I. OVERVIEW OF THE FUNDING OPPORTUNITY

Program Announcement for the Department of Defense

Defense Health Program

Congressionally Directed Medical Research Programs

Peer Reviewed Medical Research Program

Clinical Trial Award

Announcement Type: Initial

Funding Opportunity Number: W81XWH-22-PRMRP-CTA

Assistance Listing Number: 12.420 Military Medical Research and Development

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-Application Submission Deadline:** 5:00 p.m. Eastern time (ET), May 6, 2022
- **Invitation to Submit an Application:** June 17, 2022
- **Application Submission Deadline:** 11:59 p.m. ET, August 12, 2022
- **End of Application Verification Period:** 5:00 p.m. ET, August 17, 2022
- **Peer Review:** September 2022
- **Programmatic Review:** December 2022

This program announcement must be read in conjunction with the General Application Instructions, version 701. The General Application Instructions document is available for downloading from the Grants.gov funding opportunity announcement by selecting the "Package" tab, clicking "Preview," and then selecting "Download Instructions."

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II. DETAILED INFORMATION ABOUT THE FUNDING OPPORTUNITY

II.A. Program Description

Applications to the Fiscal Year 2022 (FY22) Peer Reviewed Medical Research Program (PRMRP) are being solicited by the U.S. Army Medical Research Acquisition Activity (USAMRAA) using delegated authority provided by United States Code, Title 10, Section 2358 (10 USC 2358). The execution management agent for this program announcement is the Congressionally Directed Medical Research Programs (CDMRP) at the U.S. Army Medical Research and Development Command (USAMRDC). The PRMRP was initiated in 1999 to support medical research projects of clear scientific merit and direct relevance to military health. Appropriations for the PRMRP from FY99 through FY21 totaled $3.08 billion. The FY22 appropriation is $370 million (M).

The vision of the FY22 PRMRP is to improve the health, well-being, and care of all military Service Members, Veterans, and Beneficiaries, and its mission is to encourage, identify, select, and manage medical research projects of clear scientific merit that lead to impactful advances in military health care. The PRMRP challenges the scientific and clinical communities to address the FY22 PRMRP Topic Areas with original ideas that foster new directions along the entire spectrum of research and patient care. The program seeks applications in laboratory, clinical, behavioral, epidemiological, and other areas of research to advance knowledge in disease etiology; improve prevention, detection, diagnosis, treatment, and quality of life for those affected by a relevant disease or condition; and develop and validate clinical practice or public health guidelines. ***The proposed research must be relevant to active-duty Service Members, Veterans, military beneficiaries, and/or the American public.***

II.A.1. FY22 PRMRP Topic Areas and Strategic Goals

All applications for FY22 PRMRP funding must specifically address one of the FY22 PRMRP Topic Areas as directed by the U.S. Congress and have direct relevance to military health. Additionally, the PRMRP implements a portfolio-driven approach by grouping related Topic Areas with Strategic Goals as a framework within which to address critical gaps in major research areas. ***All applications must address one of the FY22 PRMRP Strategic Goals as it relates to the portfolio-assigned FY22 PRMRP Topic Area.*** If the proposed research does not specifically address one FY22 PRMRP Topic Area and one FY22 PRMRP Strategic Goal, then the government reserves the right to administratively withdraw the application. The government reserves the right to reassign the application's Topic Area if submitted to an incorrect Topic Area. The FY22 PRMRP Topic Areas and Strategic Goals are listed in each PRMRP portfolio category below:

FY22 PRMRP Portfolio Categories with Associated FY22 PRMRP Topic Areas and FY22 PRMRP Strategic Goals

Autoimmune Disorders and Immunology

Topic Areas

- Food Allergies
- Guillain-Barré Syndrome
- Inflammatory Bowel Disease
- Rheumatoid Arthritis
- Sustained Release Drug Delivery

Strategic Goals

Foundational Studies

- Identify factors, to include environmental exposures, lifestyle triggers, and past medical history, impacting the onset and progression of associated immune-mediated diseases
- Determine the impact of the microbiome on associated immune-mediated diseases

Diagnosis

- Develop innovative noninvasive methods for continuous monitoring of inflammation
- Identify biomarkers to predict onset and/or progression of associated immune-mediated diseases

Treatment

- Develop and test therapeutic interventions to promote tissue healing
- Develop and test new treatments and/or refine existing treatment strategies to minimize toxicity, and mitigate the inflammatory and/or allergic disease state

Epidemiology

- Conduct patient-centered research on onset, exacerbation, outcomes, and treatment preferences for associated immune-mediated diseases

Cardiovascular Health

Topic Areas

- Cardiomyopathy
- Congenital Heart Disease
- Familial Hypercholesterolemia
- Hypercholesterolemia
- Hypertension
- Vascular Malformations
- Women's Heart Disease
- Sustained Release Drug Delivery

Strategic Goals

Prevention

- Predict and prevent potential impact of extreme environments, posttraumatic stress disorder, and/or infections on cardiovascular health
- Elucidate and prevent the impact of cardiovascular conditions on the heart, brain, arteries, and additional target organs across a patient's life span

