and the feasibility of accessing the population. If a non-military population will be used for the proposed research project, explain how the population simulates the targeted population (i.e., Service members or Veterans).

○ **Attachment 8: Transition Plan (one-page limit):** Upload as "Transition.pdf".

– Provide information on the methods and strategies proposed to move the anticipated research outcomes (including non-tangible knowledge products) to the next phase of research or delivery to the military practice or civilian market after successful completion of the award. The transition plan should include the components listed below:

- Details of the funding strategy that will be used to bring the outcomes to the next level of development (e.g., specific potential industry partners, specific funding opportunities to be pursued).

- A description of collaborations and other resources that will be used to provide continuity of development, such as proposed development or modification of clinical practice guidelines and a plan for dissemination of practitioner and patient educational tools.

- For knowledge outcomes, a description of how the knowledge will be further developed, disseminated, and incorporated into clinical/patient care, including proposed development or modification of clinical practice guidelines and recommendations, provider training materials, patient brochure and other clinical support tools, scientific journal publications, models, simulations, and applications.

- A description of continued efforts required to validate any newly developed or non-standard utilization of assessment measures, tools, and technologies.

- A brief schedule and milestones for bringing the outcome(s) to the next level.

- The involvement of appropriate intellectual property, licensing, and/or business professionals.

- If applicable, a risk analysis for cost, schedule, manufacturability, and sustainability.

○ **Attachment 9: Human Subject Recruitment and Safety Procedures (if applicable; required for all studies recruiting human subjects; no page limit):** Upload as "HumSubProc.pdf". The Human Subject Recruitment and Safety Procedures attachment should include the components listed below:

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

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

Inclusion of Women and Minorities in Study. Consistent with the Belmont Report, "Ethical Principles and Guidelines for the Protection of Human Subjects," and Congressional legislation, special attention is given to inclusion of women and/or minorities in studies funded or supported by the USAMRMC. This policy is intended to promote equity both in assuming the burdens and in receiving the benefits of

human subjects research. Include an appropriate justification if women and/or minorities will be excluded from the clinical research

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

- Include a detailed description of and justification for the compensation plan if the human subjects will be compensated for participation in the study.

- Describe the recruitment and advertisement materials. The recruitment materials should not be coercive or offer undue inducements and should accurately reflect the study.

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

- ***For the proposed study, provide a draft, in English, of the Informed Consent Form.***

- Identify who is responsible for explaining the study, answering questions, and obtaining informed consent. Include a plan for ensuring that human subjects' questions will be addressed during the consent process and throughout the trial.

- Include information regarding the timing and location of the consent process.

- Address issues relevant to the mental capacity of the potential human subject (e.g., altered capacity due to administration of any mind-altering substances such as tranquilizers, conscious sedation or anesthesia, brain injury, stress/life situations, or human subject age), if applicable.

- Address how privacy and time for decision making will be provided and whether or not the potential human subject will be allowed to discuss the study with anyone before making a decision.

- Consider the need for obtaining ongoing consent or for re-assessing capacity over the course of a long-term study and describe any relevant procedures to assure continued consent.

- Describe the plan for the consent of the individual's Legally Authorized Representative (LAR) to be obtained prior to the human subject's participation in the study. State law defines who may act as the LAR. The local IRB of record should be consulted for guidance regarding who can serve as LAR for research at the study site. **Note:** The PI must describe a clear intent to benefit for human

subjects who cannot give their own consent to participate in the proposed clinical research to be in compliance with 10 USC 980) (https://www.gpo.gov/fdsys/pkg/USCODE-2011-title10/pdf/USCODE-2011-title10-subtitleA-partII-chap49-sec980.pdf). If applicable, refer to the General Application Instructions, Appendix 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.

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

f. **Risks/Benefits Assessment:**

- **Foreseeable risks:** Clearly identify all study risks. Study risks include any risks that the human subject is subjected to as a result of participation in the clinical study or trial. Consider psychological, legal, social, and economic risks as well as physical risks. If the risks are unknown, this should be stated. If applicable, any potential risk to the study personnel should be identified.

