I. OVERVIEW OF THE FUNDING OPPORTUNITY

Program Announcement for the Department of Defense

Defense Health Program

Congressionally Directed Medical Research Programs

Traumatic Brain Injury and Psychological Health Research Program

Focused Program Award

Announcement Type: Initial

Funding Opportunity Number: HT942524TBIPHRPFPA

Assistance Listing Number: 12.420 Military Medical Research and Development

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-Application (Preproposal) Submission Deadline:** 5:00 p.m. Eastern time (ET), June 27, 2024
- **Invitation to Submit an Application:** August 8, 2024
- **Application Submission Deadline:** 11:59 p.m. ET, October 3, 2024
- **End of Application Verification Period:** 5:00 p.m. ET, October 8, 2024
- **Peer Review:** December 2024
- **Programmatic Review:** February 2025

This program announcement must be read in conjunction with the General Application Instructions, version 901. The General Application Instructions document is available for downloading from the Grants.gov funding opportunity announcement by selecting the "Package" tab, clicking "Preview," and then selecting "Download Instructions."

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II. DETAILED INFORMATION ABOUT THE FUNDING OPPORTUNITY

II.A. Program Description

The U.S. Army Medical Research Acquisition Activity (USAMRAA) is soliciting applications to the fiscal year 2024 (FY24) Traumatic Brain Injury and Psychological Health Research Program (TBIPHRP)using delegated authority provided by United States Code, Title 10, Section 4001 (10 USC 4001). The Congressionally Directed Medical Research Programs (CDMRP) at the U.S. Army Medical Research and Development Command (USAMRDC) is the program management agent for this funding opportunity. In FY07, Congress appropriated funding for traumatic brain injury (TBI) and psychological health research in response to the TBIs sustained and psychological health issues experienced by our deployed forces in Iraq and Afghanistan. The TBIPHRP complements ongoing Department of Defense (DOD) efforts toward promoting a better standard of care for TBI and psychological health in the areas of prevention, detection, diagnosis, treatment, and rehabilitation. Appropriations for the TBIPHRP from FY07 through FY23 totaled $2.40 billion. The FY24 appropriation is $175.0 million (M).

The TBIPHRP's vision is to optimize the prevention, assessment, and treatment of psychological health conditions and/or TBIs. The program seeks to fund research that understands, prevents, and treats psychological health conditions and/or traumatic brain injuries that accelerates solutions to improve the health and heal. ***Proposed research can be aligned with TBI, psychological health, or both in combination.***

II.A.1. FY24 TBIPHRP Focused Program Award (FPA) Focus Areas

To meet the intent of the funding opportunity, applications ***must address at least one sub-area (1a, 1b, 2a, 2b, etc.)*** within one of the three FY24 TBIPHRP FPA Focus Areas listed below. Bulleted items are provided in Appendix 3 to indicate additional context regarding programmatic intent but are not required to be specifically addressed by applications. ***Proposed research must be hypothesis driven and can be aligned with TBI, psychological health, or in combination.*** Applications consisting solely or primarily of planning, engineering, manufacturing, or formulation activities may be administratively withdrawn. Selection of the appropriate FY24 TBIPHRP FPA Focus Area(s) is the responsibility of the applicant.

Inclusion of classified research data within the application and/or proposing research of which the anticipated outcomes may be classified or deemed sensitive to national security concerns may result in application withdrawal. This includes, but is not limited to, research involving directed energy (e.g., photonic, radio frequency, acoustic energy, other non-kinetic sources), Anomalous Health Incidents, Havana Syndrome, and associated neurological syndromes/injuries. Refer to the General Submission Instructions Appendix 2, Section E.

1. **Understand:** Research will address knowledge gaps in epidemiology and etiology of psychological health conditions and/or TBI.

    a. Understanding of risk, protective, and biological factors contributing to an individual's vulnerability to, response to, and long-term outcomes of psychological health conditions and/or TBI.

    b. Understanding psychological health factors or outcomes associated with sexual harassment and assault perpetration, victimization, barriers to reporting and response. Studies that ensure participant anonymity are strongly encouraged.

2. **Prevent and Assess:** Research will address the prevention, screening, diagnosis, or prognosis of psychological health conditions and/or TBI.

    a. Identification and validation of biomarkers or other objective methods for assessment, diagnosis, prognosis, or real-time monitoring of psychological health conditions and/or TBI (including subclinical presentations) and associated sequelae of these conditions.

        – Development of decision-making frameworks or tools that incorporate objective assessments and may consider long-term outcomes to inform return to activity/duty decisions are within scope.

    b. Development and evaluation of approaches or tools to prevent or reduce risk of psychological health conditions and/or TBI.

    c. Development and evaluation of crosscutting prevention approaches[1] to address multiple adverse outcomes such as suicide, interpersonal violence (including intimate partner and family violence), and psychological health issues are within scope.

    d. Development and evaluation of solutions to support military and family readiness[2] and increase psychological resilience in individuals to the potential negative impacts of specific military and life stressors.

[1] Crosscutting prevention approaches refer to strategies that enhance protective factors and reduce risk factors at multiple socio-ecological levels (e.g., individual, relationship, and community). https://www.sapr.mil/sites/default/files/PPoA_2.0.pdf

[2] Military readiness is the ability of military forces to fight and meet the demands of assigned missions. Family readiness is the state of being prepared to effectively navigate the challenges of daily living experienced in the unique context of military service. https://www.tradoc.army.mil/wp-content/uploads/2020/10/AD1029823-DOD-Dictionary-of-Military-and-Associated-Terms-2017.pdf

3. **Treat:** Research will address novel and repurposed interventions[3] to improve outcomes of psychological health conditions and/or TBI. Efforts that address treatment, rehabilitation, and health services research are within scope.

    a. Interventions that promote sustained functional recovery, including interventions administered acutely, during the post-acute phase, or during the chronic phase of injury.

    b. Development of postvention[4] strategies to support individuals in workplace or community environments following a sexual assault, suicide event, or other trauma.

    c. Health services research to improve provider adoption of evidence-based practices, improve access, and reduce barriers. In addition, factors that influence treatment engagement, follow-up care, and improvement of long-term outcomes are of interest.

II.A.2. Award History

The TBIPHRP FPA was first offered in FY21. Since then, 60 FPA applications have been received, and 11 have been recommended for funding.

II.B. Award Information

The intent of the FY24 TBIPHRP FPA is to accelerate the development of solutions to critical question(s) related to at least one sub-area within one of the three FY24 TBIPHRP FPA Focus Areas. The award mechanism supports execution of a synergistic, multidisciplinary research program with the potential to have a significant impact on psychological health conditions and/or TBI through clinical applications, including health care products, technologies, and/or practice guidelines. Applications may propose applied/preclinical/clinical research (including clinical trials). Hypothesis-driven health services research, implementation science, and follow-up care research are also within scope for this mechanism.

Key aspects of the FY24 TBIPHRP FPA include:

- **Overarching Challenge:** FPA applications must describe a unifying, overarching challenge that will be addressed by the set of research projects proposed. The overarching challenge must be relevant to a critical problem or question in the field of research and/or patient care in at least one sub-area within one of the three FY24 TBIPHRP FPA Focus Areas.

- **Research Projects:** Applications shall include multiple, distinct research projects led by individual project leaders that address complementary aspects of the overarching challenge. Applicants are required to ***submit three to five research projects, of which, a clinical research/trial project is strongly encouraged***. While individual projects must be capable of standing on their own high scientific merits, they must also be interrelated, synergistic, and align with the overarching challenge to advance a solution beyond what would be possible

[3] Intervention repurposing is the identification of novel indication(s) for a Food and Drug Administration-approved intervention.

[4] For the TBIPHRP, "postvention" is defined the response to and care for individuals affected in the aftermath of a sexual assault, suicide event, or other trauma" (adapted from U.S. Department of Health and Human Services Office of the Surgeon General and National Action Alliance for Suicide Prevention, 2010, p. 141).

through individual efforts. The exploration of multiple hypotheses or viewpoints of the same line of questioning is encouraged. ***This award mechanism is <u>not</u> intended to support a series of research projects that are dependent on the success of one of the other projects.*** Each project should propose a unique approach to addressing the overarching challenge and be capable of producing research findings with potential to impact the field and/or patient care. ***Individual research projects may include applied research, preclinical research, clinical research, and clinical trials. Proposed research projects must not include basic research.***[5] Preliminary data must be included to support each project's hypothesis/objective(s). There should be a clear intent to progress toward translational/clinical work over the course of the effort.

- **Implementation:** The research strategy to address the overarching challenge must be supported by a detailed implementation plan that identifies critical milestones and outlines the knowledge, resources, and technical innovations that will be utilized to achieve the milestones. A robust statistical plan and statistical expertise should be included where applicable. A plan for assessing individual project performance and progress toward addressing the overarching challenge must be included in the implementation plan. Plans to include an External Advisory Board (EAB) are encouraged; however, applicants must be careful to avoid potential conflicts of interest (COIs) during review of the application by ensuring no contact with, recruiting of, or naming of specific EAB members in the application. For multi-institutional collaborations, plans for communication and data transfer among the collaborating institutions, as well as how data, specimens, and/or products obtained during the study will be handled, must be included. An appropriate intellectual and material property plan agreed to by participating organizations is required in the application's supporting documentation.

- **Research Team:** The overall effort will be led by a Principal Investigator (PI) with demonstrated success in leading large, focused collaborative projects. The PI is required to devote a minimum of 20% effort to this award. The PI should create an environment that fosters and supports collaboration and innovation in a way that engages all members of the team in all aspects of the research plan. The research team assembled by the PI should be highly qualified and multidisciplinary, with identified project leaders for each of the complementary and synergistic research projects. The resources and expertise brought to the team by each project leader should combine to create a robust, synergistic collaboration. The TBIPHRP Science Officer assigned to a resulting award should be invited to participate in research team meetings (e.g., annual meetings of the entire research team). The plan for such meetings should be noted in the application.

- **Milestone Meeting:** The PI will be required to present an update on progress toward accomplishing the goals of the award at a Milestone Meeting after the conclusion of year 2 of the period of performance. This virtual meeting will be attended by members of the TBIPHRP Programmatic Panel, CDMRP staff, the USAMRAA Grants/Contracts Officer, and other DOD stakeholders.

[5] Basic research is defined as research directed toward greater knowledge or understanding of the fundamental aspects of phenomena and of observable facts without specific applications toward process or products in mind.

Clinical trials may be designed to evaluate promising new products, pharmacologic agents (drugs or biologics), diagnostics, devices, therapies, clinical guidance, behavioral interventions, emerging approaches and technologies, and/or new indications for products currently U.S. Food and Drug Administration (FDA)-approved or -cleared. Proposed clinical trials should demonstrate feasibility or inform the design of more advanced trials that determine efficacy in relevant patient populations. For more information, a Human Subject Resource Document is provided at https://cdmrp.health.mil/pubs/pdf/Human%20Subjects%20Resource%20Document_DEC2022.pdf.

Research Scope: Applications to the FY24 TBIPHRP FPA may include preclinical applied research (including animal research), clinical research, and clinical trials/testing (or equivalent). The FY24 TBIPHRP ERA may also support ancillary studies that are associated with an ongoing or completed clinical trial and projects that optimize the design of future clinical trials. This award may not be used to support studies requiring an exception from informed consent (EFIC).

A clinical trial is defined in the Code of Federal Regulations, Title 45, Part 46.102 (45 CFR 46.102) as a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include a placebo or another control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.

Studies that do not seek to measure safety, effectiveness, and/or efficacy outcome(s) of an intervention are not considered clinical trials. For more information, a Human Subject Resource Document is provided at https://cdmrp.health.mil/pubs/pdf/Human%20Subjects%20Resource%20Document.pdf.

For the purposes of this funding opportunity, research that meets the definition of a clinical trial is distinct from clinical research. Clinical research encompasses research with human data, human specimens, and/or interaction with human subjects. Clinical research is observational in nature and includes:

(1) Research conducted with human subjects and/or material of human origin such as data, specimens, and cognitive phenomena for which an investigator (or co-investigator) does ***not*** seek to assess the safety, effectiveness, and/or efficacy outcomes of an intervention. Research meeting this definition may include but is not limited to: (a) mechanisms of human disease, (b) diagnostic or detection studies (e.g., biomarker or imaging), (c) health disparity studies, and (d) development of new technologies.

(2) Epidemiologic and behavioral studies that do ***not*** seek to assess the safety, effectiveness, and/or efficacy outcomes of an intervention.

(3) Outcomes research and health services research that do not fit under the definition of clinical trial.

Excluded from the definition of clinical research are in vitro studies that utilize human data or specimens that cannot be linked to a living individual and meet the requirements for exemption under §46.104(d)(4) of the Common Rule.

Clinical Trials Requirements: Applications that include a clinical trial as part of the proposed research will have additional submission requirements and review criteria. For more information, see Section II.D.2, Content and Form of the Application Submission and Section II.E.1, Criteria. Funded clinical trials are required to post a copy of the informed consent form used to enroll subjects on a publicly available federal website in accordance with federal requirements described in 32 CFR 219.

This award may not be used to support studies requiring an exception from informed consent (EFIC).

Multi-Institutional Clinical Research/Trials: As of January 20, 2020, U.S. institutions engaged in non-exempt cooperative research ***must*** rely on a single Institutional Review Board (IRB) to review and approve the portion of the research conducted at domestic sites (45 CFR 46.114(b)). If the proposed, non-exempt research involves more than one U.S.-based institution, a written plan for single IRB review arrangements must be provided at the time of application submission or award negotiation. The lead institution responsible for developing the master protocol and master consent form should be identified and should be the single point of contact for regulatory submissions and requirements.

Communication and data transfer between or among the collaborating institutions, as well as how specimens and/or imaging products obtained during the study will be handled, should be included in the appropriate sections of the application. A separate intellectual and material property plan agreed on by all participating institutions is also required for multi-institutional clinical research/trials.

Rigor of Preclinical Research Design: All projects should adhere to a core set of standards for rigorous study design and reporting to maximize the reproducibility and translational potential of preclinical research. The standards are described in SC Landis et al., 2012, A call for transparent reporting to optimize the predictive value of preclinical research, *Nature* 490:187-191 (www.nature.com/nature/journal/v490/n7419/full/nature11556.html). While these standards are written for preclinical studies, the basic principles of randomization, blinding, sample-size estimation, and data handling derive from well-established best practices in clinical studies. Projects that include research on animal models should describe how these standards will be addressed as part of their Research Plan (part of Attachment 1, Project Narrative). Applicants should consult the ARRIVE guidelines 2.0 (Animal Research: Reporting *In Vivo* Experiments) to ensure relevant aspects of rigorous animal research are adequately planned for and, ultimately, reported. The ARRIVE guidelines 2.0 can be found at https://arriveguidelines.org/arrive-guidelines.