Diagnosis

- Develop an affordable genetic testing panel for accurate early detection of associated cardiovascular conditions

- Develop strategies to enable detection of associated cardiovascular conditions before clinical symptoms are apparent

Treatment
- Develop novel therapeutics or advance treatment regimens for associated cardiovascular conditions that address sex/gender or ethnic/racial differences
- Develop less-invasive treatment technologies for associated cardiovascular conditions
- Advance engineered tissue technology for the treatment of associated cardiovascular conditions

Epidemiology
- Identify risk factors that contribute to associated cardiovascular conditions in civilian and/or military populations, particularly those who have sustained combat injuries
- Conduct population-based or outcomes-based research to identify sex/gender or ethnic/racial long-term impacts of associated cardiovascular conditions

Hemorrhage Control and Blood Products

Topic Areas
- Hemorrhage Control
- Pathogen-Inactivated Blood Products
- Platelet-Like Cell Production
- Sustained Release Drug Delivery
- Trauma

Strategic Goals
Diagnosis
- Develop strategies or innovative technologies (to include wearable devices) for early detection of internal bleeding, coagulopathy of trauma, or hypovolemic shock

Treatment
- Develop smart/automated tourniquets or battlefield hemostatic dressings with antimicrobial and/or analgesic effects
- Develop innovative damage control capabilities and solutions for control of non-compressible torso hemorrhage, especially interventions that can be used in austere environments
- Develop and test novel or engineered blood products that add physiological, logistical, and cost advantages over current products

Epidemiology
- Evaluate the effects of current combat blood product transfusion guidelines on immunological status and clinical outcomes
- Determine physiological impacts of blood loss (e.g., walking donors) on the ability to sustain performance in extreme environments

Infectious Diseases

Topic Areas
- Hepatitis B
- Malaria
- Sustained Release Drug Delivery
- Viral Diseases

- Plant-Based Vaccines

Strategic Goals

Foundational Studies

- Improve understanding of long-term complications of infections (e.g., long COVID [coronavirus disease], myalgic encephalomyelitis/chronic fatigue syndrome [ME/CFS], sequelae from combat wounds)

Prevention

- Develop or optimize vaccine strategies, platforms, or compounds, to include active or passive immunoprophylaxis, especially for Dengue, Lassa, and Crimean-Congo Hemorrhagic fever viruses, and beta-coronaviruses

Diagnosis

- Develop diagnostics for early/pre-symptomatic detection of viral diseases, such as novel host-based biomarkers or other predictors of early/pre-symptomatic infection
- Develop strategies for rapid prediction of protective antigens/epitopes
- Identify testable correlates of protection, especially for Dengue, Lassa, and Crimean-Congo Hemorrhagic Fever viruses

Treatment

- Establish new, and expand upon current, clinical networks for therapeutic drug testing to prevent transmission, resistance, or severe/chronic disease

Epidemiology

- Identify strategies for surveillance or develop modeling tools and/or biomarkers to predict outbreaks, epidemics, or treatment resistance

Internal Medicine

Topic Areas

- Ehlers-Danlos Syndrome
- Endometriosis
- Epidermolysis Bullosa
- Focal Segmental Glomerulosclerosis
- Interstitial Cystitis
- Nephrotic Syndrome
- Pancreatitis
- Polycystic Kidney Disease
- Pressure Ulcers
- Sustained Release Drug Delivery

Strategic Goals

Foundational Studies

- Improve understanding of long-term complications and comorbidities of associated diseases and conditions

Diagnosis

- Develop tools for early and accurate diagnosis, including non-invasive methods for associated diseases and conditions
- Develop technologies for tracking progression of associated diseases and conditions

- Develop tools to reduce time between presentation of symptoms and required specialized care for associated disease or condition management

Treatment

- Develop non-surgical treatment options or optimize surgical techniques that improve fertility and reduce endometriosis symptoms/progression
- Develop and test therapeutics or dressings that enhance wound healing
- Advance engineered tissue technology to improve wound healing and transplant outcomes
- Develop and test novel treatments, and/or improve upon existing treatments for associated diseases and conditions

Epidemiology

- Elucidate factors (e.g., medication toxicity, genetic predisposition, infections) that influence development, progression, and outcome of associated diseases and conditions
- Develop surrogate endpoints to accelerate approval of new treatments for associated diseases and conditions
- Conduct patient-centered research to decrease disease burden for military families

Neuroscience

Topic Areas

- Dystonia
- Eating Disorders
- Fragile X
- Friedreich's Ataxia
- Frontotemporal Degeneration
- Hydrocephalus
- Myalgic Encephalomyelitis/Chronic Fatigue Syndrome
- Myotonic Dystrophy
- Non-Opioid Therapy for Pain Management
- Peripheral Neuropathy
- Rett Syndrome
- Sleep Disorders and Restriction
- Suicide Prevention
- Sustained Release Drug Delivery
- Trauma

Strategic Goals

Foundational Studies

- Identify mechanisms underlying neurological diseases and psychological conditions including potential relationships to environmental/neurotoxic exposures, injury, stress, or infections