- **Risk management and emergency response:**

  ○ Describe all safety measures to minimize and/or eliminate risks to human subjects and study personnel or to manage unpreventable risks. Include safeguards and planned responses such as dose reduction or stopping criteria based on toxicity grading scales or other predetermined alert values.

  ○ Discuss the overall plan for provision of emergency care or treatment for an adverse event for study-related injuries, to include who will be responsible for the cost of such care.

  ○ Address any special precautions to be taken by the human subjects before, during, and after the study (e.g., medication washout periods, dietary restrictions, hydration, fasting, and pregnancy prevention).

  ○ Describe any special care (e.g., wound dressing assistance, transportation due to side effects of study intervention impairing ability to drive) or equipment (e.g., thermometers, telemedicine equipment) needed for human subjects enrolled in the study.

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

○ **Attachment 10: Standard Operating Procedures (SOPs) and Manuals of Operations (MOPs), if available:** Upload as "SOPs.pdf". Provide draft SOPs and MOPs for the proposed Consortium efforts to include Consortium governance, research core operations, site operations, and Consortium procedures. For applications leveraging existing resources, current SOPs may be used to demonstrate established frameworks.

○ **Attachment 11: Representations, if applicable (extramural submissions only):** Upload as "MandatoryReps.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 12: VA Site Budgets, if applicable:** Upload as "VABudgets.pdf". If any VA Sites or VA investigators are requesting VA funds under the LIMBIC Award, VA budgets must be completed using the SF424 and submitted as a single PDF. This attachment (VA budgets only) must also be submitted to the local Research Office and ORD, specifying the appropriate Research Service, for verification prior to submission. VA funding must not be included in the overall DoD Budget.

○ **Attachment 13: 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.7, 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, 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.2, for detailed information.

- ○ PI Biographical Sketch (5-page limit): Upload as "Biosketch_LastName.pdf". The suggested biographical sketch format is available on the "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) in eBRAP. The National Institutes of Health Biographical Sketch may also be used. All biographical sketches should be submitted in the PDF format that is not editable.

- ○ PI Previous/Current/Pending Support (no page limit): Upload as "Support_LastName.pdf".

- ○ Key Personnel Biographical Sketches (5-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.4, and for intramural submissions (via eBRAP), refer to the General Application Instructions, Section IV.A.3, 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.5, and for intramural submissions (via eBRAP), refer to the General Application Instructions, Section IV.A.4, for detailed information.

- **Extramural Applications Only**

R&R Subaward Budget Attachment(s) Form (if applicable): Refer to the General Application Instructions, Section III.A.6, for detailed information.

- ○ **Extramural Subaward:** Complete the Research & Related Subaward Budget Form through Grants.gov. (Refer to the General Application Instructions, Section III.A.6, 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 13. (Refer to the General Application Instructions, Section III.A.7, 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.

Applicants Requesting VA Funds: Complete the VA Forms using the SF424 and upload to Grants.gov attachment form as [Attachment 12](). **VA budgets should not be included on the Grants.gov DoD Research and Budget form under subaward costs.** VA Budget forms must also be submitted to the local Research Office and ORD, specifying the appropriate Research Service, for verification prior to submission.

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.