If animal models are proposed, consider the following:

- Pairing clinical populations to animal models in order to validate the clinical relevance and development of prevention, assessment, and treatment solutions is encouraged.
- Proposed animal models should be well justified, supported within the literature, and clearly align with clinical relevance to the human condition.

Relevance to Military Health: Relevance to the health care needs of Service Members, their Families, and Veterans is a key feature of this award. Investigators are encouraged to consider the following characteristics as examples of how a project may demonstrate relevance to military health:

- Explanation of how the project addresses an aspect of psychological health conditions and/or TBI that has direct relevance to the health and/or readiness Service Members, their Families, and Veterans.
- Description of how the knowledge, information, products, or technologies gained from the proposed research could be implemented in a dual-use capacity to benefit the civilian population and also address a military need.
- Use of military or Veteran populations, samples, or datasets in the proposed research, if appropriate.

Collaborations between researchers or consultants at military or Veterans organizations and non-military organizations are encouraged. These relationships can leverage knowledge, infrastructure, and access to unique data and research resources that the partners bring to the research effort, ultimately advancing TBI and psychological health research of significance to Service Members, their Families, and Veterans. A list of websites that may be useful in identifying additional information about ongoing DOD and VA areas of research interest or potential opportunities for collaboration can be found in Appendix 2.

Conducting DOD-Funded Human Research with Military Populations: There are unique requirements and prohibitions for compensating DOD-affiliated personnel for study participation and for conducting research with military families/children and U.S. Army Special Operations Command populations. Additional information regarding conducting DOD-funded human research with military populations can be found at https://cdmrp.health.mil/pubs/pdf/Conducting%20Research%20Military%20Pop%20DoD_funded_7NOV2022.pdf.

Use of DOD or VA Resources: If the proposed research involves access to VA or DOD patient populations, resources, or databases, the application must describe the access at the time of submission and include a plan for maintaining access as needed throughout the proposed research. Refer to Section II.D.2.b.ii, Full Application Submission Components, for detailed information. Refer to the General Submission Instructions, Appendix 1, Section C, for additional information. ***Note, the CDMRP will not serve as the government sponsor or signatory on any access applications or agreements for DOD or VA patient populations, resources, or databases.***

Nuclear Medicine: Innovative research involving nuclear medicine and related techniques to support early diagnosis, more effective treatment, and improved health outcomes of Service Members and their Families is encouraged. Such research could improve diagnostic and targeted treatment capabilities through noninvasive techniques and may drive the development of precision imaging and advanced targeted therapies.

Women's Health: The CDMRP encourages research on health areas and conditions that affect women uniquely, disproportionately, or differently from men, including studies analyzing sex as

a biological variable. Such research should relate anticipated project findings to improvements in women's health outcomes and/or advancing knowledge for women's health.

Optimizing Research Impact Through Community Collaboration: Research funded by the FY24 TBIPHRP should be responsive to the psychological health conditions and/or TBI needs of the lived experience/consumer, family, and care provider communities. Through the establishment and utilization of effective and equitable collaborations and partnerships, the translational and impact potential of the proposed research can be maximized. ***For the FY24 TBIPHRP FPA, inclusion of Community-Based Participatory Research (CBPR) approaches is required***. The inclusion of CBPR can be documented in Attachment 8, CBPR Documentation.

CBPR supports collaborative research that involves scientific researchers and community members working together to address diseases and conditions, particularly those that disproportionately affect health disparity populations. Recognizing the strength of each partner, scientific researchers and community members ***collaborate and contribute equitably their expertise on all aspects of the project, which may include a needs assessment, planning, research intervention design, implementation, evaluation, and dissemination***. CBPR features shared responsibility for and ownership of the research project, and the research results are jointly interpreted, disseminated, and fed back to affected communities and may be translated into interventions or policy. CBPR methods are critically important for community-level interventions and conditions affecting health disparity populations. CBPR methods, such as collaborative planning, data collection, analysis/interpretation, dissemination and implementation, actively engage consumers and communities in research. These interactions can accelerate "bench to bedside" translation and augment the potential impact of research on people living with psychological health conditions and/or TBI.

CBPR collaborative relationships are often established through integrating community members into research teams as co-researchers, advisors, and consultants. Some examples of CBPR collaborations include:

- Lived Experience Consultants/Consumers: The research team includes at least one member with lived psychological health conditions and/or TBI experience who will provide advice and consultation throughout the planning and implementation of the research project. Lived Experience Consultants (LECs) may include individuals with a TBI or psychological health condition, their family members, or care partners. Ideally an LEC should an individual(s) nominated by a foundation or advocacy group in order to represent the diversity of those with TBI or psychological health conditions vs. individual experiences.

- Partnership with a community-based organization: The research team establishes partnerships with at least one community-based organization that provides advice and consultation throughout planning and implementation of the research project. Community-based organizations may include advocacy groups, service providers, policymakers, or other formal organizational stakeholders.

- Community Advisory Board (CAB): A CAB is composed of multiple community stakeholders and can take many forms, from a board of LECs to a coalition of community-based organizations or any combination thereof. As with LEC and organizational partners,

the CAB provides advice and consultation throughout planning and implementation of the research project.

Additional information on CBPR can be found here:

- Chung B, Jones L, Dixon EL, et al. 2010. Using a community partnered participatory research approach to implement a randomized controlled trial: Planning the design of community partners in care. *Journal of Health Care for the Poor and Underserved* 21(3):780-795. doi: 10.1353/hpu.0.0345.

- Wallerstein N and Duran B. 2010. Community-based participatory research contributions to intervention research: The intersection of science and practice to improve health equity. *American Journal of Public Health* 100(S1):S40-S46. doi: 10.2105/AJPH.2009.184036.

- Patient-Centered Outcomes Research Institute's Engagement Tool and Resource Repository, https://www.pcori.org/engagement/engagement-resources/Engagement-Tool-Resource-Repository

- Toolkit to Better Understand and Measure Stakeholder Engagement, https://icdr.acl.gov/resources/reports/getting-most-out-stakeholder-engagement-toolkit-better-understand-and-measure.

Data Sharing Requirement for Traumatic Brain Injury or Psychological Health Human Subjects Research: The CDMRP intends that information, data, and research resources generated under this funding opportunity will be made available to the research community (including both the scientific and consumer advocacy communities) and the public at large. Note that the CDMRP will not serve as the government sponsor or signatory on any data-sharing agreements. For additional guidance, refer to the General Application Instructions, Appendix 2, Section L.

- **All Prospective Human Subject Research**

    - Applicants ***must*** include language in informed consent documents to allow for submission of de-identified data to a repository or for secondary use/meta-analyses of the data.

    - Applicants are also strongly encouraged to include language in consent forms to enable optional passive follow-up via electronic health record.

    - ***The TBIPHRP requires applicants to incorporate Common Data Elements (CDEs) appropriate to each field of study*** such as the PhenX Core and Specialty collections and National Institute of Neurological Disorders and Stroke (NINDS) TBI CDEs. ***Justification is required*** if CDEs are not utilized.

    - As applicable, applicants are strongly encouraged to include secondary outcomes in proposed studies to address potential crosscutting impacts.

- As appropriate, the inclusion of TBI, psychological health, and caregiver/family outcomes measures is encouraged, regardless of the primary focus of the study.

- **Psychological Health Research**

  - The TBIPHRP requires that all psychological health-related clinical research data with at least 50 subjects funded by this program be shared through the National Institute of Mental Health (NIMH) Data Archive (NDA). The NDA provides an infrastructure for sharing research data, tools, methods, and analyses enabling collaborative science and discovery. The NDA mission is to accelerate scientific research and discovery through data sharing, data harmonization, and the reporting of research results. Consult the NDA website at https://nda.nih.gov/ for additional information.

  - While there is no direct charge to users of the NDA, a project estimation tool is available to help estimate costs and manpower needs that may be associated with data submission.

- **Traumatic Brain Injury Research**

  - The TBIPHRP requires that all TBI-related clinical research data with at least 50 subjects funded by this program be shared through the jointly supported DOD-National Institutes of Health (NIH) Federal Interagency TBI Research Information System (FITBIR). Recipients will be required to upload study data annually and in accordance with the FITBIR data submission policies. There is no fee to use FITBIR, and detailed guidance and policies, including a cost estimator tool for budgeting considerations, can be found at https://fitbir.nih.gov.

  - While there is no direct charge to users of the FITBIR Informatics System, a project estimation tool is available to help estimate costs and manpower needs that may be associated with data submission.

- **Traumatic Brain Injury Research and Psychological Health Research**

  - Applicants proposing to conduct research collecting both TBI and psychological health human subject data may follow the requirements for either TBI research, psychological health research, or both as appropriate. Applicants should justify their choice.

The types of awards made under the program announcement will be assistance agreements. An assistance agreement can take the form of a grant or cooperative agreement. The level of involvement on the part of the CDMRP during the project's period of performance is the key factor in determining whether to award a grant or cooperative agreement. If "no substantial involvement" on the part of the CDMRP is anticipated, a grant will be made (31 USC 6304). Conversely, if "substantial involvement" on the part of the CDMRP is anticipated, a cooperative agreement will be made (31 USC 6305). Substantial involvement means that, after award, CDMRP staff will assist, guide, coordinate, or participate in project activities including but not limited to:

- Make recommendations for continued funding based on (a) overall study progress, including sufficient patient and/or data accrual and/or (b) maintenance of a high quality of research.

The award type, along with the start date, will be determined during the negotiation process.

The anticipated direct costs budgeted for the entire period of performance for an FY24 TBIPHRP FPA should not exceed **$5.0M**. Refer to Section II.D.5, Funding Restrictions, for detailed funding information.

Awards supported with FY24 funds will be made no later than September 30, 2025.

The CDMRP expects to allot approximately $46.5M to fund approximately six FPA applications. Funding of applications received is contingent upon the availability of federal funds for this program, the number of applications received, the quality and merit of the applications as evaluated by peer and programmatic review, and the requirements of the government. Funds to be obligated on any award resulting from this funding opportunity will be available for use for a limited time period based on the fiscal year of the funds. It is anticipated that awards made from this FY24 funding opportunity will be funded with FY24 funds, which will expire for use on September 30, 2030.

II.C. Eligibility Information

II.C.1. Eligible Applicants

II.C.1.a. Organization: Extramural and Intramural organizations are eligible to apply, including foreign or domestic organizations, for-profit and non-profit organizations, and public entities.

Extramural Organization: An eligible non-DOD organization. Examples of extramural organizations include academic institutions, biotechnology companies, foundations, federal government organizations other than the DOD (i.e., intragovernmental organizations), and research institutes.

Intramural DOD Organization: Refers specifically to DOD organizations including DOD laboratories, DOD military treatment facilities, and/or DOD activities embedded within a civilian medical center.

Awards are made to eligible ***organizations***, not to individuals. Refer to the General Application Instructions, Appendix 1, for additional recipient qualification requirements.

II.C.1.b. Principal Investigator

Principal Investigator: Independent investigators at all academic/career levels (or equivalent) may be named by organizations as the PI on the application. For titles outside of academia that may not be analogous to traditional hierarchies, investigators at or above an independent scientist level may be named by their organization as the PI on the application. ***Postdoctoral fellows are not considered independent investigators.***

- Project leaders for each of the complementary and synergistic research projects must be independent investigators.

- The PI is required to devote a minimum of 20% effort to this award.

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

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 to fulfill the financial and technical deliverable requirements of the award and submit invoices for payment.

Refer to Section II.H.2, Administrative Actions, for a list of administrative actions that may be taken if a pre-application or full application does not meet the administrative, eligibility, or ethical requirements defined in this program announcement.

II.D. Application and Submission Information

II.D.1. Location of Application Package

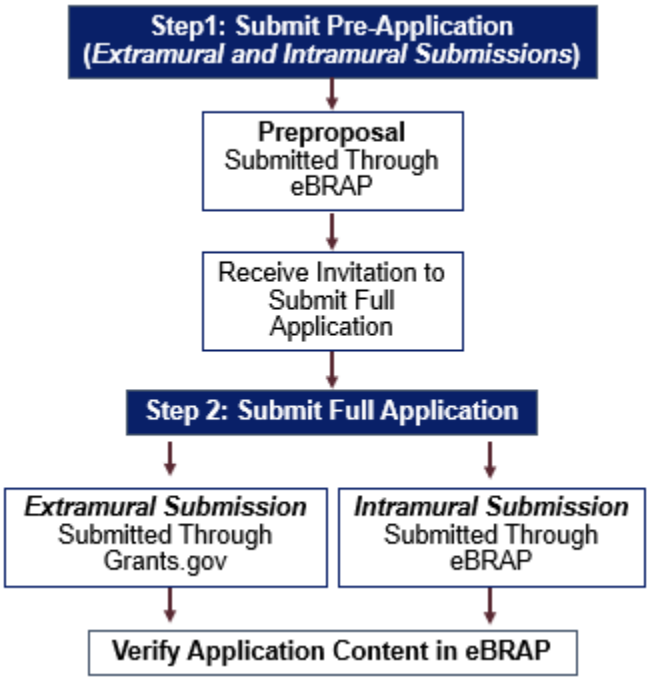
Submission is a two-step process requiring both a ***pre-application*** submitted via the Electronic Biomedical Research Application Portal (eBRAP.org) and a ***full application*** (eBRAP.org or Grants.gov). Depending on the type of submission (i.e., extramural vs. intramural), certain aspects of the submission process will differ.

The CDMRP uses two portal systems to accept pre- and full application submissions.

eBRAP (https://ebrap.org) is a secure web-based system that allows PIs and/or organizational representatives from both extra- and intramural organizations to receive communications from the CDMRP and submit their pre-applications. Additionally, eBRAP allows extramural applicants to view and verify full applications submitted to Grants.gov and allows intramural DOD applicants to submit and verify full applications following their pre-application submission.

Grants.gov (https://grants.gov) is a federal system that must be used by funding agencies to announce extramural grant applications. Full applications for CDMRP funding opportunities can only be submitted to Grants.gov after submission of a pre-application through eBRAP.