Prevention

- Develop strategies, including predictive analytics and artificial intelligence, to provide early identification of associated neurological diseases and psychological conditions, with the goal of providing early intervention
- Develop tools to reduce complications of physical and/or psychological trauma

Diagnosis

- Improve diagnostic and/or develop objective diagnostic criteria (e.g., diagnostic biomarkers) for ME/CFS

Treatment

- Develop and evaluate novel treatments, strategies or therapeutic targets, including research to repurpose existing drugs, for associated neurological diseases and psychological conditions
- Develop capabilities to monitor, and therapies or countermeasures to maintain, optimal cognitive functioning and mental resilience in occupational environments or under sleep restriction (e.g., shift work, insufficient sleep, jet lag)
- Develop and test pain therapies that will not affect the cardiorespiratory system and cognitive abilities for use in trauma, battlefield, or resource-limited environments
- Develop and test treatment strategies to manage symptoms and improve quality of life for those affected by associated neurological and psychological conditions

Epidemiology

- Conduct population-based studies to identify risk factors (e.g., military-specific lifestyle) that contribute to onset and progression of associated neurological diseases and psychological conditions

Nutrition and Metabolism

Topic Areas

- Diabetes
- Mitochondrial Disease
- Nutrition Optimization
- Sustained Release Drug Delivery

Strategic Goals

Foundational Studies

- Understand correlations between nutrition and disease susceptibility (e.g., infectious, autoimmune, neurological, metabolic, cardiac)
- Develop and test novel nutrition-based approaches for recovery from injury/illness or to enhance performance in operational environments, extreme climates, or resource-limited settings

Prevention

- Develop evidence-based diet and exercise recommendations to decrease obesity, improve nutrition, and optimize energy balance to prevent metabolic diseases

Diagnosis

- Develop improved diagnostics for metabolic diseases
- Develop tools, devices, and/or strategies to monitor and optimize real-time nutritional intake at the individual level

Treatment

- Develop and test strategies to decrease the burden of treatment regimens, including improved insulin formulations or delivery methods, or smart/automated glucose-monitoring or implantable biosensor systems
- Develop and test novel treatment strategies for mitochondrial diseases, especially those ready to progress to the clinic, including repurposing existing drugs or non-prescription treatment options
- Treat obesity and develop strategies for weight management, especially for Veterans

Orthopaedic Medicine

Topic Areas

- Arthritis
- Fibrous Dysplasia
- Musculoskeletal Disorders (related to acute and chronic bone conditions and injuries)
- Sustained Release Drug Delivery

Strategic Goals

Foundational Studies

- Understand mechanisms underlying the pathobiology of associated musculoskeletal disorders
- Determine factors that lead to accelerated degeneration following joint injuries

Prevention

- Develop strategies for improved care at point of injury to prevent musculoskeletal disorder onset

Diagnosis

- Develop novel tools/technologies for early and precision diagnosis of associated musculoskeletal disorders

Treatment

- Develop and test novel and improved intra-articular treatments for joint injuries
- Develop and test strategies to increase quality of life or halt/slow disease progression, including regenerative medicine approaches and biologics for associated musculoskeletal disorders

Epidemiology

- Conduct patient-reported outcomes research to inform treatment guidelines and improve exercise recommendations to optimize joint longevity

Respiratory Health

Topic Areas

- Pulmonary Fibrosis
- Respiratory Health
- Sustained Release Drug Delivery
- Trauma

Strategic Goals

Foundational Studies

- Determine how airborne hazards, toxins, or nanomaterial exposure cause respiratory injury/disease

Prevention

- Prevent lung injury caused by trauma, transfusion, mechanical ventilation, infection, or hemorrhagic shock

Diagnosis

- Develop and validate sensors to assess environmental and/or physiological levels of exposure to airborne hazards or toxins
- Develop a fieldable toolset to monitor lung dysfunction/failure
- Improve early detection for interstitial lung disease

Treatment

- Develop and test novel treatments, including precision medicine approaches, to slow progression or reverse lung injury/disease
- Develop improved fieldable devices to treat traumatic/acute lung injury in far forward settings, including toolsets to enable correct airway placement, oxygenation in austere settings, or miniature and/or semi-automated ventilator
- Develop novel delivery mechanisms and/or improved pharmaceuticals to prevent/treat high-altitude pulmonary edema (HAPE)

II.B. Award Information

The FY22 PRMRP Clinical Trial Award (CTA) supports the rapid implementation of clinical trials with the potential to have a significant impact on a disease or condition addressed in one of the congressionally directed FY22 PRMRP Topic Areas and FY22 PRMRP Strategic Goals. Clinical trials may be designed to evaluate promising new products, pharmacologic agents (drugs or biologics), devices, clinical guidance, and/or emerging approaches and technologies. Proposed projects may range from small proof-of-concept trials (e.g., pilot, first in human, phase 0) to demonstrate the feasibility or inform the design of more advanced trials through large-scale trials to determine efficacy in relevant patient populations.