New Requirement: In March 2018, the General Services Administration (GSA) implemented fraud prevention security measures in the SAM that require every *new* contractor registrant to provide a written (hard copy), notarized letter confirming that the entity's Administrator is authorized to register the entity in the SAM database or to make changes to its registration. Effective April 29, 2018, the notarized letter process is now mandatory on all *current* registrants at SAM who have a requirement to update data on their SAM record. The notarized letter is mandatory and is required before the GSA Federal Service Desk (FSD) will activate the entity's registration. The Office of the Secretary of Defense and GSA realize the length of time needed to transmit, receive, process, and approve the notarized letters presents a significant impact on the ability of the contracting activity to make timely awards, but these steps must be taken to mitigate fraud concern. ***Notarized letters are required for all new and existing SAM-registered entities.*** The notarized letters must be postal service mailed (not emailed or faxed) to the "Federal Service Desk" and must contain the information outlined in the SAM-posted Frequently Asked Questions (FAQs) at [https://www.gsa.gov/about-us/organization/federal-acquisition-service/office-of-systems-management/integrated-award-environment-iae/sam-update](). Instructions for domestic entities and instructions for international entities with embedded templates for use are also provided within the SAM Update notice with FAQs at [https://www.gsa.gov/about-us/organization/federal-acquisition-service/office-of-systems-management/integrated-award-environment-iae/sam-update]().

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 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 **5** years.

The anticipated total DoD award costs budgeted for the entire period of performance will not exceed **$25M**. It is anticipated that $5M per year may be available in FY19, FY20, FY21, and FY22, dependent on the availability of funds. 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 **$25M** total DoD award 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 anticipated total VA costs for the entire budgeted period of performance will not exceed **$25M** (up to $5M per year for 5 years, depending upon availability of funds). Requests for VA funds will be detailed in Attachment 12 and through separate applications to the VA as Service

Directed Research programs in the out-years. VA funding is restricted to individuals and sites that meet VA research funding criteria (see Section II.C, Eligibility Information).

For this award mechanism, direct costs:

Must be requested for:

- Preparation and submission of data to FITBIR.

- Travel cost for the Consortium Coordinating Center and Study Site PIs to travel to two GSC meetings per year. For planning purposes, it should be assumed that the GSC meetings are held in the National Capital Area. These travel costs are in addition to those allowed for annual/scientific technical meetings.

- Travel costs for the Consortium Coordinating Center and Study Site PIs to present project information and disseminate results at two DoD or VA-sponsored meetings (e.g., Military Health System Research Symposium) during the period of performance. These travel costs are in addition to those allowed for scientific/technical meetings.

May be requested for (not all-inclusive):

- Salary

- Research supplies

- Research-related subject costs

- Clinical research costs

- Support for multidisciplinary collaborations, including travel

- Travel costs for Consortium Coordinating Center and Study Site PIs to attend one scientific/technical meeting per year, in addition to the required meetings described above, to present Consortium research and outcomes/results.

Must not be requested for:

- Animal studies

- Clinical trials

- VA costs. VA sites will be funded using intramural VA funding mechanisms. VA costs must not be included in the DoD budget. Costs for VA-funded sites must be detailed in Attachment 12: VA Site Budgets (see Full Application Instructions)

Awards made to extramural organizations will consist solely of 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.4, for budget regulations and instructions for the Research & Related Budget. ***For Federal agencies or organizations collaborating with Federal agencies, budget restrictions apply as are noted in the General Application Instructions, Section III.A.4***.

The JPC-6 expects to allot approximately $5M of the FY18 PH/TBIRP appropriation and $5M per year of the anticipated FY19, FY20, FY21, and FY22 DHP RDT&E appropriations to fund approximately one LIMBIC Award application, depending on the quality and number of applications received. Funding of applications received in response to this Program Announcement is contingent upon the availability of Federal funds for this program.

Funds to be obligated on any award resulting from this Program Announcement/Funding Opportunity will be available for use for a limited time period based on the fiscal year appropriation of funds. The time is considered when establishing the award's period of performance. It is anticipated that awards made from this Program Announcement/Funding Opportunity will be funded with the DHP RDT&E FY18-FY22 funds. FY18 funds will expire for use on September 30, 2024; FY19 funds will expire for use on September 30, 2025; FY20 funds will expire for use on September 30, 2026; FY21 funds will expire for use on September 30, 2027; FY22 funds will expire for use on September 30, 2028. VA funding will follow the budgetary policies of the Department of Veterans Affairs, Office of Research and Development.

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:

- **Consortium Road Map**

  ○ How well the proposed Road Map provides a plan for addressing the overarching goal of the LIMBIC Award.