Application Submission Workflow



Extramural Submission: An application submitted by an extramural organization for an extramural or intramural PI working within an extramural or intramural organization. For example, a research foundation submitting an application for a DOD employee working within a DOD organization would be considered an extramural submission and should follow instructions specific to extramural submissions. Download application package components for HT942524TBIPHRPFPA from Grants.gov (https://grants.gov). Full applications from extramural organizations ***must*** be submitted through Grants.gov.

Intramural Submission: An application submitted by an intramural DOD organization for an investigator employed by that organization. Intramural DOD organizations may submit full applications to either eBRAP or Grants.gov. Download application package components for HT942524 TBIPHRPFPA from the anticipated submission portal eBRAP (https://ebrap.org) or Grants.gov.

The submission process should be started early to avoid missing deadlines. Regardless of submission type or portal used, all pre- and full application components must be submitted by the deadlines stipulated on the first page of this program announcement. There are no grace periods for deadlines; failure to meet submission deadlines will result in application rejection. ***The USAMRAA cannot make allowances/exceptions for submission problems encountered by the applicant organization using system-to-system interfaces with Grants.gov.***

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

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

Unnecessary duplication of funding or accepting funding from more than one source for the same research, is prohibited. See the CDMRP's full position on research duplication at https://cdmrp.health.mil/funding/researchDup.

Including classified research data within the application and/or proposing research that may produce classified outcomes, or outcomes deemed sensitive to national security concerns, may result in application withdrawal. Refer to the General Application Instructions, Appendix 7, Section B.

FY24 TBIPHRP Programmatic Panel members should not be involved in any pre-application or full application. For questions related to panel members and pre-applications or applications, refer to Section II.H.2.c, Withdrawal, or contact the eBRAP Help Desk at help@eBRAP.org or 301-682-5507.

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

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

During the pre-application process, eBRAP assigns each submission a unique log number. This unique log number is required during the full application submission process. The eBRAP log number, application title, 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 eBRAP Help Desk at help@eBRAP.org or 301-682-5507 prior to the application submission deadline.

No change in PI will be allowed after the pre-application deadline. If any other changes are necessary after submission of the pre-application, the PI must contact the eBRAP Help Desk at help@eBRAP.org or 301-682-5507.

II.D.2.a.i. Pre-Application Components

Pre-application submissions must include the following components (refer to the General Application Instructions, Section III.B, for additional information on pre-application submission):

Note: Upload documents as individual PDF files unless otherwise noted.

- **Preproposal Narrative (four-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:

- **Focus Area:** Describe how the proposed research program is relevant to the selected sub-area(s) within one of the three FY24 TBIPHRP FPA Focus Areas.

- **Overarching Challenge:** Describe the unifying challenge or question to be addressed and how it is relevant to a critical problem or question in psychological health conditions and/or TBI research and/or patient care. Clearly articulate the scientific rationale for the overarching challenge, including relevant preliminary data and literature citations.

- **Specific Aims and Study Design:** The FY24 TBIPHRP FPA requires three to five individual but complementary research projects addressing the overarching challenge. ***The inclusion of a clinical research/trial project is strongly encouraged***. For each proposed project, state the hypothesis to be tested, the specific aims, and the objectives to be reached. Specific aims should be independent and not depend on the successful completion of prior aims or other research projects. Briefly describe the experimental approach. Describe how the projects are interrelated, synergistic, and align with the overarching challenge to advance a solution beyond what would be possible through individual efforts. If applicable, identify the availability of and accessibility to the research resources and subject population.

- **Research Team:** Briefly describe the composition, expertise, and organization of the research team. Identify the project leaders and describe their role in and commitment to the projects, with additional emphasis on the leadership role and commitment of the PI. Briefly describe how these features will facilitate the success of the key aspects of the projects.

- **Impact and Relevance to Military Health:** Describe the potential near-term and long-term impact of the proposed research on a critical problem or question in psychological health and/or TBI. Explain how the effort is relevant to the health care needs of Service Members, their Families, and/or Veterans.

- **Clinical Trial (if applicable):** If one or more of the proposed research projects includes a clinical trial, briefly state the clinical intervention(s), subject population(s), and the type and phase of the clinical trial(s). Describe the objectives of the proposed clinical trial(s), how it addresses the overarching challenge, and how it complements the other projects. As applicable, provide the regulatory status (including device classification) and identify the regulatory sponsor.

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

  - **References Cited (one-page limit):** List the references cited (including URLs if available) in the Preproposal Narrative using a standard reference format that includes the full citation (i.e., author[s], year published, reference title, and reference source, including volume, chapter, page numbers, and publisher, as appropriate).

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

- **Key Personnel Biographical Sketches (six-page limit per individual):** ***All biographical sketches should be uploaded as a single combined file.*** Biographical sketches should be used to demonstrate background and expertise through education, positions, publications, and previous work accomplished.

II.D.2.a.ii. Pre-Application Screening Criteria

To determine the technical merits of the pre-application and the relevance to the mission of the Defense Health Program (DHP) and the TBIPHRP, pre-applications will be screened based on the following criteria:

- **Focus Area:** The degree to which the proposed research program is relevant to the selected sub-area(s) within one of the three FY24 TBIPHRP FPA Focus Areas.

- **Overarching Challenge:** How well the unifying challenge or question addresses a critical problem or question in psychological health conditions and/or TBI research and/or patient care. How well the scientific rationale supports the overarching challenge.

- **Specific Aims and Study Design:** How well a hypothesis and specific aims are defined for each proposed project and to what extent each project's approach will address them. How well the proposed projects complement each other and synergistically address the overarching challenge to advance a solution beyond what would be possible through individual efforts. If applicable, to what extent the availability of and accessibility to the research resources and subject population will support successful completion of the research.

- **Research Team:** To what degree the composition, expertise, and commitment of the PI and project leaders are appropriate with respect to their abilities to successfully complete the projects and the extent to which the PI is prepared and committed to lead the research team and proposed projects.

- **Impact and Relevance to Military Health:** Whether the proposed research will have a potential near-term and long-term impact on a critical problem or question in psychological health and/or TBI. To what degree the project is relevant to the health care needs of Service Members, their Families, and/or Veterans.

- **Clinical Trial (if applicable):** How well the objectives of the proposed clinical trial(s) address the overarching challenge and complement the other projects.

II.D.2.a.iii. Notification of Pre-Application Screening Results

Following the pre-application screening, PIs will be notified as to whether they are invited to submit full applications. The estimated date when PIs can expect to receive notification of an invitation to submit a full application is indicated in Section I, Overview of the Funding Opportunity. No feedback (e.g., a critique of the pre-application's strengths and weaknesses) is provided at this stage. Because the invitation to submit a full application is based on the contents

of the pre-application, investigators should not change the title or research objectives after the pre-application is submitted.

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

Applicants must receive an invitation to submit a full application. Uninvited full application submissions will be rejected.

II.D.2.b.i. Full Application Submission Type

Extramural Submissions: Full applications from extramural organizations ***must*** be submitted through Grants.gov Workspace. Full applications from extramural organizations, including non-DOD federal organizations, received through eBRAP will be withdrawn. Refer to the General Application Instructions, Section IV, for considerations and detailed instructions regarding extramural full application submission.

Intramural Submissions: Intramural DOD organizations may submit full applications through either eBRAP or Grants.gov. There is no preference from the CDMRP for which submission portal is utilized; submission through one portal or the other does not provide the application any advantage during the review process. Intramural DOD organizations that choose to submit through Grants.gov should follow Extramural Submission instructions. Intramural DOD organizations that are unable to submit through Grants.gov should submit through eBRAP. For the remainder of this program announcement, it will be assumed intramural DOD submissions will proceed through eBRAP. Refer to the General Application Instructions, Section V, for considerations and detailed instructions regarding intramural DOD full application submission.

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

Each application submission must include the completed full application package for this program announcement. See Section II.H.3 of this program announcement for a checklist of the required application components.

(a) SF424 Research & Related Application for Federal Assistance Form *(Extramural Submissions Only)*: Refer to the General Application Instructions, Section IV.B, for detailed information.

(b) 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 2.

- **Attachment 1: Project Narrative (40-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 (uniform resource locators) that provide additional information that expands 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.

Overall Program: Provide a description of the comprehensive effort using the following outline. Applicants are required to submit three to five research projects. ***The inclusion of a clinical research/trial project is strongly encouraged***. Emphasize areas of synergy throughout the narrative.

- **Overarching Challenge:** Describe the unifying, overarching challenge or question to be addressed and how it is relevant to a critical problem or question in psychological health conditions and/or TBI research and/or patient care. Describe how the proposed research addresses the selected sub-area(s) within one of the three FY24 TBIPHRP FPA Focus Areas. Clearly articulate the rationale for the overarching challenge, including relevant literature citations. Clearly describe how the proposed research projects are not dependent upon each other but are interrelated and synergistic and will advance toward a solution through a multidisciplinary research program. Describe how each project will address the overarching challenge in a unique but complementary way and how the combined efforts of the projects will address the overarching challenge more effectively than if the projects were conducted independently. Describe how the proposed program aligns with the intent of the mechanism.

- **Leadership:** Describe how the PI's research experience, leadership skills, and commitment to making an impact in psychological health and/or TBI research and patient care demonstrates substantial qualifications to coordinate this collaborative effort. Describe the PI's demonstrated success in leading large, focused collaborative projects and how it will contribute to achieving the overarching goal(s) of the proposed effort. Outline the PI's responsibilities during the conduct of the proposed research effort. ***Note that these responsibilities should align with the minimum 20% PI effort required for this award.*** Discuss the qualifications of the research team being brought together by the PI and how the assembled expertise will create a robust, synergistic collaboration necessary to address the overarching challenge and enable the success of the proposed research.

- **Implementation Plan:** Provide a detailed strategic implementation plan for completing the proposed projects that identifies critical milestones and explain how these milestones will be achieved. Outline the knowledge, expertise, and technical innovations that the investigative team will utilize to make decisions, allocate resources, and accomplish the milestones. Describe how CBPR/ stakeholder engagement will make meaningful contributions to the success of the overall program. ***Full details of the CBPR approach are required for all applications and should be provided in Attachment 8.*** Describe and/or provide evidence that the research can be initiated without delay once the award is made. Present an overall management plan to facilitate a consistent and intensive flow of ideas and information among all team members, including aspects such as adherence

to regulatory requirements, administrative support, and oversight to accelerate translation of the projects' outcomes to patients and/or for clinical use. Outline shared research resources and/or cores that will be created and/or leveraged throughout the research program. Describe plans for communication, data transfer among the collaborating institutions, and how data, specimens, and/or imaging products obtained during the study will be handled. If applicable, describe how Standard Operating Procedures will be created, reviewed, implemented, and modified during the course of the award. Describe how individual project performance will be assessed during the course of the award, including progression toward defined milestones, realization of study objectives, and addressing the overarching challenge. If an EAB is to be utilized, describe the role of the board and the expertise to be sought in its members. To avoid potential COIs in the review of the proposal/ application, potential candidates for an EAB should not be contacted, recruited, or named during the application process.

- **Data and Research Resources Sharing Plan:** Describe how data or resources generated during the performance of the project will be shared with the research community, including the sharing of de-identified data with repositories. Refer to CDMRP's Policy on Data & Resource Sharing located on the eBRAP "Funding Opportunities & Forms" web page https://ebrap.org/eBRAP/public/Program.htm for more information about CDMRP's expectations for making data and research resources publicly available. NIH-supported Data Repositories can be found at https://www.nlm.nih.gov/NIHbmic/domain_specific_repositories.html.

  - ***For applications involving FITBIR-eligible TBI research:***

    - Identify and describe the planned NINDS TBI CDEs, alignment to FITBIR data elements and forms, and timelines for integrating data to the FITBIR Informatics System. Provide a justification as to why existing CDEs are not applicable or appropriate.

    - Provide a justification as to why existing CDEs are not applicable or appropriate.

    - For applications not using FITBIR, please justify and identify the alternative data-sharing platform.

  - ***For applications involving NIMH NDA-eligible psychological health research:***

    - Identify and describe the planned CDEs appropriate to each field of study, data elements and forms, and timelines for integrating data to the NIMH NDA.

    - Provide a justification as to why existing CDEs are not applicable or appropriate.

    - For applications not using NIMH NDA, please justify and identify the alternative data-sharing platform.

Research Plan: Provide the following details for each proposed research project, organizing each project clearly and separately. ***Start each project on a separate page.***

- **Title:** Provide a title for each project.

- **Project Leader:** Identify the project leader and any key personnel, as appropriate, describing each person's qualifications, specific contributions, and evidence of strong commitment to the project.

- **Background:** For each project, the project leader must describe in detail the scientific rationale for the study and include a literature review, unpublished data, preliminary studies/data, and/or preclinical data that support the development of the proposed project. The background section should clearly support the choice of study variables and should explain the basis for the study questions and/or hypotheses. If proposing translational or clinical research, it is important to describe the project showing proof of concept and, if applicable, efficacy in an in vivo system(s) to support relevance to the intended patient population, translational feasibility, and promise of the approach. ***Full details of the CBPR approach are required for all studies enrolling human subjects and should be provided in Attachment 8.*** Establish the relevance and applicability of the proposed research and findings to the intent of the mechanism and selected sub-area(s) within one of the three FY24 TBIPHRP FPA Focus Areas.

- **Objectives/Specific Aims/Hypothesis:** Provide a description of the purpose and objectives of the study with detailed specific aims and hypotheses. Specific aims should be independent and not depend on the successful completion of prior aims. The aims should align with the associated tasks described in the Statement of Work (SOW; Attachment 5).

- **Environment:** Describe the research environment and the availability of and accessibility to facilities and resources (including patient populations, samples, and collaborative arrangements) that will support the research requirements.

- **Research Strategy and Feasibility:** Describe the experimental design, methods, and analyses in sufficient detail for evaluation and their relevance to the completion of the specific aims. Provide a description of how the study will be controlled and how the study variables will be measured. Explain how the research strategy will address the overarching challenge and meet appropriate milestones. Identify potential problem areas and present alternative methods and approaches to mitigate any risks that are identified. Describe how the proposed project is feasible and will be completed within the proposed performance period.