Funding from this award mechanism must support a clinical trial. A clinical trial is defined as a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes. For more information, a Human Subject Resource Document is provided at https://cdmrp.army.mil/pubs/pdf/Human%20Subjects%20Resource%20Document.pdf. Principal Investigators (PIs) seeking funding for a preclinical research project should consider one of the other FY22 PRMRP program announcements being offered. For information about these award mechanisms, see https://cdmrp.army.mil/funding/prmrp.

Two different application categories, based on the phase of planning for the clinical trial, are available under this program announcement (summary available in Appendix 3):

- **Planning Phase with Clinical Trial:** This is intended to support the final phase of regulatory activities necessary to initiate the planned clinical trial.
    - The proposed clinical trial must address one of the FY22 PRMRP Topic Areas and one of the FY22 PRMRP Strategic Goals.
    - Funding of the clinical trial will be considered an optional research effort.

- ***Within the 18-month period of performance of the planning phase, recipients are expected to submit an Investigational New Drug/Investigational Device Exemption (IND/IDE) application to the U.S. Food and Drug Administration (FDA) (or equivalent) if required, and obtain an FDA acknowledgment letter (or equivalent), to include submission date and receipt date, and a statement that the FDA (or equivalent) did not raise concerns and/or did not place the clinical trial on hold. The PRMRP will not exercise the option for the initiation of the proposed clinical trial if any of the following milestones are not met (for additional details refer to Attachment 1, Project Narrative):***

  - A copy of the FDA acknowledgment letter, to include submission date and receipt date, and a statement that the FDA did not raise concerns and/or did not place the clinical trial on hold, or

  - A copy of the FDA acknowledgment letter and meeting minutes (pre-IND/pre-IDE and/or Type C) that ascertain the FDA's concurrence with the proposed regulatory approach if a technical or a protocol amendment to an active IND/IDE is necessary to complete the clinical trial, or

  - A copy of the relevant national regulatory agency approval if the clinical trial will be conducted at an international site(s), or

  - Evidence in writing from the Institutional Review Board (IRB) of record, or the FDA, or the national regulatory agency for clinical trials conducted at an international site(s) that the proposed investigational drug/agent/device is exempt or the proposed investigational device qualifies for an abbreviated IDE.

- Research milestones to be accomplished by the end of the planning phase must be clearly defined in the project Statement of Work (SOW) and will be finalized during negotiations. The PI will be required to present an update on progress toward accomplishing research milestones and goals of the project at a Milestone Meeting, to be held in person or virtually, at the discretion of the government, in the National Capital Region. Milestone Meetings will be held nearing the conclusion of the planning phase and will be attended by members of the PRMRP Programmatic Panel, CDMRP staff, and the USAMRAA Grants Officer.

- The agreement to support optional clinical trial efforts will be contingent upon (1) all necessary regulatory approvals obtained under the base award; (2) the availability of funds; and (3) accomplishment of research milestones and goals as determined by the PRMRP Programmatic Panel and USAMRAA Grants Officer.

- Important tasks to consider under the Planning Phase with Clinical Trial include, but are not limited to:

  - Planning for appropriate regulatory approvals (for example, IRB submissions, FDA submissions such as FDA IND/IDE applications, and Department of Defense (DOD) Human Research Protection Office [HRPO] submissions)

- Obtaining IRB and FDA IND/IDE approval for clinical trials involving emergency research whereby exception from informed consent is required ***(under Title 21, Code of Federal Regulations, Part 50.24 [21 CFR 50.24])***
- Developing the clinical protocol
- Establishing access to appropriate patient populations or resources
- Developing training procedures

- **Clinical Trial Only:** This is intended to support a clinical trial having either FDA (or other regulatory agency) approval or an exemption at the time of application submission; the clinical trial is expected to begin no later than 9 months after the award date.

  - If the proposed clinical trial involves the use of a drug that has not been approved by the FDA for the proposed investigational use, then an IND application to the FDA that meets all requirements under 21 CFR 312 may be required. It is the responsibility of the applicant to provide evidence from the IRB of record or the FDA if an IND is not required. If an IND is required, an active IND deemed safe to proceed that covers the proposed trial ***must be in place by the PRMRP Clinical Trial Award application submission deadline (this includes clinical trials requesting exception from informed consent under 21 CFR 50.24).*** The IND should be specific for the product (i.e., the product should not represent a derivative or alternate version of the investigational agent described in the IND application) and indication to be tested in the proposed clinical trial. For more information on IND applications, the FDA has provided guidance at https://www.fda.gov/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/approvalapplications/investigationalnewdrugindapplication/default.htm. More information about the requirements for obtaining approval for a study involving emergency research can be found within the FDA guidance document "*Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors Exception from Informed Consent Requirements for Emergency Research"* at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/exception-informed-consent-requirements-emergency-research.

  - If the investigational product is a device, then IDE application to the FDA that meets all requirements under 21 CFR 812 may be required. It is the responsibility of the applicant to provide evidence from the IRB of record or the FDA if an IDE is not required or if the device qualifies for an abbreviated IDE. If an IDE is required, an active IDE deemed safe to proceed that covers the proposed trial ***must be in place by the PRMRP Clinical Trial Award application submission deadline (this includes clinical trials requesting exception from informed consent under 21 CFR 50.24).*** The IDE should be specific for the device (i.e., should not represent a derivative or modified version of the device described in the IDE application) and indication to be tested in the proposed clinical trial.