  ○ To what extent the proposed Road Map and studies will advance the knowledge of TBI and related comorbidities to improve care for individuals with chronic TBI.

- **Consortium Structure, Expertise, Resources, and Previous Collaborations**

  ○ How well the proposed Consortium structure identifies key personnel and resources necessary for achieving the overarching goal of the LIMBIC Award.

  ○ To what extent the proposed overall organizational structure of the Consortium is appropriate.

  ○ To what extent the Coordinating Center personnel's background, track record, and expertise are appropriate with respect to the ability to manage and oversee the Consortium.

  ○ To what extent the previous experience and level of effort of key Study Site personnel are appropriate for the successful execution of the Consortium studies.

  ○ How well ongoing and previous collaborations involving Study Sites and/or the Coordinating Center are described and relate to the current effort.

  ○ To what extent the Consortium application builds upon and streamlines existing collaborations.

  ○ To what extent the patient populations and resources at proposed Study Sites are appropriate for the overarching goal and required research areas of the LIMBIC Award.

  ○ The degree to which the facilities and resources are appropriate for the conduct of Consortium operations.

  ○ How well existing translational resources support the Consortium's goals.

  ○ The degree to which the proposed organizational structure supports implementation of multi-institutional communication and collaboration.

- **Plan of Operations**

  ○ The degree to which the Plan of Operations establishes plans for coordination and communication between the Government, Coordinating Center, Study Sites, and any related partner organizations.

  ○ How well the Consortium Coordinating Center and Study Sites will function as an integrated unit.

  ○ How well the Plan of Operations demonstrates a sound strategy for synergy and collaboration throughout the Consortium.

  ○ How well the Study Management and Monitoring Plan addresses monitoring of Consortium research.

- How well the Plan of Operations addresses the ability of the Coordinating Center to oversee and coordinate Consortium sites to include procedures to redirect resources and funds, as necessary, in response to Study Site activation and/or closure.

- The degree to which the Plan of Operations is appropriate for a large multi-institutional research effort.

- To what degree the proposed core facilities are appropriate and integrated for the proposed effort.

- To what degree the Plan of Operations describes plans and procedures for clinical protocol development and regulatory approval. How appropriate the plans are for addressing human subjects protection requirements as described by HRPO and coordinating IRB submissions and approvals at participating sites.

- The degree to which plans for the proposed project development, and any required external peer review of clinical protocols and associated clinical documents are appropriate for the proposed period of performance.

The main longitudinal study and associated sub-studies will be evaluated using the following criteria:

- **Research Strategy**

  - Whether the proposed longitudinal study and any related sub-studies are appropriate to the overarching goal of the LIMBIC Award.

  - How well the overall Research Plan addresses the required research areas of the award mechanism.

  - The degree to which the overall Research Plan addresses secondary research areas of the award mechanism, if applicable.

  - How well the scientific rationale for testing the overall hypothesis(es) is(are) supported by the preliminary data, critical review and analysis of the literature, and/or prior clinical evidence supporting the relationship to chronic TBI.

  - How well the study aims, hypotheses or objectives, experimental design, methods, data collection procedures, and analyses are designed to clearly answer the clinical objective.

  - As applicable, how appropriate the questionnaires, surveys, and other tools included in the study are and how well their psychometrics are described.

  - How well the scientific rationale and preliminary data support each proposed study's design and objectives.

  - The degree to which the patient populations and sample size are appropriate for the main study and any associated sub-study.

- The degree to which proposed methods and outcome measures are appropriate for the purposes of the main study and each sub-study.

- How well the inclusion criteria meets the needs of the proposed clinical study(ies).

- How well the exclusion criteria are justified.

- **Clinical Impact**

  - How the proposed study addresses the overarching Consortium goal.

  - To what degree the anticipated results of the proposed clinical study will impact research and/or patient care related to chronic TBI.

  - How well the study population represents the target patient population that may benefit from the proposed research.