For research involving animals:

- When the proposed study involves animals, the applicant is required to submit a summary describing the animal research that will be conducted. Applicants should not submit a verbatim replica of the protocol(s) to be submitted to the Institutional Animal Care and Use Committee (IACUC) as the summary. Applicants should

consult the ARRIVE 2.0 guidelines to ensure relevant aspects of rigorous animal research are adequately planned for and, ultimately, reported. The ARRIVE 2.0 guidelines can be found at https://arriveguidelines.org/arrive-guidelines The summary should address the following points for each proposed animal study:

- Briefly describe the research objective(s) of the animal study.
- Provide evidence that the chosen animal model(s) is validated and well justified in the literature. Explain how and why the animal species, strain, and model(s) being used can address the scientific objectives and the relevance to human biology.
    - ❖ Describe approaches that will be undertaken to validate or corroborate findings from animal studies to relevant human data sources/populations. This could include, but is not limited to, validation of animal transcriptomic data using publicly available human transcriptomic datasets, confirmation of histological findings in a human postmortem case series, and validation against fluid-based or imaging biomarkers.
    - ❖ Describe how the proposed validation approaches or corroborative studies "de-risk" the possibility that the findings from the animal study cannot be translated into human populations.
- Summarize the procedures to be conducted. Describe how the study will be controlled.
- Describe the randomization and blinding procedures for the study, and any other measures to be taken to minimize the effects of subjective bias during animal treatment and assessment of results. If randomization and/or blinding will not be utilized, provide justification.
- Describe how data will be handled, including rules for stopping data collection, criteria for inclusion and exclusion of data, how outliers will be defined and handled, statistical methods for data analysis, and identification of the primary endpoint(s).
- Describe how data will be reported and how it will be assured that the documentation will support a regulatory filing with the U.S. Food and Drug Administration (FDA) (or international equivalent) or next stage of development, if applicable.

For research involving human subjects/samples/data:

- Justify how the chosen human subjects/samples/datasets are appropriate for the proposed research project.
- For studies performing retrospective or prospective human subject recruitment or observation, describe the population(s) of interest and how access to the population(s)

or dataset(s) will be achieved; ***full details on human subject recruitment will be required in the Human Subject Recruitment and Safety Procedures (Attachment 10).***

- Describe the availability of the proposed study population and past successes in recruiting similar populations. If active-duty military, military families, and/or Veteran population(s) or datasets will be used in the proposed research project, describe how access to the population(s)/dataset(s) will be obtained.

- If applicable, describe how data will be reported and how it will be assured that the documentation will support a regulatory filing with the FDA (or international equivalent) or next stage of development; ***full details will be required in the Regulatory Strategy (Attachment 12)***.

For clinical trials:

- Provide detailed plans for initiating and conducting the clinical trial during the course of this award.

- As appropriate, state the investigational product regulatory exemption (e.g., FDA IND/IDE or international equivalent) application status or approvals. ***Note that an active investigational product regulatory exemption (e.g., FDA Investigational New Drug [IND]/ Investigational Device Exemption [IDE]) application for the proposed indication has been submitted or authorized (without clinical hold status) OR a statement and associated justification that an investigational product regulatory exemption (e.g., FDA IND/IDE) application for the proposed indication is not required must be in the FY24 TBIPHRP FPA application (full details will be required in the Regulatory Strategy, Attachment 12).***

- Describe the type of clinical trial to be performed (e.g., treatment, prevention, diagnostic), the phase of trial and/or class of device (as appropriate), and the study model (e.g., single group, parallel, crossover). Provide preclinical and/or clinical evidence to support the safety of the intervention.

- Identify the intervention to be tested and describe the projected endpoints/outcomes. Define the primary, secondary, or interim endpoints/outcome measures, why they were chosen, and how and when they will be assessed. If the study design (e.g., selection of outcome measures) was guided by communications/interactions with the FDA or international equivalent, please describe. Outline the timing and procedures planned during the follow-up period.

- Describe the study population, and how the sample population represents the targeted patient population that might benefit from the proposed intervention. Explain the methods that will be used to recruit a sample of human subjects from the accessible population (e.g., convenience, simple random, stratified random); ***full details will be required in the Human Subject Recruitment and Safety Procedures (Attachment 10).***

- Define each arm/study group of the proposed trial, if applicable. Describe the human subject-to-group assignment process (e.g., randomization, block randomization, stratified randomization, age-matched controls, alternating group, or other procedures) and how it meets the needs of the proposed clinical research/trial. Explain the specific actions to accomplish the group assignment (e.g., computer assignment, use of table of random numbers). If multiple site studies are involved, state the approximate number of subjects to be enrolled at each site.

  - Outline the timing and procedures planned during the follow-up period. Estimate the potential for subject loss to follow-up, and how such loss will be handled/ mitigated.

  - Provide evidence to document the availability of and access to all critical reagents, including the intervention itself, if applicable, for the duration of the proposed clinical trial.

  - Describe the composition of the clinical trial team. Provide details on how the team (including investigator(s), study coordinator, and statistician) possesses the appropriate expertise in conducting clinical trials; ***full details will be required in the Study Personnel (Attachment 13).***

- **Statistical Plan:** Describe the statistical model and data analysis plan with respect to the study objectives. Include a complete power analysis (including method by which it was derived) to demonstrate that the sample size is appropriate to meet the objectives of the study and all proposed correlative studies. Ensure sufficient information is provided to allow thorough evaluation of all statistical calculations during review of the application. If applicable, specify the approximate number of human subjects to be enrolled. If multiple study sites are involved, state the approximate number to be enrolled at each site. If a subpopulation of a recruited sample population will be used for analysis, complete a statistical analysis to ensure appropriate power can be achieved within the subpopulation study. For phase 3 clinical trials, describe plans for the valid analysis of group differences on the basis of sex/gender, race, and/or ethnicity as appropriate for the scientific goals of the study.

- **Attachment 2: Supporting Documentation: Combine and upload as a single file named "Support.pdf".** Start each document on a new page. 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.

- **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 government-furnished facilities or equipment are proposed for use. If so, reference should be made to the original or present government award under which the facilities or equipment items are now accountable. There is no form for this information.

- **Publications and/or Patents:** Include a list of relevant publication URLs and/or patent abstracts. If articles are not publicly available, then copies of up to five published manuscripts may be included in Attachment 2. Extra items will not be reviewed.

- **Letters of Organizational Support (three-page limit is recommended):** 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 Commitment (if applicable, two-page limit per letter is recommended):** If the proposed study involves use of a commercially produced investigational drug, device, or biologic, provide a letter of commitment from the commercial entity indicating availability of the product for the duration of the study, support for the proposed phase of research, and support for the indication to be tested.

- **Letters of Collaboration (if applicable, two-page limit per letter is recommended):** 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.

- **Intellectual Property:** Information can be found in the 2 CFR 200.315, "Intangible Property."

  - **Intellectual and Material Property Plan:** Provide a plan for resolving intellectual and material property issues among participating organizations.

- **Data Management Plan (if applicable, two-page limit is recommended):** If a Data Management Plan is provided within Attachment 10, Human Subject Recruitment and Safety Procedures, then submission of the Data Management Plan under "Supporting Documentation" is not required. Describe the data management plan in accordance with Section 3.c, Enclosure 3, DoD Instruction 3200.12. ***Do not***

duplicate the Data and Research Resources Sharing Plan. Refer to General Application Instructions, Section IV.B, Attachments Form, Attachment: Supporting Documentation, for detailed information regarding Data Management Plan content.

- **Use of DOD Resources (if applicable):** Provide a letter of support signed by the lowest-ranking person with approval authority confirming access to active-duty military populations and/or DOD resources or databases.

- **Use of VA Resources (if applicable):** Provide a letter of support signed by 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, confirming access to VA patients, resources, and/or VA research space. If the VA-affiliated non-profit corporation is not identified as the applicant organization for administering the funds, include a letter from the VA ACOS/R&D confirming this arrangement and identifying the institution that will administer the funds associated with the proposed research.

- **Quad Chart:** Provide a Quad Chart for the proposed project. The format for the Quad Chart is available on the eBRAP "Funding Opportunities & Forms" web page at (https://ebrap.org/eBRAP/public/Program.htm)

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

  Technical abstracts must be provided for the overall program, as well as each individual project, with the abstract for each project starting on a separate page. Clarity and completeness within the space limits of the technical abstract are highly important. Describe the proposed research effort of the overall project and each individual project, including the following elements:

  - ***Overarching Challenge:*** Identify the unifying, overarching challenge or question that will be addressed by the research plan and describe how it relates to a critical problem or question in psychological health conditions and/or TBI research and/or patient care.

  - **Background:** Briefly articulate the rationale for the overarching challenge and the proposed research.

  - **Research Plan:** Provide a brief description of the studies proposed, including hypotheses, objectives, specific aims, model system(s)/research participant population(s), and scientific approach. If proposing a clinical trial(s), identify the phase.

  - **Impact:** Briefly describe the potential near-term and long-term impact of the results of the proposed research on psychological health conditions and/or TBI research,

patient care, and the sub-area(s) within one of the three FY24 TBIPHRP FPA Focus Areas to be addressed.

- **Relevance to Military Health:** Explain how the project is relevant to the health care needs of Service Members, their Families, and/or Veterans.

- **Attachment 4: Lay Abstract (one-page limit per abstract): Upload as "LayAbs.pdf".** The lay abstract is used by all reviewers, and addresses issues of particular interest to the affected community. ***Abstracts of all funded research projects will be posted publicly.*** Use only characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed. ***Do not duplicate the technical abstract.***

  Lay abstracts must be provided for the overall program, as well as each individual project, with the abstract for each project starting on a separate page. Lay abstracts should address the points outlined below ***in a manner that will be readily understood by readers without a background in science or medicine***. Avoid overuse use of scientific jargon, acronyms, and abbreviations.

  - Describe how the proposed research program addresses the selected sub-area(s) within one of the three FY24 TBIPHRP FPA Focus Areas.

  - Clearly describe the critical problem or question to be addressed and the ultimate applicability and impact of the research.

  - Describe the CBPR approach and implementation in the study.

  - Include a concise overview of the effort.

- **Attachment 5: Statement of Work (no page limit): Upload as "SOW.pdf".** Refer to the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) for the suggested SOW format and recommended strategies for assembling the SOW.

  For the FY24 TBIPHRP FPA, refer to either the "Example: Assembling a Clinical Research and/or Clinical Trial Statement of Work" or "Example: Assembling a Generic Statement of Work", whichever example is most appropriate for the proposed effort, for guidance on preparing the SOW. Use the "Suggested SOW Format" to develop the SOW for the proposed research. Submit as a PDF.

  The SOW should state the specific aims described in the Project Narrative and include a list of major tasks and subtasks that support the completion of the stated aims, including milestones for completing the aims during 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 following tasks/subtasks:

  - If applicable, cross-mapping of data elements to psychological health conditions and/or TBI CDEs.

- Including language in informed consent documents to allow for submission of de-identified data to a repository or for secondary use/meta-analysis of the data.
- FITBIR- or NIMH NDA-eligible research should also include the following subtasks:
  - investigator and study registration within the first 30 days of the award
  - Sharing of draft data collection forms with FITBIR or NIMH NDA, as applicable
  - Annual data submission

- **Attachment 6: Impact Statement (two-page limit per statement): Upload as "Impact.pdf".** For the overall program and for each individual project, the Impact Statement should be written in a manner that will be ***readily understood by readers without a background in science or medicine.***

  An Impact Statement is required for the overall program as well as for each individual project. The Impact Statement for each project should begin on a new page.

  - Describe how the proposed research will the development of solutions to critical question(s) research in the selected sub-area(s) within the FY24 TBIPHRP FPA Focus Areas and will lead to the development of health care products, technologies, and/or clinical practice guidelines that improve patient outcomes.
    - Describe the anticipated short-term (immediate to 5 years) and long-term (greater than 5 years) impact of the proposed work on research or improved patient care.
  - Describe any potential issues that might limit the impact of the proposed research and provide approaches to overcome.

- **Attachment 7: Relevance to Military Health Statement (two-page limit): Upload as "Military.pdf".** Describe how the proposed effort is responsive to the health care needs of Service Members, their Families, and/or Veterans.
  - If applicable, clearly articulate how the proposed research is likely to enhance readiness and recovery on the battlefield, during training, or in resource-limited environments. ***Note that, per DOD Instruction 6200.02, the DOD preferentially uses medical countermeasures that are approved by the United States Food and Drug Administration.*** Applicants should address this requirement if appropriate.
  - If applicable, describe how the study team composition can provide military-relevant subject matter expertise to the proposed research.
  - If applicable, describe how the proposed research project complements DOD and/or VA areas of research interest and/or patient care for psychological health conditions and/or TBI.

- Provide a description of how the knowledge, information, products, or technologies gained from the research could be implemented in a dual-use capacity to benefit the civilian population and address a military need, as appropriate.

- **Attachment 8: CBPR Documentation (no-page limit): Start each document on a new page. Combine and upload as "CBPR.pdf.**

  - **CBPR Letters of Support (two-page limit per letter is recommended):** Provide a letter signed by each LEC/consumer or community-based partner(s) confirming their role and commitment to participate on the research team. The letter should include the qualifications and background of the LEC(s) or community-based partner(s) and their relevance to the proposed research project.

  - **CBPR Statement (three-page limit is recommended):** Description of the CBPR approach that will be used (e.g., LEC/consumer, partner organization, CAB, co-researcher model) and at what points it will contribute to the research project. Description of the CBPR input that will be captured and how this input will be meaningfully integrated and incorporated into the needs assessment, planning, design, execution, analysis, and dissemination of the research. Include a description of how CBPR effectiveness will be assessed. Description of training that will be provided to both scientific researchers and community members on CBPR approaches, decision-making, and equitable participation. Description of resource allocation, decision-making processes, and authorship between scientific researchers and community partners (whether individuals or organizations). Description of dissemination activities that will share research findings with the stakeholder communities.

- **Attachment 9: Transition Plan (three-page limit): Upload as "Transition.pdf".** Research funded by the TBIPHRP should accelerate the development of tangible or knowledge products that optimize the prevention, assessment, and treatment of psychological health conditions and/or traumatic brain injuries. In the Transition Plan, provide information on the methods and strategies proposed to move the proposed research to the next phases of development or commercialization/clinical use following the successful completion of the proposed effort. ***Articulate this information for the overall effort as well as the individual projects.*** Applicants are encouraged to work with their organization's Technology Transfer Office (or equivalent) to develop the transition plan. The transition plan should include the components listed below, as appropriate.

  For the purposes of this funding opportunity Regulatory Agency refers to the FDA or any relevant international regulatory agency unless otherwise noted.