  - If the clinical trial of an investigational product will be conducted at international sites, evidence that an application to the relevant national regulatory agency of the host

country(ies) ***has been submitted by the FY22 PRMRP Clinical Trial Award application submission deadline*** is required.

- Refer to Attachment 10, Regulatory Strategy, for additional details on documentation of FDA applications. The government reserves the right to withdraw the application if an active IND or IDE and/or international regulatory approval is necessary but is not in place prior to the application submission deadline.

- ***For the Clinical Trial Only category, a copy of the FDA or relevant national regulatory agency approval, or evidence that the proposed investigational drug/agent/device is exempt or the proposed investigational device qualifies for an abbreviated IDE is required in Attachment 10, Regulatory Strategy.***

- Research milestones to be accomplished throughout each phase of the clinical trial must be clearly defined in the project SOW and will be finalized during negotiations. The government reserves the right to fund the clinical trial under a base award and subsequent optional research phases. Continued funding of the clinical trial and approval of research options will be contingent upon meeting mutually agreed upon milestones and goals as determined by the USAMRAA Grants Officer.

Key Aspects of the FY22 PRMRP CTA:

- **Clinical Trial Start Date:** The proposed clinical trial is expected to begin no later than 9 months after the award date of the Clinical Trial Only or no later than 9 months after exercising the option for the clinical trial in the Planning Phase with Clinical Trial.

- **Impact:** The proposed intervention(s) to be tested should offer significant potential impact for one of the FY22 PRMRP Topic Areas and address one of the FY22 PRMRP Strategic Goals.

- **Preliminary Data are Required:** Inclusion of preliminary data relevant to the proposed clinical trial is required. The proposed clinical trial must be based on a sound scientific rationale that is established through logical reasoning and critical review and analysis of the relevant literature.

- **Study Population:** The application should demonstrate the availability of and access to a suitable patient population that will support a meaningful outcome for the study. The application should include a discussion of how accrual goals will be achieved, as well as the strategy for inclusion of women and minorities in the clinical trial appropriate to the objectives of the study.

- **Intervention Availability and Indication:** The application should demonstrate the documented availability of and access to the drug/compound, device, and/or other materials needed, as appropriate, for the proposed duration of the study. The quality and stability of the product should be documented and commensurate with current FDA manufacturing standards applicable to the type and phase of product being developed (i.e., Quality System Regulation, Good Manufacturing Practice [GMP] guidelines). The application should also

describe the planned indication for the product label, if appropriate, and include an outline of the product development plan required to support that indication.

- **Personnel and Environment:** The application should demonstrate the study team's expertise and experience in all aspects of conducting clinical trials, including appropriate statistical analysis, knowledge of FDA processes (if applicable), and data management. The application should include a study coordinator(s) who will guide the clinical protocol through the local IRB of record and other federal agency regulatory approval processes, coordinate activities from all sites participating in the trial, and coordinate participant accrual. The application should show strong institutional support and, if applicable, a commitment to serve as the FDA regulatory sponsor, ensuring all sponsor responsibilities described in 21 CFR 312, Subpart D, are fulfilled.

- **Statistical Analysis and Data Management Plans:** The application should include a clearly articulated statistical analysis plan, a power analysis reflecting sample size projections that will answer the objectives of the study and a data management plan and use of an appropriate database to safeguard and maintain the integrity of the data. If FDA-regulated, the trial must use a 21 CFR 11-compliant database and appropriate data standards. For more on data standards, see https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/UCM511237.pdf

Funded trials are required to post a copy of the informed consent form used to enroll subjects on a publicly available federal website in accordance with federal requirements described in 32 CFR 219. Funded studies are required to register the study in the National Institutes of Health (NIH) clinical trials registry, www.clinicaltrials.gov, prior to initiation of the study. Refer to the General Application Instructions, Appendix 1, Section B, for further details.

The types of awards made under the program announcement will be assistance agreements. An assistance agreement is appropriate when the federal government transfers a "thing of value" to a "state, local government," or "other recipient" to carry out a public purpose of support or stimulation authorized by a law of the United States instead of acquiring property or service for the direct benefit and use of the U.S. government. An assistance agreement can take the form of a grant or cooperative agreement. The level of involvement on the part of the DOD during project performance is the key factor in determining whether to award a grant or cooperative agreement. If "no substantial involvement" on the part of the funding agency is anticipated, a grant award will be made (31 USC 6304). Conversely, if substantial involvement on the part of the funding agency is anticipated, a cooperative agreement will be made (31 USC 6305), and the award will identify the specific substantial involvement. Substantial involvement may include, but is not limited to, collaboration, participation, or intervention in the research to be performed under the award. The award type, along with the start date, will be determined during the negotiation process.