  - To what degree the potential clinical research outcomes will provide short- and long-term improvements in the care of individuals with chronic TBI.

  - To what degree the proposed research outcomes are an improvement over current standards of care for individuals with chronic TBI (e.g., available interventions, patient-related outcomes, and/or clinical practice guidelines).

- **Feasibility**

  - Whether there is sufficient evidence that the PI has the experience and resources to conduct the research successfully. Whether the described study population is feasible, with respect to access, recruitment strategies, inclusion/exclusion criteria, etc.

  - How well the PI addresses the availability of human subjects for the clinical research 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 research.

  - How well the application identifies possible delays (e.g., slow accrual, attrition) and presents adequate contingency plans to resolve them.

  - Acknowledgement of potential problems and alternative approaches.

- **Statistical and Data Analysis Plan**

  - How the statistical plan, including sample size projections and power analysis, is adequate to achieve the study objectives and is appropriate to type and phase of study.

- ○ Description of the population(s) of interest, demonstration of access to these populations, and identification of sampling methods to gain a representative sample from the population(s) of interest.

- ○ How well the longitudinal study and each proposed sub-study utilizes the Consortium resources.

- ○ To what degree the data collection instruments (e.g., surveys, questionnaires), if applicable, are appropriate to support statistical significance of the proposed study.

- **Ethical Considerations**

  - ○ Whether the level of risk to human subjects is minimized and communicated through informed consent.

  - ○ 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.

  - ○ How well safeguards are described and in place for vulnerable populations.

- **Personnel**

  - ○ How the background and expertise of the Clinical Study Site PI(s) demonstrate ability to perform the proposed work.

  - ○ How the levels of effort by the Clinical Study Site PI(s) and key personnel are appropriate to ensure success of this study.

  - ○ How each investigator's record of accomplishment demonstrates the ability to accomplish the work.

  - ○ Whether the composition of the study team is appropriate.

- **Data Management and Data Sharing**

  - ○ The degree to which the overall approach to data collection, management, analysis, and security measures is appropriate.

  - ○ How clearly the PI and key personnel have demonstrated (1) effective application of methods to monitor quality and consistency of data collection, and (2) methods to measure outcomes in previously conducted clinical research.

  - ○ How adequate the plan is for real-time data transfer with regard to supporting the Consortium-associated activities.

  - ○ The degree to which plans for the publication, dissemination, and sharing of data are appropriate.

○ How well the study utilizes TBI CDEs and describes processes and timelines for integrating data to the FITBIR Informatics System. If UDEs are utilized, how well the application justifies the rationale for UDE collection.

- **Military and Veteran Benefit**

  ○ The degree to which the Consortium efforts are responsive to the health needs of Service members and Veterans with chronic TBI, their families and beneficiaries and the American public.

  ○ The degree to which Service member and Veteran populations are included in Consortium Studies.

  ○ How well relevant non-military populations represent the health needs of a military population.

  ○ The degree to which the Consortium complements ongoing DoD and VA research in chronic TBI, if applicable.

- **Transition Plan**

  ○ Whether the funding strategy described to bring the outcome(s) to the next level of development (e.g., higher-phase clinical trial, transition to industry, delivery to the market, incorporation into standard practice) is appropriate.

  ○ Whether appropriate collaborations and other resources for providing continuity of development are established and/or well-described.

  ○ To what degree the schedule and milestones for bringing the proposed outcome(s) to the next level of development (e.g., potential clinical trial, transition to industry, delivery to the market, incorporation into standard practice) are appropriate.

  ○ How well the application identifies intellectual property ownership, describes any appropriate intellectual and material property plan among participating organizations (if applicable), and addresses any impact of intellectual property issues on product development and subsequent Government access to products supported by this Program Announcement/Funding Opportunity.

  ○ For knowledge products, to what degree the transition plan includes appropriate strategies for further knowledge development, dissemination, and/or incorporation into clinical care toward improved patient-related outcomes.