  - Details of the overall strategy to transition to the research to commercialization or clinical use. Include a description of collaborations and other resources that will be used to provide continuity of development.

  - A brief schedule and milestones for transitioning to a clinical product (even if Regulatory Agency approval/clearance is not needed). This can include the next logical step of preclinical or clinical research, next-phase clinical trials,

commercialization, delivery to the military or civilian market, incorporation into clinical practice, and/or approval by a Regulatory Agency.

- For knowledge products, a description of collaborations and other resources that will be used to provide continuity of development, including proposed development or modification of clinical practice guidelines and recommendations, provider training materials, patient brochures, and other clinical support tools, scientific journal publications, models, simulations, and applications.

  - A "knowledge product" is a non-materiel product that addresses an identified need, topic area, or capability gap; is based on current evidence and research; aims to transition into medical practice, training, or tools or to support materiel solutions (systems to develop, acquire, provide, and sustain medical solutions and capabilities); and educates or impacts behavior throughout the continuum of care, including primary prevention of negative outcomes.

- If applicable, ownership rights and/or access to the intellectual property necessary for the development and/or commercialization of products or technologies supported with this award and the government's ability to access such products or technologies in the future.

- A risk analysis for cost, schedule, manufacturability, and sustainability.

- **Attachment 10: Human Subject Recruitment and Safety Procedures (no page limit): If proposing multiple human subjects research projects, start each Human Subject Recruitment and Safety Procedures on a new page and clearly identify the supported project. Combine and upload as "HumSubProc.pdf".** ***(Attachment 10 is only applicable and required for research recruiting human subjects.)*** As applicable, the Human Subject Recruitment and Safety Procedures attachment should include the components listed below.

  - **Study Population:** Describe the target population (to whom the study findings will be generalized) and the nature, approximate number, and pertinent demographic characteristics of the accessible population at the study site(s) (population from whom the sample will be recruited/drawn). Provide a table of anticipated enrollment counts at each study site. ***Demonstrate that the research team has access to the proposed study population at each site and describe the efforts that will be made to achieve accrual goals.*** Provide justification related to the scientific goals of the proposed study for limiting inclusion of any group by age, race, ethnicity, or sex/gender. ***For clinical research/trials proposing to include military personnel, refer to the General Submission Instructions, Appendix 1, for more information.***

  - **Inclusion/Exclusion Criteria:** List the inclusion and exclusion criteria for the proposed clinical research/trial(s). Describe how the inclusion and exclusion criteria meet the needs of the proposed clinical research/trial(s). 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 Enrollment Plan:** Describe the strategy for the inclusion of women and minorities in the clinical research/trial appropriate to the objectives of the study, including a description of the composition of the proposed study population in terms of sex/gender, race, and ethnicity, and an accompanying rationale for the selection of subjects. Provide an anticipated enrollment table(s) for the inclusion of women and minorities using the Public Health Service (PHS) Inclusion Enrollment Report, a three-page fillable PDF form, that can be downloaded from eBRAP at https://ebrap.org/eBRAP/public/Program.htm. The enrollment table(s) should be appropriate to the objectives of the study with the proposed enrollment distributed on the basis of sex/gender, race, and ethnicity. Studies utilizing human biospecimens or datasets that cannot be linked to a specific individual, gender, ethnicity, or race (typically classified as exempt from IRB review) are exempt from this requirement.

- **Description of the Recruitment Process:** Explain methods for identification of potential human subjects (e.g., medical record review, obtaining sampling lists, health care provider identification). Describe the recruitment process in detail. Address who will identify potential human subjects, who will recruit them, and what methods will be used to recruit them. If human subjects will be compensated for participation in the study, include a detailed description of and justification for the compensation plan. Describe the recruitment and advertisement materials. The recruitment materials should not be coercive or offer undue inducements and should accurately reflect the study. Address any potential barriers to accrual and plans for addressing unanticipated delays, including a mitigation plan for slow or low enrollment or poor retention. Identify ongoing clinical trials that may compete for the same patient population and how they may impact enrollment progress.

- **Description of the Informed Consent Process:** Specifically describe the plan for obtaining informed consent from human subjects (including vulnerable populations). ***This program announcement may not be used to support studies requiring an EFIC.***

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

    - Applicants must include language in informed consent documents to allow for submission of de-identified data to a repository or for secondary use/meta-analyses of the data. Provide justification if this is not possible.

    - Applicants are also strongly encouraged to include language in consent forms to allow for optional passive follow-up via electronic health record.

  - 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 the potential human subject will be allowed to discuss the study with anyone before making a decision.
- Consider the need for obtaining ongoing consent or for re-assessing capacity over the course of a long-term study and describe any relevant procedures to assure continued consent.
- Describe the plan for the consent of the individual's Legally Authorized Representative (LAR) to be obtained prior to the human subject's participation in the study. State law defines who may act as the LAR. The local IRB of record should be consulted for guidance regarding who can serve as LAR for research at the study site. ***Note:*** In compliance with 10 USC 980 (https://www.gpo.gov/fdsys/pkg/USCODE-2011-title10/pdf/USCODE-2011-title10-subtitleA-partII-chap49-sec980.pdf), the application must describe a clear intent to benefit for human subjects who cannot give their own consent to participate in the proposed clinical research/trial(s). If applicable, refer to the General Submission Instructions, Appendix 1, for more information.
- ***Assent:*** If minors or other populations that cannot provide informed consent are included in the proposed clinical research/trial(s), a plan to obtain assent (agreement) from those with capacity to provide it, or a justification for a waiver of assent, should be provided. PIs should consult with their local IRB to identify the conditions necessary for obtaining assent.

– **Screening Procedures:** List and describe any evaluations (e.g., laboratory procedures, history, or physical examination) that are required to determine eligibility/suitability for study participation and the diagnostic criteria for entry. ***Note:*** Some screening procedures may require a separate consent or a two-stage consent process.

– **Risks/Benefits Assessment:**

- **Foreseeable risks:** Clearly identify all study risks, including potential safety concerns and adverse events. 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:**
  - ❖ Appropriate to the study's level of risk, describe how safety monitoring and reporting to the IRB and Regulatory Agency (if applicable) will be managed

and conducted. Describe all safety measures to minimize and/or eliminate risks to human subjects and study personnel or to manage unpreventable risks. Include safeguards and planned responses such as dose reduction or stopping criteria based on toxicity grading scales or other predetermined alert values. Discuss the overall plan for provision of emergency care or treatment for an adverse event for study-related injuries, including who will be responsible for the cost of such care.

- **Potential benefits:** Describe known and potential benefits of the study to the human subjects who will participate in the study. Articulate the importance of the knowledge to be gained as a result of the proposed research. Discuss why the potential risks to human subjects are reasonable in relation to the anticipated benefits to the human subjects and others that may be expected to result.

– **Data Management Plan:** Describe the data to be gathered and all methods used for collection, including the following:

- **Data:** The types of data, software, or other materials to be produced.

- **Acquisition and processing:** How the data will be acquired, including the time and location of data acquisition, if scientifically pertinent. If use of existing data resources is proposed, describe the origin of the dataset. Provide an account of the standards to be used for data and metadata format and content. Explain how the data will be processed.

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

- **Confidentiality:**

  - Explain measures taken to protect the privacy of human subjects and maintain confidentiality of study data. Strategies to protect the privacy and confidentiality of study records, particularly those containing identifying information, should be addressed.

  - Address who will have access to study records, data, and specimens, including an acknowledgment that representatives of the DOD are eligible to review study records.

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

- **Data capture, verification, and disposition:** Describe how data will be captured and verified. Describe where data (both electronic and hard copy) will be stored who will keep the data; how the data will be stored, if applicable; the file formats and the naming conventions that will be used; the process for locking the database at study completion; and the length of time data will be stored, along with a justification for the time frame of preservation, which may include considerations

related to the balance between the relative value of data preservation and other factors such as the associated cost and administrative burden of data storage. Describe the proposed database, how it will be developed and validated, and its capability to safeguard and maintain the integrity of the data. Describe the database lock process. For Regulatory Agency oversight, compliance with 21 CFR 11 and appropriate data standards (such as those established by the Clinical Data Interchange Standards Consortium) is required.

- **Data reporting:** Describe how data will be reported and how it will be assured that the documentation will support a regulatory filing with a Regulatory Agency, if applicable.

- **Sharing study results:** In cases where the human subject could possibly benefit medically or otherwise from the information, explain whether the results of screening and/or study participation will be shared with human subjects or their primary care provider, including results from any screening or diagnostic tests performed as part of the study. In cases of national security or controlled unclassified information concerns, include a statement that the data cannot be made available to the public (e.g., "This data cannot be cleared for public release in accordance with the requirements in DoD Directive 5230.09.").

- **Attachment 11: Intervention (no page limit): If using multiple interventions, provide the information for each intervention on a new page and clearly identify the supported project(s). Combine and upload as "Intervention.pdf".** ***(Attachment 11 is only applicable and <u>required</u> for applications proposing clinical trials.)*** The Intervention attachment should include the components listed below.

  - **Description of the Intervention:** Identify the intervention to be tested and describe the particular outcomes. Describe how the intervention addresses the clinical needs and how it compares with currently available interventions and/or standards of care. As applicable, the description of the intervention should include the following components: complete name and composition, storage and handling information, source, dose, schedule, administration route, washout period, duration of the intervention, and concomitant medications allowed. Provide evidence indicating availably of the intervention from its source for the duration of the proposed clinical trial (if applicable). Description of devices should include general concept of design, detailed operational instructions, any potential risks to users, and intended benefits. ***Other types of interventions (diagnostics, devices, therapies, clinical guidance, behavioral interventions) should be fully described.*** Indicate who holds the intellectual property rights to the intervention, if applicable, and how the PI has obtained access to those rights for conduct of the clinical trial.

    Summarize key preclinical findings, dosage studies, and/or other clinical studies (if applicable) that examine the safety and stability (as appropriate) of the intervention. Describe measures to ensure consistency of dosing (e.g., active ingredients for nutritional supplements, rehabilitation interventions).

- **Laboratory Evaluations:** State the biospecimen that will be collected along with the collection schedule and amount. 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). Describe the specimen storage plan, including location of storage, how long specimens will be stored, any special conditions required, labeling, and specimen disposition. Outline the actions to be taken to allow the use of stored specimens in future research studies, if applicable. Identify the laboratory performing each evaluation, the applicable quality standard, and any special precautions that should be taken in handling the samples. If transport of samples is required, describe provisions for ensuring proper storage during transport.

- **Questionnaires and Other Research Data Collection Instruments, if applicable:** Include a copy of the most recent version of questionnaires, data collection forms, rating scales, interview guides, or other instruments. For each instrument, describe how the information collected is related to the objectives of the study. Describe how and when the instrument(s) will be administered. Describe how the instrument(s) will be adapted to the subject population, if applicable.

- **Study Procedures:** Describe the interaction with the human subject, including the study intervention that they will experience. Provide sufficient detail in chronological order for a person uninvolved in the study to understand what the human subject will experience. Provide a schedule (e.g., flowchart or diagram) of study evaluations and follow-up procedures. Clearly delineate research procedures from routine clinical procedures. Discuss how compliance with current Good Laboratory Practice (GLP) guidelines, Good Manufacturing Practice (GMP), and other regulatory considerations will be established, monitored, and maintained, as applicable.

- **Clinical Monitoring Plan:** Describe how the study will be conducted by and monitored for current ICH E6 (International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use) Good Clinical Practice (GCP) compliance by an independent clinical trial monitor (or clinical research associate). The monitoring plan should describe the types of monitoring visits to be conducted, the intervals (based on level of risk), how corrective actions will be reported to the Sponsor and PI, and how they will be corrected and prevented by the clinical trial site/PI.

- **Attachment 12: Regulatory Strategy: If submitting multiple documents, start each document on a new page. Combine and upload as a single file named "Regulatory.pdf".** ***(Attachment 12 is only applicable and <u>required</u> for applications that include a clinical trial[s].)*** Address the following and provide supporting documentation as applicable. If more than one clinical trial is proposed, provide the below information for each trial/intervention. For the FY24 TBIPHRP FPA, evidence of investigational product regulatory exemption (e.g., IND or IDE) application submission, clearance or authorization has been submitted/cleared/authorized or will be submitted to the appropriate Regulatory Agency ***within the first 60 days of the award*** must be included in the application.

– State the product/intervention name.

For products/interventions that do not require regulation by a Regulatory Agency:

– Provide evidence that the product/intervention does not require regulation by a Regulatory Agency. Note that this request includes but limited to software applications, algorithms, nutraceuticals, or behavioral health interventions. ***Submissions providing "not applicable," "none," or similar responses do not satisfy this request and may be administratively withdrawn.*** If the clinical trial will be conducted at international sites, provide equivalent information relevant to the host country[ies] regulatory requirements. No further information for this attachment is required.

For products that require regulation by a Regulatory Agency:

– For investigator-sponsored investigational product regulatory exemptions (e.g., IND, IDE) provide evidence of appropriate institutional support, including capabilities to ensure monitoring as required by the Regulatory Agency.

– State whether the product is FDA-approved, -licensed, or -cleared and marketed in the United States. State whether the product is approved, licensed, cleared and marketed outside of in the United States.

– If the product is marketed in the United States, state the product label indication. State whether the proposed research involves a change to the approved label indication for the route of administration, dosage level, and/or subject population. Indicate whether the proposed research involves a change that increases the risks associated with using the product. State whether the product is being promoted for an off-label use (where promotion involves the sale of a marketed product).

– If the product is not currently Regulatory Agency-approved, -licensed, or -cleared, state the planned indication/use. Indicate whether the product would be classified as a drug, device, biologic, or combination product. Indicate whether the FDA or international regulatory agency has confirmed the proposed classification. Identify the regulatory sponsor. Include a signed sponsor commitment letter acknowledging the regulatory sponsor's understanding of all sponsor responsibilities and commitment to oversee execution of the study.