The anticipated direct costs budgeted for the entire period of performance for an FY22 PRMRP Clinical Trial Award – Planning Phase with Clinical Trial award will not exceed **$500,000** for the planning phase, while the budget for the proposed clinical trial is not restricted to a predetermined cost limit. The requested budget for the clinical trial must be justified and appropriate to the scope proposed.

Applications to the FY22 PRMRP Clinical Trial Award – Clinical Trial Only are not restricted to a predetermined cost limit. The requested budget must be justified and appropriate to the scope of the clinical trial proposed. Refer to Section II.D.5, Funding Restrictions, for detailed funding information.

Awards will be made no later than September 30, 2023. For additional information, refer to Section II.F.1, Federal Award Notices.

The CDMRP expects to allot approximately $52M to fund approximately eight FY22 PRMRP Clinical Trial Award applications. Funding of applications received is contingent upon the availability of federal funds for this program as well as the number of applications received, the quality and merit of the applications as evaluated by scientific and programmatic review, and the requirements of the government. Funds to be obligated on any award resulting from this funding opportunity will be available for use for a limited time period based on the fiscal year of the funds. It is anticipated that awards made from this FY22 funding opportunity will be funded with FY22 funds, which will expire for use on September 30, 2028.

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

- Explanation of how the project addresses an aspect of the target disease/condition/technology that has direct relevance to the health of military Service Members, Veterans, and/or other Military Health System beneficiaries
- Description of how the knowledge, information, products, or technologies gained from the proposed research could be implemented in a dual-use capacity to benefit the civilian population and also address a military need
- Use of military or Veteran populations, samples, or datasets in the proposed research, if appropriate
- Collaboration with DOD or Department of Veterans Affairs (VA) investigators or consultants

Applicants are encouraged to integrate and/or align their research projects with DOD and/or VA research laboratories and programs. Collaboration with the DOD or VA is also encouraged. Potential for future development partnerships with the U.S. Army Medical Materiel Development Activity (https://www.usammda.army.mil) may be available depending on the maturity and impact of the product on the military. 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 within the FY22 PRMRP Topic Areas can be found in Appendix 2.

Use of DOD or VA Resources: If the proposed research involves access to active-duty military patient populations and/or DOD or VA 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 Application Instructions, Appendix 1, for additional information.

Research Involving Human Anatomical Substances, Human Subjects, or Human Cadavers: All DOD-funded research involving new and ongoing research with human anatomical substances, human subjects, or human cadavers must be reviewed and approved by the USAMRDC Office of Research Protections (ORP), HRPO, prior to research implementation. This administrative review requirement is in addition to the local IRB or Ethics Committee (EC) review. Local IRB/EC approval at the time of submission is ***not*** required. Allow up to 3 months to complete the HRPO regulatory review and approval process following submission of ***all required and complete*** documents to the HRPO. Refer to the General Application Instructions, Appendix 1, and the Human Research Protections Office Resources and Overview document available on the electronic Biomedical Research Application Portal (eBRAP) "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) for additional information.

Multi-Institutional Clinical Trials: If the proposed research involves more than one institution, plans for the multi-institutional structure governing the research protocol(s) should be outlined. A written plan for single IRB review arrangements must be provided for cooperative research conducted in the United States. 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. The master protocol and consent form must be reviewed by the HRPO prior to distribution to the additional sites for IRB/EC review. Communication and data transfer 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 trials.

II.C. Eligibility Information

II.C.1. Eligible Applicants

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

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

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

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

Intramural DOD Organization: A DOD laboratory, DOD military treatment facility, and/or DOD activity embedded within a civilian medical center. ***Intramural Submission: An application submitted by a DOD organization for an intramural investigator working within a DOD laboratory or military treatment facility or in a DOD activity embedded within a civilian medical center.***

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

II.C.1.b. Principal Investigator

Investigators at or above the level of Assistant Professor (or equivalent) may be named by the organization as the PI on the application.

Each investigator may be named on only one FY22 PRMRP CTA application as a PI.

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

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

II.C.2. Cost Sharing

Cost sharing/matching is not an eligibility requirement.

II.C.3. Other

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

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

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

II.D. Application and Submission Information

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

II.D.1. eBRAP and Grants.gov

eBRAP (https://ebrap.org) is a secure web-based system that allows PIs to submit their pre-applications, view and verify extramural full applications submitted to Grants.gov (https://grants.gov), receive communications from the CDMRP, and submit documentation during award negotiations and throughout the period of performance. eBRAP also allows intramural organizations to submit full applications following pre-application submission.

Grants.gov is a federal system required to be utilized by agencies to receive and process extramural grant applications. Full applications may only be submitted to Grants.gov after submission of a pre-application through eBRAP.

Contact information for the eBRAP Help Desk and the Grants.gov Contact Center can be found in Section II.G, Federal Awarding Agency Contacts.

Extramural Submission:

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

Intramural DOD Submission:

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

Note: Applications from an intramural DOD organization or from an extramural federal government organization may be submitted to Grants.gov through a research foundation.