- **Environment**

  ○ To what extent the scientific environment is appropriate for Consortium efforts.

  ○ How well the research requirements are supported by the availability of and accessibility to facilities and resources (including collaborative arrangements).

  ○ To what extent the quality and level of institutional support are appropriate for the proposed research project.

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

- **Budget**

  ○ Whether the **total** maximum costs are equal to or less than the allowable total maximum costs as published in the Program Announcement/Funding Opportunity.

  ○ Whether the budget is appropriate for the proposed research.

- **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 and FY18 PH/TBIRP, as evidenced by the following:

  ○ Adherence to the intent of the award mechanism

  ○ Program portfolio composition

  ○ Programmatic relevance to DoD and VA TBI research priorities

  ○ Relative impact

  ○ Relative military and VA benefit

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 of applications against established criteria for determining technical merit. Each application is evaluated for its own merit, independent of other applications. The second tier is a programmatic review that makes recommendations for funding to the Commanding General, USAMRMC, on behalf of the DHA and the OASD(HA), based on technical merit, the relevance to the mission of the DHP, JPC-6/CCCRP, and PH/TBIRP, and to the VA ORD the specific intent of the award mechanism, and to other specified evaluation criteria in the Program Announcement. Programmatic review is a comparison-based process in which applications with scientific and technical merit compete in a common pool. ***The highest-***

scoring applications from the first tier of review are not automatically recommended for funding. Funding recommendations depend on various factors as described in [Section II.E.1.b, Programmatic Review](#). Additional information about the two-tier process used by the CDMRP can be found at http://cdmrp.army.mil/about/fundingprocess.

All CDMRP review processes are conducted confidentially to maintain the integrity of the merit-based selection process. 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 will be made no later than September 30, 2019. 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 Organizations: Awards 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

Changes in Coordinating Center PI are not allowed, except under extenuating circumstances that will be evaluated on a case-by-case basis and at the discretion of the Grants Officer. An organizational transfer of an award will not be allowed in the last year of the (original) period of performance or any extension thereof.

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

II.F.2. Administrative and National Policy Requirements

If additional conference travel is proposed, prior to the re-budgeting and in advance of the incurrence of the travel costs, the Grants Officer should be consulted to determine the reasonableness of the expense in accordance with 2 CFR 200.407.

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 LIMBIC 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.

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 full text of the USAMRAA General Research Terms and Conditions with Institutions of Higher Education, Hospitals, and Non-Profit Organizations: Addendum to the DoD R&D 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.***

Report-out at biannual GSC meetings is required for this award mechanism.

Annual progress reports as well as a final progress report will be required. Quarterly technical progress reports, quad charts, and in-person presentations are required.

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 Terms and Conditions (see General Application Instructions, Section III.A.4).

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 20180329h. The Program Announcement numeric version code will match the General Applications Instructions version code 20180329.

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 exceeds page limit.

- Preproposal Narrative is missing.

The following will result in administrative rejection of the application:

- Submission of an application for which a letter of invitation was not received.

- Project Narrative exceeds page limit.

- Project Narrative is missing.

- Budget is missing.

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 FY18 PH/TBIRP LIMBIC GSC 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 FY18 PH/TBIRP LIMBIC GSC members can be found at* http://cdmrp.army.mil/phtbi/panels/panels18_limbic.

- 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 FY18, the identities of the peer review contractor and the programmatic review contractor may be found at the CDMRP website (http://cdmrp.army.mil/about/2tierRevProcess). Applications that include names of personnel from either of these companies will be administratively withdrawn unless plans to manage COIs are provided and deemed appropriate by the Grants Officer. Refer to the General Application Instructions, Appendix 3, for detailed information.

- 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 application proposes animal research.

- The application proposes a clinical trial.

- The invited application does not propose the same research project described in the pre-application.

- An application for which the PI does not meet the eligibility criteria will be withdrawn.