– For the FY24 TBIPHRP FPA, ***evidence that an investigational product exemption application (e.g., IDE/IND) has been submitted/cleared/authorized has been secured or will be submitted to the appropriate Regulatory Agency within 60 days of the award must be included.*** The application should be specific for the investigational product (i.e., not a derivative or alternate version of the product) and indication to be tested in the proposed clinical trial. If an application has already been submitted to the Regulatory Agency, provide the date of submission, the application number, and a copy of the Regulatory Agency letter acknowledging the submission. Clearly identify whether a member of the study team holds the regulatory exemption (e.g., IND/IDE). If there are any existing cross-references in place, provide the

investigational product regulatory exemption application (e.g., IND/IDE) number(s) and associated sponsor(s). Provide an explanation of the status of the investigational product regulatory exemption (e.g., IND/IDE) application (e.g., past the critical 30-day period, pending response to questions raised by the Regulatory Agency, on clinical hold, on partial clinical hold). Provide a summary of previous meetings with the Regulatory Agency on development of this product, if appropriate. A copy of the Regulatory Agency meeting minutes should be included if available. Provide copies of communications from the Regulatory Agency relevant to the most recent status of the investigational product regulatory exemption (e.g., IND/IDE). If the regulatory exemption application (e.g., IND/IDE) has not been submitted to the Regulatory Agency yet, indicate when the application will be submitted to the FDA, provide a timeline for obtaining the investigational product regulatory exemption within the first 60 days of award, document in the SOW (Attachment 5).

- If available, provide a copy of the communication from the Regulatory Agency indicating the investigational product regulatory exemption (e.g., IND/IDE) application is active/safe to proceed.

- If an active investigational product regulatory exemption (e.g., IND/IDE) for the investigational product is in effect but an amendment is needed to include the proposed trial, describe the type and nature of the amendment(s) ***and provide evidence of the submission within the application***. Indicate whether the amendment increases the risk of the intervention.

- If the proposed clinical trial will be conducted at international sites, provide equivalent information and supporting documentation relevant to the product indication/label and regulatory approval and/or filings in the host country(ies).

- If applicable, provide the current status for manufacturing development (e.g., manufacturer's name, GMP-compliant lots available, status of stability testing), non-clinical development (e.g., test facility name, status of pivotal GLP toxicology studies to support phase 1 testing), and clinical development (e.g., clinical site name, safety profile, status of any completed or ongoing clinical trials).

- Describe the overall regulatory strategy and product development plan that will support the planned product indication or product label change (if applicable). Include a description of the numbers and types of studies proposed to reach approval, licensure, or clearance, the types of Regulatory Agency meetings that will be held/planned, and the submission filing strategy. Include considerations for compliance with current GMP, GLP, and GCP guidelines.

- **Attachment 13: Study Personnel (no page limit): Upload as "Personnel.pdf".**

  - Discuss the qualifications and relevant experience of the research team, including each project leader, and each individual's specific contributions are incorporated to address the overarching challenge, individual projects' research question(s), and enable the success of the proposed project(s).

- Describe the PI's record of accomplishment and their ability to lead the research team to accomplish the proposed research projects.

- Clearly state if key personnel are not receiving salary from the award. If applicable, provide assurances/letters of commitment that the unpaid personnel will contribute the required level of effort to complete the project.

- Provide an organizational chart that identifies key members of the study team and provides an outline of the governing structure for multi-institutional studies. Identify collaborating organizations, centers, and/or departments and name each person's position on the project. Include any separate laboratory or testing centers. Identify the data and clinical coordinating center(s) and note any involvement from Contract Research Organizations, as appropriate. Identify and provide justification for the inclusion of international sites, as appropriate. If applicable, identify the Regulatory Agency sponsor and any external consultants or other experts who will assist with Regulatory Agency sponsor applications. While there is no specified format for this information, a table(s) or diagram is recommended. ***Note:*** This item may be made available for programmatic review.

- **Attachment 14: Representations *(Extramural Submissions Only)*: Upload as "RequiredReps.pdf".** All extramural applicants must complete and submit the Required Representations template available on eBRAP (https://ebrap.org/eBRAP/public/Program.htm). For more information, see the General Application Instructions, Appendix 8, Section B, Representations.

- **Attachment 15: Suggested Intragovernmental/Intramural Budget Form *(if applicable)*: Upload as "IGBudget.pdf".** If an intramural DOD organization will be a collaborator in performance of the project, complete a separate budget using the "Suggested Intragovernmental/Intramural Budget Form", available for download on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm). The budget should cover the entire period of performance for each intramural DOD site and include a budget justification as instructed. The ***total*** costs per year for each subaward (direct and indirect costs) should be included on the Grants.gov Research & Related Budget Form under subaward costs. Refer to the General Application Instructions, Section V.A.(e), for additional information and considerations.

(c) Research & Related Personal Data: For extramural submissions, refer to the General Application Instructions, Section IV.B.(c), and for intramural submissions, refer to the General Application Instructions, Section V.A.(c), for detailed instructions.

(d) Research & Related Senior/Key Person Profile (Expanded): For extramural submissions, refer to the General Application Instructions, Section IV.B.(d), and for intramural submissions, refer to the General Application Instructions, Section V.A.(d), for detailed instructions.

- **PI Biographical Sketch (six-page limit):** Upload as "Biosketch_LastName.pdf".
  - Include a biographical sketch for each Project Leader.
  - CBPR: Biographical sketches, or an equivalent document, should also be included for CBPR team member(s) to demonstrate background and experience relevant to their role in the proposed research project.
- **PI Previous/Current/Pending Support (no page limit):** Upload as "Support_LastName.pdf".
- **Key Personnel Biographical Sketches (six-page limit each):** Upload as "Biosketch_LastName.pdf".
- **Key Personnel Previous/Current/Pending Support (no page limit):** Upload as "Support_LastName.pdf".
  - Include previous/current/pending support for each Project Leader.

(e) Research & Related Budget: For extramural submissions, refer to the General Application Instructions, Section IV.B.(e), and for intramural submissions, refer to the General Application Instructions, Section V.A.(e), for detailed instructions.

- **Budget Justification (no page limit):** For extramural submissions, refer to the General Application Instructions, Section IV.B.(e), Section L, for instructions. For intramural submissions, refer to General Application Instructions, Section V.A.(e), Budget Justification Instructions.

(f) Project/Performance Site Location(s) Form: For extramural submissions, refer to the General Application Instructions, Section IV.B.(f), and for intramural submissions, refer to the General Application Instructions, Section V.A.(f), for detailed instructions.

(g) Research & Related Subaward Budget Attachment(s) Form *(if applicable, Extramural Submissions Only)*: Refer to the General Application Instructions, Section IV.B.(g), for detailed instructions.

- **Extramural Subaward:** Complete the Research & Related Subaward Budget Form and upload through Grants.gov.
- **Intramural DOD Subaward:** Complete a separate "Suggested Intragovernmental/Intramural Budget Form" for each intramural DOD subaward and upload as a single document titled **IGBudget.pdf** to Grants.gov as Attachment 15.

II.D.2.c. Applicant Verification of Full Application Submission in eBRAP

Independent of submission type, once the full application is submitted it is transmitted to and processed in eBRAP. At this stage, the PI and organizational representatives will receive an email from eBRAP instructing them to log into eBRAP to review, modify, and verify the full

application submission. Verification is strongly recommended but not required. eBRAP will validate full application files against the specific program announcement requirements, and discrepancies will be noted in the "Full Application Files" tab in eBRAP. However, 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. ***The Project Narrative and Research & Related Budget Form cannot be changed after the application submission deadline. 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 full application submission deadline.*** Other application components, including subaward budget(s) and subaward budget justification(s), may be changed until the end of the application verification period. The full application cannot be modified once the application verification period ends.

II.D.3. Unique Entity Identifier (UEI) and System for Award Management (SAM)

The applicant organization must be registered as an entity in SAM (https://www.sam.gov/content/home) and receive confirmation of an "Active" status before submitting an application through Grants.gov. Organizations must include the UEI generated by SAM in applications to this funding opportunity.

II.D.4. Submission Dates and Times

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.

All submission dates and times are indicated in Section I, Overview of the Funding Opportunity.

II.D.5. Funding Restrictions

The maximum period of performance is **4** years.

The application's direct costs budgeted for the entire period of performance should not exceed **$5.0M**. If indirect cost rates have been negotiated, indirect costs are to be budgeted in accordance with the organization's negotiated rate. Collaborating organizations should budget associated indirect costs in accordance with each organization's negotiated rate.

All direct and indirect costs of any subaward or contract must be included in the direct costs of the primary award.

The applicant may request the entire maximum funding amount for a project that may have a period of performance less than the maximum **4** years.

For this award mechanism, direct costs:

Must be requested for:

- In years three and four, travel costs for the PI to present project information or disseminate project results at a DOD-sponsored meeting (e.g., Interim/In-Progress Review [IPR] meeting or Military Health System Research Symposium). For planning purposes, it should be assumed that the meeting will be held in the Central Florida Area.

May be requested for (not all-inclusive):

- Travel costs in support of multidisciplinary collaborations.
- Starting in year two, travel costs for the PI and one investigator per research project to attend one scientific/technical meeting per year in addition to the required meetings described above. The intent of travel costs to scientific/technical meetings is to present project information or disseminate project results from the FY24 TBIPHRP FPA.
- Costs associated with CBPR implementation.
- Research subject compensation and reimbursement for trial-related out-of-pocket costs (e.g., travel, lodging, parking, costs associated with caregiving, and resources/equipment to enable participation).
- Costs associated with data and research resource sharing (i.e., making a large dataset available to the public or developing an important resource for the scientific community):
    - Considerations:
        - If recommended for funding, the government reserves the right to reduce the data/resource sharing budget request during award negotiations in order to maximize funding available for research.
        - The TBIPHRP will not provide future TBIPHRP funds to preserve or share data/resources indefinitely.
    - Curation and developing supporting documentation, including formatting according to accepted community standards; de-identification; preparing metadata to foster discoverability, interpretation, and reuse; and formatting for transmission to and storage at a selected repository for long-term preservation and access.
    - Local management considerations, such as unique and specialized information infrastructure necessary to provide local management and preservation (e.g., before deposit into an established repository).
    - Preserving and sharing through established repositories, such as data deposit fees necessary for making data available and accessible. For example, if a Data Management and Sharing Plan proposes preserving and sharing scientific data for 3 years in an established repository with a deposition fee, the cost for the entire 3-year period must be

paid prior to the end of the period of performance. If the Plan proposes deposition to multiple repositories, costs associated with each proposed repository may be included.

II.D.6. Other Submission Requirements

Refer to the General Application Instructions, Appendix 2, 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 individually evaluated according to the following **scored criteria**, which are of equal importance:

- **Overall Program**
    - To what extent the unifying, overarching challenge addresses a relevant critical problem or question in psychological health and/or TBI research and addresses the selected sub-area(s) within one of the three FY24 TBIPHRP FPA Focus Areas.
    - To what extent the research projects are not dependent upon each other but are interrelated and synergistic and will advance toward a solution through a multidisciplinary research program.
- **Leadership**
    - How well the PI demonstrates research experience, leadership skills, and commitment to making an impact in psychological health conditions and/or TBI research and patient care.
    - To what degree the PI's experience in successfully leading large, focused collaborative projects will contribute to achieving the overarching goal(s) of the proposed effort.
    - Whether the PI's responsibilities align with the minimum 20% effort required for this award.
    - To what degree the quality and extent of organizational support are appropriate for the proposed research.
    - To what extent the qualifications of the research team being brought together by the PI and the assembled expertise will create a robust, synergistic collaboration necessary to address the overarching challenge and enable the success of the proposed research.

- **Implementation Plan**
    - How well the proposed projects are supported by a detailed implementation plan that identifies critical milestones and outlines the knowledge, resources, and technical innovations that will be utilized to achieve the milestones.
    - How well the research resources and/or cores that will be created are leveraged throughout the research program.
    - To what extent the plans to assess individual project performance during the course of the award, including progression toward defined milestones, realization of study objectives, and addressing the overarching challenge are appropriate.
    - How well the overall management plan will facilitate a consistent and intensive flow of ideas and information among all team members.
    - How the proposed plans for communication, data transfer among the collaborating institutions, and how plans for sharing data, specimens, and/or imaging products obtained during the study are appropriate.
    - To what extent the plans for creating, reviewing, implementing, and modifying Standard Operating Procedures are appropriate, if applicable.
- **Overall Impact**
    - To what degree the anticipated outcome(s) or knowledge/materiel product(s) will make important scientific advances and improve the understanding, prevention, assessment, and/or treatment of psychological health conditions and/or TBI.
    - To what extent the long-range vision of the proposed research will impact the field of study and/or the lives of relevant patient or community populations.
    - If applicable, to what degree the proposed materiel or knowledge product represents an improvement to currently available pharmacologic agents, non-pharmacologic interventions, devices, or clinical practice guidance devices, or clinical guidance.
    - To what degree the study identifies potential issues that might limit the impact of the proposed research and provides strategies that may be employed to overcome those issues.
- **Community-Based Participatory Research**
    - How CBPR/stakeholder engagement will make meaningful contributions to the success of the overall program.
    - To what extent the CBPR Letter(s) of Commitment describe the role and commitment of the lived experience or community-based partners on the research team.

- How well the CBPR approach that will be used (e.g., LEC, partner organization, CAB, co-researcher model) is described and at what points it will contribute to the overall program or proposed project(s).

- To what extent the CBPR input will be captured and meaningfully integrated and incorporated into the needs assessment, planning, design, execution, analysis, and dissemination of the research.

- To what extent training that will be provided to both scientific researchers and community members on CBPR approaches, decision making, and equitable participation.

- To what degree dissemination activities will share research findings with the stakeholder communities.

- **Data and Research Resources Sharing Plan**

  - To what extent the data and resources generated during the performance of the project will be shared with the research community, including the sharing of de-identified data with data repositories.

  - For studies with prospective human subject enrollment, how thoroughly the application incorporates CDEs appropriate to each field of study.

  - For studies with prospective human subject enrollment, how well the application justifies any instances where existing CDEs are not applicable or appropriate (if applicable).

Scored Review Criteria for Individual Proposed Research Projects: Research Strategy and Feasibility is of most importance and the remaining criteria listed are of equal importance.

- **Research Strategy and Feasibility:**

  - How well the scientific rationale, literature review, unpublished data, preliminary studies, and/or preclinical data support the development of the proposed project and provide the basis for the study questions and/or hypotheses.

  - How relevant and applicable the proposed research and findings are to the intent of the mechanism and selected sub-area(s) within one of the three FY24TBIPHRP FPA Focus Areas.

  - How well the purpose and objectives of the study with detailed specific aims and hypotheses are described and aligned with the tasks in the SOW.

  - To what extent the experimental design, methods, and analyses are relevant to the completion of the specific aims.