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

Submission is a two-step process requiring both ***pre-application*** (eBRAP.org) and ***full application*** (eBRAP.org or Grants.gov) as indicated below. The submission process should be started early to avoid missing deadlines. There are no grace periods. Full application submission guidelines differ for extramural (Grants.gov) and intramural (eBRAP.org) organizations (refer to Table 1, Full Application Guidelines).

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

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

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

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

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

When starting the pre-application, PIs should ensure that they have selected the appropriate application category:

- "No option" for the Clinical Trial Only, *or*
- "With Planning Phase" for the Planning Phase with Clinical Trial

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

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

PIs with an ORCID identifier should enter that information in the appropriate field in the "My Profile" tab in the "Account Information" section of eBRAP.

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

- **Tab 1 – Application Information**

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

  Select the application category that is most appropriate for the proposed work (as described in Section II.A.1, FY22 PRMRP Topic Areas and Strategic Goals or summarized in Appendix 3).

Select the FY22 PRMRP Portfolio addressed by the proposed research.

Select the FY22 PRMRP Topic Area addressed by the proposed research.

Select the FY22 PRMRP Continuum of Care category addressed by the proposed research.

Select the FY22 PRMRP Strategic Goal addressed by the proposed research.

- **Tab 2 – Application Contacts**

  Enter contact information for the PI. Enter the organization's Business Official responsible for sponsored program administration (the "person to be contacted on matters involving this application" in Block 5 of the Grants.gov SF424 Research & Related Form). The Business Official must be either selected from the eBRAP list or invited in order for the pre-application to be submitted.

  Select the performing organization (site at which the PI will perform the proposed work) and the contracting organization (organization submitting on behalf of the PI, which corresponds to Block 5 on the Grants.gov SF424 Research & Related Form), and click on "Add Organizations to this Pre-application." The organization(s) must be either selected from the eBRAP drop-down list or invited in order for the pre-application to be submitted.

  It is recommended that PIs identify an Alternate Submitter in the event that assistance with pre-application submission is needed.

- **Tab 3 – Collaborators and Key Personnel**

  Enter the name, organization, and role of all collaborators and key personnel associated with the application.

  FY22 PRMRP Programmatic Panel members should not be involved in any pre-application or application. For questions related to panel members and pre-applications or applications, refer to Section II.H.2.c, Withdrawal, or contact the eBRAP Help Desk at help@eBRAP.org or 301-682-5507.

- **Tab 4 – Conflicts of Interest**

  List all individuals other than collaborators and key personnel who may have a conflict of interest in the review of the application (including those with whom the PI has a personal or professional relationship).

- **Tab 5 – Pre-Application Files**

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

  - **Preproposal Narrative (five-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:

- **Research Idea:** Describe how the proposed project relates to an FY22 PRMRP Topic Area. Additionally, describe how the proposed research project addresses an FY22 PRMRP Strategic Goal. Describe the ideas and scientific rationale on which the proposed clinical trial is based; include relevant literature citations. State the clinical intervention, subject population(s), phase of the clinical trial proposed, regulatory status, and sponsor.

  Briefly describe the project readiness to include the level of scientific evidence that supports the initiation of the proposed clinical trial, and the availability of, and accessibility to, the intervention and the proposed subject population.

- **Research Strategy:** Concisely state the project's hypothesis and/or objectives and specific aims. Briefly describe the experimental approach, including study design and endpoints/outcome measures.

- **Personnel:** Briefly state the qualifications of the PI and key personnel to perform the clinical trial. Note any DOD- or VA-relevant collaborations.

- **Impact and Relevance to Military Health:** Describe how the proposed work will have an impact on accelerating the movement of a promising intervention into clinical application. Explain how the project is relevant to the healthcare needs of military Service Members, Veterans, and/or beneficiaries.

- **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.

  - **Budget:** Provide an estimated budget for direct costs for the clinical trial, and if applicable, the planning phase, and include a brief justification of those costs. A detailed budget is not required at this time but will be required if invited to submit a full application.

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

- **Tab 6 – Submit Pre-Application**

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

Pre-Application Screening

- **Pre-Application Screening Criteria**

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

  - **Research Idea:** The degree to which the proposed clinical trial addresses an important question in one of the FY22 PRMRP Topic Areas and one of the FY22 PRMRP Strategic Goals. How well the scientific rationale is supported, and how well the background and availability of and accessibility to resources and subject population indicates the research is ready to move into the phase of clinical trial proposed.

  - **Research Strategy:** How well the specific aims, patient population, and proposed methodology will address the hypothesis and/or reach the desired objectives.

  - **Personnel:** How the background and experience of the PI and other key personnel are appropriate to successfully complete the clinical trial.

  - **Budget:** How the estimated budget and justification are reasonable for the proposed work.

  - **Impact and Relevance to Military Health:** The degree to which the proposed clinical trial, if successful, will have an impact on accelerating the movement of a promising intervention into clinical application. How well the research will address a healthcare issue relevant to military Service Members, Veterans, and/or beneficiaries.

- **Notification of Pre-Application Screening Results**

  Following the pre-application screening, PIs will be notified as to whether or not they are invited to submit applications; however, they will not receive feedback (e.g., a critique of strengths and weaknesses) on their pre-application. The estimated timeframe for notification of invitation to submit an application is indicated in Section I, Overview of the Funding Opportunity. Invitations to submit a full application are based on the Pre-Application Screening Criteria listed above.