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 (R&R) 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".	
	Data and Research Resources Sharing and Management: Upload as Attachment 6 with file name "Data_Manage.pdf".	
	Military and Veteran Benefit Statement: Upload as Attachment 7 with the file name "MilBen.pdf".	
	Transition Plan: Upload as Attachment 8 with the file name "Transition.pdf".	
	Human Subject Recruitment and Safety Procedures: Upload as Attachment 9 with the file name "HumSubProc.pdf".	
	Standard Operating Procedures and Manuals of Operations: Upload as Attachment 10 with the file name "SOPs.pdf".	
	Representations (Extramural Submissions only): Upload as Attachment 11 with file name "MandatoryReps.pdf" if applicable.	
	VA Site Budgets: Upload as Attachment 12 with the file name "VABudgets.pdf".	
	DoD Military Budget Form(s): Upload as Attachment 13 with file name "MFBudget.pdf" if applicable.	
Research & Related Personal Data	Complete form as instructed.	

Application Components	Action	Completed
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.	
R&R Subaward Budget Attachment(s) Form, if applicable	Complete form as instructed.	
Additional Application Components	**Action**	**Completed**
Confidential Letters of Recommendation	Confirm upload to eBRAP.	

APPENDIX 1: ACRONYM LIST

ACOS/R&D	Associate Chief of Staff for Research and Development
CCCRP	Combat Casualty Care Research Program
CDEs	Common Data Elements
CDMRP	Congressionally Directed Medical Research Programs
CFR	Code of Federal Regulations
COI	Conflict of Interest
CRADA	Cooperative Research and Development Agreement
CTE	Chronic Traumatic Encephalopathy
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
DVBIC	Defense and Veterans Brain Injury Center
eBRAP	Electronic Biomedical Research Application Portal
EC	Ethics Committee
ET	Eastern Time
FAD	Funding Authorization Document
FAPIIS	Federal Awardee Performance and Integrity Information System
FAQs	Frequently Asked Questions
FDA	U.S. Food and Drug Administration
FISMA	Federal Information Security Management Act
FITBIR	Federal Interagency TBI Research
FSD	Federal Service Desk
FY	Fiscal Year
GOR	Grants Officer's Representative
GSA	General Services Administration
GSC	Government Steering Committee
GUID	Global Unique Identifier
HIPAA	Health Information Portability and Accountability Act
HRPO	Human Research Protection Office
IRB	Institutional Review Board
IT	Information Technology
JPC-6	Joint Program Committee-6
LAR	Legally Authorized Representative

LIMBIC	Long-Term Impact of Military-Relevant Brain Injury Consortium
M	Million
MAAWS	Multi-Role Anti-Armor Anti-Personnel Weapon System
MIPR	Military Interdepartmental Purchase Request
MIRECC	Mental Illness Research, Education and Clinical Center
MOP	Manual of Operations
MTA	Material Transfer Agreement
mTBI	Mild Traumatic Brain Injury
MTF	Military Treatment Facility
NINDS	National Institute of Neurological Disorders and Stroke
NPC	Non-Profit Corporation
NRAP	National Research Action Plan
NTP	Neurotrauma Portfolio
OASD(HA)	Office of the Assistant Secretary of Defense for Health Affairs
ORCID	Open Researcher and Contributor ID, Inc.
ORP	Office of Research Protections
PH/TBIRP	Psychological Health and Traumatic Brain Injury Research Program
PI	Principal Investigator
PII	Personally Identifiable Information
PTSD	Post-Traumatic Stress Disorder
R&D	Research and Development
RDT&E	Research, Development, Test, and Evaluation
SAM	System for Award Management
SOP	Standard Operating Procedure
SOW	Statement of Work
STEM	Science, Technology, Engineering, and Mathematics
TBI	Traumatic Brain Injury
UDE	Unique Data Element
USAMRAA	U.S. Army Medical Research Acquisition Activity
USAMRMC	U.S. Army Medical Research and Materiel Command
USC	United States Code
VA	Department of Veterans Affairs
VHA	Veterans Health Administration