  - How well the research requirements are supported by the availability of and accessibility to facilities and resources (including patient populations, samples, and collaborative arrangements).

- How well the application identifies potential problem areas and presents methods and approaches to mitigate any risks that are identified.
- Whether the proposed project is feasible and will be completed within the proposed period of performance.

For research involving animals:

- To what extent the choice of animal model is validated and well-justified in the literature.
- How well the study explains how and why the animal species, strain, and model(s) being used can address the scientific objectives and the relevance to human biology.
- How the approaches to validate or corroborate findings from animal studies to human data sources/populations are relevant.
- If applicable, to what extent the proposed validation approaches or corroborative studies "de-risk" the possibility that the findings from the animal study cannot be translated into human populations.

For research involving human subjects/samples/datasets:

- To what extent the chosen human subjects/samples/datasets are appropriate for the proposed research project.
- How well plans to collect specimens and conduct laboratory evaluations are relevant to the study objectives, if applicable.
- If applicable, how well the inclusion of international sites is justified.
- Whether the application demonstrates access to the proposed study population at each site.
- To what degree the data collection instruments are appropriate to the proposed study.
- The degree to which the recruitment, screening, and retention processes for human subjects will meet the needs of the proposed clinical research/trial.
- How well the application identifies any potential barriers to accrual and provides mitigation plans for addressing unanticipated delays (e.g., slow accrual, attrition).
- How well the inclusion and exclusion criteria and group assignment process (if applicable) meet the needs of the proposed clinical research/trial.
- Whether the strategy for the inclusion of women and minorities and distribution of proposed enrollment are appropriate for the proposed research. Studies utilizing human biospecimens or datasets that cannot be linked to a specific individual, gender, ethnicity, or race (typically classified as exempt from IRB review) are exempt from this requirement.

For clinical trials:

- Whether the clinical trial is designed with the appropriate primary, secondary, or interim endpoints/outcome measures.
- To what degree the intervention addresses the clinical need described.
- Whether there is evidence indicating availability of the intervention from its source for the duration of the proposed clinical trial (if applicable).
- To what degree the application includes key preclinical findings, dosage studies, and/or other clinical evidence (if applicable) to support the safety and stability (as appropriate) of the intervention.
- How well research procedures are clearly delineated from routine clinical procedures.
- Whether measures are described to ensure the consistency of dosing (e.g., active ingredients for nutritional supplements, rehabilitation interventions).

- **Impact**
  - To what extent the proposed research will accelerate research in the selected sub-area(s) within the FY24 TBIPHRP FPA Focus Areas and will lead to the development of health care products, technologies, and/or clinical practice guidelines that improve patient outcomes.
  - How well the application acknowledges potential issues that might limit impact and provides approaches to overcome.
- **Regulatory Strategy and Transition Plan**
  - If applicable, whether evidence that the product/intervention does not require regulation by a Regulated Agency is provided and reasonable.
  - As appropriate, whether the application includes evidence that the IND or IDE application (or international equivalent) has submitted/cleared/authorized or will be submitted to the appropriate Regulatory Agency within the first 60 days of the award.
  - How the overall regulatory strategy and product development plan that will support the planned product indication or product label change.
  - For investigator-sponsored investigational product regulatory exemptions (e.g., IND, IDE), whether there is evidence of appropriate institutional support.
  - Whether plans to comply with current GLP, GMP, and GCP guidelines are appropriate.
  - Whether a member of the study team is the regulatory sponsor and holds the investigational product regulatory exemption (e.g., IND/IDE) for the proposed indication.

- Whether the overall strategy described to transition the research to commercialization or clinical use is reasonable and achievable.

- Whether the schedule and milestones for transitioning the research to a clinical product are achievable.

- Whether the potential risk analysis for cost, schedule, manufacturability, and sustainability is realistic and reasonable.

- How well the application identifies intellectual property ownership and demonstrates the appropriate access to all intellectual property rights necessary for development and commercialization.

- If applicable, how the application describes an appropriate intellectual and material property plan among participating organizations.

- If applicable, how well the application addresses any impact of intellectual property issues on product development and the government's ability to access such products or technologies in the future.

- **Ethical Considerations** ***(for research recruiting human subjects)***

  - To what degree the level of risk to human subjects is minimized and how the safety monitoring and reporting is appropriate for the level of risk.

  - To what degree privacy and confidentiality of study records are appropriately considered.

  - To what degree the process for seeking informed consent is appropriate and whether safeguards are in place for vulnerable populations.

- **Statistical Plan**

  - How the statistical plan, including sample size and power analysis, is adequate for the study and all proposed correlative studies.

  - As applicable, how appropriate the randomization and blinding procedures for the study are, and how well any other measures to be taken to minimize the effects of subjective bias during animal treatment and assessment of results are described.

  - How the justification for not utilizing randomization and/or blinding is appropriate, if applicable.

  - Whether the statistical plan compensates for the use of a subpopulation of a recruited sample population to ensure appropriate power can be achieved within the subpopulation study.

- If applicable, whether the plans for the valid analysis of group differences on the basis of sex/gender, race, and/or ethnicity for phase 3 clinical trials are appropriate for the proposed research.

- **Personnel**

  - To what degree the research team's qualifications and relevant experience, including each project leader, and each individual's specific contributions are incorporated to address the overarching challenge, individual projects' research question(s), and enable the success of the proposed project(s).

  - To what degree the levels of effort are appropriate for successful conduct of the proposed work.

In addition, the following criteria will also contribute to the overall evaluation of the application, but will not be individually scored and are therefore termed **unscored criteria**:

- **Budget**

  - Whether the **direct costs** exceed the allowable direct costs as published in the program announcement.

  - Whether the budget is appropriate for the proposed research.

- **Application Presentation**

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

II.E.1.b. Programmatic Review

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

- Ratings and evaluations of the peer reviewers

- Relevance to the priorities of the DHP and FY24 TBIPHRP, as evidenced by the following:

  - Adherence to the intent of the award mechanism

  - Program portfolio composition

  - Relative impact

  - Relevance to military health

II.E.2. Application Review and Selection Process

All applications are evaluated by scientists, clinicians, and consumers in a two-tier review process. The first tier is **peer review**, the evaluation of applications against established criteria to determine technical merit, where each application is assessed for its own merit, independent of other applications. The second tier is **programmatic review**, a comparison-based process in which applications with high scientific and technical merit are further evaluated for programmatic relevance. Final recommendations for funding are made to the Commanding General, USAMRDC. ***The highest-scoring applications from the first tier of review are not automatically recommended for funding. Funding recommendations depend on various factors as described in Section II.E.1.b, Programmatic Review.*** Additional information about the two-tier process used by the CDMRP can be found at https://cdmrp.health.mil/about/2tierRevProcess.

All CDMRP review processes are conducted confidentially to maintain the integrity of the merit-based selection process. Panel members sign a statement declaring that application and evaluation information will not be disclosed outside the review panel. Violations of confidentiality can result in the dissolution 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 a 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 200.1, over the period of performance, the federal awarding agency is required to review and consider any information about the applicant that is available in SAM.

An applicant organization may review SAM and submit comments on any information currently available about the organization that a federal awarding agency previously entered. 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.F. Federal Award Administration Information

II.F.1. Federal Award Notices

Each applicant organization and PI will receive email notification when the funding recommendations are posted to eBRAP. At this time, each PI will receive a peer review summary statement on the strengths and weaknesses of the application and an information paper describing the funding recommendation and review process for the TBIPHRP award mechanisms. The information papers and a list of organizations and PIs recommended for funding are also posted on the program's page within the CDMRP website.

If an application is recommended for funding, after the email notification is posted to eBRAP, a government representative will contact the person authorized to negotiate on behalf of the recipient organization.

Only an appointed USAMRAA Grants Officer may obligate the government to the expenditure of funds to an extramural organization. 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 (i.e., assistance agreement).***

Intra-DOD obligations of funding will be made according to the terms of a negotiated Inter-Agency Agreement and managed by a CDMRP Science Officer.

Funding obligated to ***intragovernmental and intramural DOD organizations*** will be sent through the Military Interdepartmental Purchase Request (MIPR), Funding Authorization Document (FAD), or Direct Charge Work Breakdown Structure processes. Transfer of funds is contingent upon appropriate safety and administrative approvals. Intragovernmental and intramural DOD investigators and collaborators must coordinate receipt and commitment of funds through their respective Resource Manager/Task Area Manager/Comptroller or equivalent Business Official.

An organization may, at its own risk and without the government's prior approval, incur obligations and expenditures to cover costs up to 90 days before the beginning date of the initial budget period of a new award. For extramural submissions, refer to the General Application Instructions, Section IV.B.(e), Pre-Award Costs section, and for intramural submissions, refer to the General Application Instructions, Section V.A.(e), Pre-Award Costs section, for additional information about pre-award costs.

If there are technical reporting requirement delinquencies for any existing CDMRP awards at the applicant organization, no new awards will be issued to the applicant organization until all delinquent reports have been submitted.

II.F.2. PI Changes and Award Transfers

Changes in PI are not allowed, except under extenuating circumstances that will be evaluated on a case-by-case basis.

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

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 7, Section F, for general information on organization or PI changes.

II.F.3. Administrative and National Policy Requirements

Applicable requirements in the DoDGARs found in 32 CFR, Chapter I, 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 7, for general information regarding administrative requirements.

Refer to the General Application Instructions, Appendix 8, for general information regarding national policy requirements.

Refer to full text of the latest DoD R&D Terms and Conditions and the USAMRAA Research Terms and Conditions: Addendum to the DoD R&D Terms and Conditions for further information.

Funded trials are required to post a copy of the informed consent form used to enroll subjects on a publicly available federal website in accordance with federal requirements described in 32 CFR 219. Funded studies are required to register the study in the NIH clinical trials registry, , prior to initiation of the study. Refer to the General Application Instructions, Appendix 6, Section F, for further details.

Applications recommended for funding that involve animals, human data, human specimens, human subjects, or human cadavers must be reviewed for compliance with federal and DOD animal and/or human subjects protection requirements and approved by the USAMRDC Office of Human and Animal Research Oversight prior to implementation. This administrative review requirement is in addition to the local IACUC, IRB, or Ethics Committee review. Refer to the General Application Instructions, Appendix 6, for additional information.

II.F.4. Reporting

Annual technical progress reports and quad charts as well as a final technical progress report and quad chart will be required. Annual and final technical reports must be prepared in accordance with the Research and Performance Progress Report (RPPR).

Award Expiration Transition Plan: An Award Expiration Transition Plan must be submitted with the final progress report. Use the one-page template "Award Expiration Transition Plan," available on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) under the "Progress Report Formats" section.

The Award Expiration Transition Plan must outline whether and how the research supported by this award will progress and must include source(s) of funding, either known or pending.

PHS Inclusion Enrollment Reporting Requirement: Enrollment reporting on the basis of sex/gender, race, and/or ethnicity will be required with each annual and final progress report. The PHS Inclusion Enrollment Report is available on the "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) in eBRAP. Studies utilizing human biospecimens or datasets that cannot be linked to a specific individual, gender, ethnicity, or race (typically classified as exempt from IRB review) are exempt from this requirement.

The Award Terms and Conditions will specify whether additional and/or more frequent reporting is required.

Awards resulting from this program announcement may entail 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 $10.0M are required to provide information to SAM 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. These recipients are required to disclose, semiannually, information about criminal, civil, and administrative proceedings as specified in the applicable Representations (see General Application Instructions, Appendix 8, Section B).

II.G. Federal Awarding Agency Contacts

II.G.1. eBRAP Help Desk

Questions regarding program announcement content or submission requirements as well as technical assistance related to pre-application or intramural application submission:

Phone: 301-682-5507

Email: help@eBRAP.org

II.G.2. Grants.gov Contact Center

Questions regarding Grants.gov registration and Workspace

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

Email: support@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 901a. The program announcement numeric version code will match the General Application Instructions version code 901.

II.H.2. Administrative Actions

After receipt of pre-applications or full 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 full 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.
- Attachment 6, Impact Statement, is missing.
- Attachment 7, Relevance to Military Health Statement, is missing.
- Attachment 8, CBPR Documentation, is missing.

For applications recruiting human subjects:

- Attachment 10, Human Subject Recruitment and Safety Procedures, is missing.

For applications proposing a clinical trial:

- Attachment 11, Intervention, is missing.
- Attachment 12, Regulatory Strategy, is missing.

II.H.2.b. Modification

- Pages exceeding the specific limits will be removed prior to review for all documents other than the 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 full application:

- An FY24 TBIPHRP Programmatic Panel member is named as being involved in the research proposed or is found to have assisted in the pre-application or application processes including, but not limited to, concept design, application development, budget preparation, and the development of any supporting documentation, including letters of support/recommendation. ***A list of the FY24 TBIPHRP Programmatic Panel members can be found at https://cdmrp.health.mil/tbiphrp/panels/panels24***.
- 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.
- Applications that include names of personnel from either of the CDMRP peer or programmatic review companies. For FY24, the identities of the peer review contractor and the programmatic review contractor may be found at the CDMRP website (https://cdmrp.health.mil/about/2tierRevProcess).
- 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.
- Applications submitted by a federal government organization (including an intramural DOD organization) may be withdrawn if (a) the organization cannot accept and execute the entirety of the requested budget in current year (FY24) funds and/or (b) the federal government organization cannot coordinate the use of contractual, assistance, or other appropriate agreements to provide funds to collaborators.
- Application includes research data that are classified and/or proposes research that may produce classified outcomes, or outcomes deemed sensitive to national security concerns.
- The invited application proposes a different research project than that described in the pre-application.
- Application consists solely or primarily of planning, engineering, manufacturing, or formulation activities.

- Basic research is proposed.
- Application consists of less than three or more than five research projects.
- Submission of the same research project to different funding opportunities within the same program and fiscal year. Refer to Section II.D, Application and Submission Information, for exceptions.
- PI and/or project leaders do not meet the eligibility criteria.
- A clinical research/trial is proposed that requires an EFIC.
- Application does not include a CBPR approach.
- Application failed to address a unifying overarching challenge that will be addressed by the set of research projects proposed.
- Application failed to address at least one sub-area within one of the three FY24 TBIPHRP FPA Focus Areas.
- Evidence is not provided that the investigational product regulatory exemption (e.g., IND/IDE) application has been submitted/authorized/cleared or will be submitted in the first 60 days of the award.
- Application does not demonstrate support for and access to relevant population(s) and/or resources(s)

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. Full Application Submission Checklist

Full Application Components	Uploaded
SF424 Research & Related Application for Federal Assistance *(Extramural submissions only)*	☐
Summary (Tab 1) and Application Contacts (Tab 2) *(Intramural submissions only)*	☐
Attachments	
Project Narrative – Attachment 1, upload as "ProjectNarrative.pdf"	☐
Supporting Documentation – Attachment 2, upload as "Support.pdf"	☐
Technical Abstract – Attachment 3, upload as "TechAbs.pdf"	☐
Lay Abstract – Attachment 4, upload as "LayAbs.pdf"	☐
Statement of Work – Attachment 5, upload as "SOW.pdf"	☐
Impact Statement – Attachment 6, upload as "Impact.pdf"	☐
Relevance to Military Health Statement– Attachment 7, upload as "Military.pdf"	☐
CBPR Documentation – Attachment 8, upload as "CBPR.pdf"	☐
Transition Plan – Attachment 9, upload as "Transition.pdf"	☐
Human Subject Recruitment and Safety Procedures *(if applicable)* – Attachment 10, upload as "HumSubProc.pdf"	☐
Intervention *(if applicable)* – Attachment 11, upload as "Intervention.pdf"	☐
Regulatory Strategy *(if applicable)* – Attachment 12, upload as "Regulatory.pdf"	☐
Study Personnel – Attachment 13, upload as "Personnel.pdf"	☐
Representations *(Extramural submissions only)* – Attachment 14, upload as "RequiredReps.pdf"	☐
Suggested Intragovernmental/Intramural Budget Form (*if applicable)* – Attachment 15, upload as "IGBudget.pdf"	☐
Research & Related Personal Data	☐
Research & Related Senior/Key Person Profile (Expanded)	☐
Attach PI Biographical Sketch (Biosketch_LastName.pdf)	☐
Attach PI Previous/Current/Pending Support (Support_LastName.pdf)	☐
Attach Biographical Sketch (Biosketch_LastName.pdf) for each senior/key person	☐
Attach Previous/Current/Pending (Support_LastName.pdf) for each senior/key person	☐

Full Application Components	Uploaded
Research & Related Budget *(Extramural submissions only)* Include budget justification	☐
Budget *(Intramural submissions only)* Include budget justification	☐
Project/Performance Site Location(s) Form	☐
Research & Related Subaward Budget Attachment(s) Form *(if applicable)*	☐

APPENDIX 1: ACRONYM LIST

ACOS/R&D	Associate Chief of Staff for Research and Development
ARRIVE	Animal Research: Reporting In Vivo Experiments
ASR	Acute Stress Reaction
CAB	Community Advisory Board
CBPR	Community-Based Participatory Research
CDE	Common Data Element
CDMRP	Congressionally Directed Medical Research Programs
CFR	Code of Federal Regulations
COI	Conflict of Interest
DHP	Defense Health Program
DOD	Department of Defense
DoDGARs	Department of Defense Grant and Agreement Regulations
eBRAP	Electronic Biomedical Research Application Portal
EAB	External Advisory Board
EFIC	Exception from Informed Consent
ET	Eastern Time
FAD	Funding Authorization Document
FDA	U.S. Food and Drug Administration
FITBIR	Federal Interagency Traumatic Brain Injury Research
FPA	Focused Program Award
FY	Fiscal Year
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
IACUC	Institutional Animal Care and Use Committee
IDE	Investigational Device Exemption
IND	Investigational New Drug
IRB	Institutional Review Board
LAR	Legally Authorized Representative
LEC	Lived Experience Consultant
M	Million
MIPR	Military Interdepartmental Purchase Request
NDA	NIMH Data Archive
NIH	National Institutes of Health
NIMH	National Institute of Mental Health
NINDS	National Institute of Neurological Disorders and Stroke

PDF	Portable Document Format
PHS	Public Health Service
PI	Principal Investigator
PTSD	Posttraumatic Stress Disorder
RPPR	Research Performance Progress Report
SAM	System for Award Management
SOW	Statement of Work
TBI	Traumatic Brain Injury
TBIPHRP	Traumatic Brain Injury and Psychological Health Research Program
UEI	Unique Entity Identifier
URL	Uniform Resource Locator
USAMRAA	U.S. Army Medical Research Acquisition Activity
USAMRDC	U.S. Army Medical Research and Development Command
USC	United States Code
VA	U.S. Department of Veterans Affairs

APPENDIX 2: DOD AND VA WEBSITES

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

Air Force Office of Scientific Research
https://www.afrl.af.mil/AFOSR/

Air Force Research Laboratory
https://www.afrl.af.mil/

Armed Forces Radiobiology Research Institute
https://afrri.usuhs.edu/home

Combat Casualty Care Research Program
https://cccrp.health.mil/Pages/default.aspx

Congressionally Directed Medical Research Programs
https://cdmrp.health.mil/

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

Defense Health Agency
https://health.mil/About-MHS/OASDHA/Defense-Health-Agency

Defense Suicide Prevention Office
https://www.dspo.mil/

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

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

Military Health System Research Symposium
https://mhsrs.health.mil/sitepages/home.aspx

Military Infectious Diseases Research Program
https://midrp.health.mil/

Military Operational Medicine Research Program
https://momrp.health.mil/

Navy Bureau of Medicine and Surgery
https://www.med.navy.mil/

Naval Health Research Center
https://www.med.navy.mil/Naval-Medical-Research-Command/R-D-Commands/Naval-Health-Research-Center/

Navy and Marine Corps Public Health Center
https://www.med.navy.mil/Navy-and-Marine-Corps-Force-Health-Protection-Command/

Naval Medical Research Command
https://www.med.navy.mil/Naval-Medical-Research-Command/

Office of Naval Research
https://www.med.navy.mil/

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

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

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

U.S. Army Aeromedical Research Laboratory
https://usaarl.health.mil/

U.S. Army Combat Capabilities Development Command
https://www.army.mil/devcom

U.S. Army Institute of Surgical Research
https://usaisr.health.mil/

U.S. Army Medical Materiel Development Activity
https://usammda.health.mil/

U.S. Army Medical Research and Development Command
https://mrdc.health.mil/

U.S. Army Medical Research Institute of Infectious Diseases
https://usamriid.health.mil/

U.S. Army Research Institute of Environmental Medicine
https://usariem.health.mil/

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

U.S. Army Sharp, Ready and Resilient Directorate
https://www.armyresilience.army.mil/sharp/index.html

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

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

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

Walter Reed Army Institute of Research
https://wrair.health.mil/

APPENDIX 3: ADDITIONAL FOCUS AREA INFORMATION

The information below in italics provides additional context regarding programmatic intent but **are not required** to be specifically addressed by applications.

Psychedelic clinical trials involving eligible Service Members are allowed: Section 723 of the National Defense Authorization Act for Fiscal Year 2024 authorizes the DOD to conduct research involving psychedelic substances (e.g., 3,4-Methylenedioxy-methamphetamine, psilocybin, ibogaine, 5-Methoxy-N,N-dimethyltryptamine, and other plant-based alternative therapies) as treatments for TBI or posttraumatic stress disorder (PTSD). The Secretary of the DOD may authorize any member of the Armed Forces serving on active duty who is diagnosed with a covered condition (TBI or PTSD) to participate in a clinical trial. ***Submissions including a clinical trial involving psychedelic interventions and Service Members are allowed and will openly compete with other research submissions during the application review and selection process.*** *Such trials recommended for funding may be subject to additional review and approval processes.*

1. **Understand:** Research will address knowledge gaps in epidemiology and etiology of psychological health conditions and/or TBI.

    a. Understanding of risk, protective, and biological factors contributing to an individual's vulnerability to, response to, and long-term outcomes of psychological health conditions and/or TBI.

        - *Understanding psychological health trajectories associated with trauma (e.g., acute stress reactions, adjustment disorders, PTSD) and suicidality that incorporate internal and external factors. For example, factors could include time course, demographic characteristics, career progression, history of trauma exposure, and community and cultural factors.*

        - *Understanding how the approach to psychiatric diagnosis (e.g., acute stress reactions, adjustment disorders, PTSD) in the military relates to occupational impairment and/or military separation.*

        - *Understanding the role of genetics, endophenotypes, health demographics, previous injuries or repetitive exposures, psychological health conditions, pathophysiology, and environmental factors (e.g., extreme temperatures/pressures) on TBI.*

        - *Understanding the contribution of pre- and post-injury patient, family,[6] and caregiver education, as well as cultural, demographic, stigma, and bias factors that may relate to treatment-seeking and adherence.*

        - *Development and analysis of modeling from clinical data and other human data (e.g., electronic health records, exposure, training, and/or occupational data) to forecast*

[6] "Family" should be broadly defined to include not just spouses, but also parents, significant others/fiancés/partners, children, caregivers, or close friends.

the long-term and/or late effects of brain exposures, such as TBI, and co-occurring conditions.

- *Development and analysis of communication and tools/technology adoption that would facilitate clinical translation and identification of risk factors, educational barriers, social determinates of health, and other factors that may impede clinical translation.*

b. Understanding psychological health factors or outcomes associated with sexual harassment and assault perpetration, victimization, barriers to reporting and response. Studies that ensure participant anonymity are strongly encouraged.

- *Understanding processes of shame, stigma, and institutional betrayal among sexual assault victims and their units/teams and evaluation of approaches to mitigate these experiences. Experiences of marginalized groups, male victims, and victims of intimate partner and family violence are of particular interest.*

- *Understanding how interpersonal and individual conditions, choices, behaviors, and psychological health are influenced by organizational-level factors relate to sexual assault and harassment prevention, perpetration, and response. Measurement and analysis of organizational-level factors, such as culture, climate, and training, beyond aggregating individual perceptions, are encouraged. Research could include the progression from sexual harassment to sexual assault and factors influencing sexual harassment.*

- *Understanding barriers to reporting sexual assault and factors that contribute to retaliation within units/teams and evaluation of approaches to mitigate barriers, prevent retaliation, and improve psychological health outcomes of victims. Research could include data from influencers, bystanders, and perpetrators, as well as environmental, structural, and demographic factors (e.g., workplace culture, climate, senior leader diversity, age, gender).*

- *Understanding the psychological health consequences of intimate partner and family violence.*

2. **Prevent and Assess:** Research will address the prevention, screening, diagnosis, or prognosis of psychological health conditions and/or TBI.

a. Identification and validation of biomarkers or other objective methods for assessment, diagnosis, prognosis, or real-time monitoring of psychological health conditions and/or TBI (including subclinical presentations) and associated sequelae of these conditions.

- *Development of decision-making frameworks or tools that incorporate objective assessments and may consider long-term outcomes to inform return to activity/duty decisions are within scope*.

b. Development and evaluation of approaches or tools to prevent or reduce risk of psychological health conditions and/or TBI.

   - *Evaluation of environmental sensor data in aspects related to brain health and risk from brain blast and impact exposures.*

   - *Development of innovative materials and technologies that can prevent or reduce risk of TBI.*

   - *Generation of physiological evidence regarding the safety, efficacy, and utility of candidate neuroprotective measures. Animal models, if used, should be validated and well justified within the literature and should demonstrate clear alignment to clinical populations.*

   - *Validation of objective tools/methods for assessing and real-time health status monitoring of psychological health conditions and/or TBI.*

   - *Development of clinical decision-making frameworks or tools that incorporate objective assessments and long-term outcomes to return to activity/duty decisions.*

c. Development and evaluation of crosscutting prevention approaches to address multiple adverse outcomes such as suicide, interpersonal violence (including intimate partner and family violence), and psychological health issues are within scope.

   - *Optimized messaging for successful dissemination and implementation.*

   - *Inclusion of families[6] and evaluation of family impact.*

   - *Culturally acceptable approaches to reducing access to lethal means and promoting means safety for suicide and violence prevention.*

d. Development and evaluation of solutions to support military and family readiness and increase psychological resilience in individuals to the potential negative impacts of specific military and life stressors.

   - *Effective pharmacologic or non-pharmacologic prevention interventions. Solutions for prevention of acute stress reactions (ASRs) and PTSD or adjustment disorders may be proposed.*

   - *Preparation of Service Members and units for missions and to help reset and improve resilience between deployments.*

   - *Effective solutions to support relationships and parenting, prepare families for potential secondary trauma exposure, and empower families to access tailored support and resources.*

3. **Treat:** Research will address novel and repurposed interventions[7] to improve outcomes of psychological health conditions and/or TBI. Efforts that address treatment, rehabilitation, and health services research are within scope.

    a. Interventions that promote sustained functional recovery, including interventions administered acutely, during the post-acute phase, or during the chronic phase of injury.

        - *Rapid assessments and treatments for psychological health conditions. Interventions addressing adjustment disorders, ASRs, and PTSD may be proposed.*
        - *Mobile health technologies to improve mental health and well-being.*
        - *Interventions focused on sensory and motor dysfunction after brain injury.*
        - *Interventions that address neurodegenerative processes associated with TBI.*
        - *Interventions that restore cognitive reserve and functioning.*
        - *Novel therapeutic candidates based on evolving changes of pathophysiology and/or theoretical mechanisms of psychological health conditions and/or TBI.*
        - *Interventions and/or the delivery of health care services to improve the ability to treat co-occurring TBI and psychological health conditions.*
        - *Personalized medicine approaches to treatment that may include tailoring treatment to the biological and endophenotypic elements present. Treatment approaches may consider how TBI, PTSD, depression, or other psychological health conditions are interrelated.*
        - *Considerations for sequencing and optimal combinations of pharmacologic and non-pharmacologic interventions.*
        - *Effective, early interventions for delivery in rural or other resource-limited environments (e.g., far-forward military environments), and/or by non-clinicians (e.g., peers, teams, first responders/medics).*

    b. Development of postvention strategies to support individuals in workplace or community environments following a sexual assault, suicide event, or other trauma.

[7] Intervention repurposing is the identification of novel indication(s) for an FDA-approved intervention.

c. Health services research to improve provider adoption of evidence-based practices, improve access, and reduce barriers. In addition, factors that influence treatment engagement, follow-up care, and improvement of long-term outcomes are of interest.

- *Research of interest includes, but is not limited to individual, peer/unit/team, leader, family, caregivers, community, and enterprise level methods.*

- *Clinical effectiveness studies comparing emerging capabilities to existing evidence-based treatments and/or the standard of care.*

- *Identification and evaluation of methods for successful dissemination and implementation of interventions.*