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

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

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

Each application submission must include the completed full application package for this program announcement. The full application package is submitted by the Authorized Organizational Representative through Grants.gov (https://grants.gov/) for extramural organizations or through eBRAP (https://ebrap.org/) for intramural organizations. See Table 1 below for more specific guidelines.

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

Extramural organizations must submit full applications through Grants.gov. Applicants must create a Grants.gov Workspace for submission, which allows the application components to be completed online and routed through the applicant organization for review prior to submission. Applicants may choose to download and save individual PDF forms rather than filling out webforms in Workspace. A compatible version of Adobe Reader **must** be used to view, complete, and submit an application package consisting of PDF forms. If more than one person is entering text into an application package, the ***same version*** of Adobe Reader software should be used by each person. Check the version number of the Adobe software on each user's computer to make sure the versions match. Using different versions of Adobe Reader may cause submission and/or save errors – even if each version is individually compatible with Grants.gov. Refer to the General Application Instructions, Section III, and the "Apply For Grants" page of Grants.gov (https://www.grants.gov/web/grants/applicants/apply-for-grants.html) for further information about the Grants.gov Workspace submission process. Submissions of extramural applications through eBRAP may be withdrawn.

Do not password protect any files of the application package, including the Project Narrative.

Table 1. Full Application Submission Guidelines

Extramural Submissions	Intramural DOD Submissions
Application Package Location	
Download application package components for W81XWH-22-PRMRP-CTA from Grants.gov (https://grants.gov/) and create a Grants.gov Workspace. Workspace allows online completion of the application components and routing of the application package through the applicant organization for review prior to submission.	Download application package components for W81XWH-22-PRMRP-CTA from eBRAP (https://ebrap.org).

Extramural Submissions	Intramural DOD Submissions
Full Application Package Components	
SF424 Research & Related Application for Federal Assistance Form: Refer to the General Application Instructions, Section III.A.1, for detailed information.	**Tab 1 – Summary:** Provide a summary of the application information. **Tab 2 – Application Contacts:** This tab will be pre-populated by eBRAP; add Authorized Organizational Representative.
Descriptions of each required file can be found under Full Application Submission Components: • Attachments • Research & Related Personal Data • Research & Related Senior/Key Person Profile (Expanded) • Research & Related Budget • Project/Performance Site Location(s) Form • Research & Related Subaward Budget Attachment(s) Form	**Tab 3 – Full Application Files:** Upload files under each Application Component in eBRAP. Descriptions of each required file can be found under Full Application Submission Components: • Attachments • Key Personnel • Budget • Performance Sites **Tab 4 – Application and Budget Data:** Review and edit proposed project start date, proposed end date, and budget data pre-populated from the Budget Form.
Application Package Submission	
Create a Grants.gov Workspace. Add participants (investigators and Business Officials) to Workspace, complete all required forms, and check for errors before submission. **Submit a Grants.gov Workspace Package.** An application may be submitted through Workspace by clicking the "Sign and Submit" button on the "Manage Workspace" page, under the "Forms" tab. Grants.gov recommends submission of the application package **at least 24-48 hours prior to the close date** to allow time to correct any potential technical issues that may disrupt the application submission. ***Note:*** If either the Project Narrative or the budget fails eBRAP validation or needs to be modified, an updated Grants.gov application package must be submitted via Grants.gov as a "Changed/ Corrected Application" with the previous Grants.gov Tracking ID ***prior to*** the application submission deadline. ***Do not***	**Submit package components to eBRAP (https://ebrap.org).** **Tab 5 – Submit/Request Approval Full Application:** After all components are uploaded and prior to the full application submission deadline, enter your password in the space provided next to "Enter Your Password Here" and press the "Submit Full Application" button. eBRAP will notify your Resource Manager/Comptroller/Task Area Manager or equivalent Business Official by email. ***Do not password protect any files of the application package, including the Project Narrative.***

Extramural Submissions	Intramural DOD Submissions
password protect any files of the application package, including the Project Narrative.	
Application Verification Period	
The full application package submitted to Grants.gov may be viewed and modified in eBRAP until the end of the application verification period. During the application verification period, the full application package may be modified ***with the exception of the Project Narrative and Research & Related Budget Form***.	After eBRAP has processed the full application, the organizational Resource Manager/Comptroller/Task Area Manager or equivalent Business Official and PI will receive email notification of this status and will be able to view and modify application components in eBRAP. During the application verification period, the full application package may be modified ***with the exception of the Project Narrative and Research & Related Budget Form***. Your Resource Manager/Comptroller/Task Area Manager or equivalent Business Official should log into eBRAP to review and to approve prior to the application verification deadline.
Further Information	
Tracking a Grants.gov Workspace Package. After successfully submitting a Workspace package, a Grants.gov Tracking Number is automatically assigned to the package. The number will be listed on the "Confirmation" page that is generated after submission. Refer to the General Application Instructions, Section III, for further information regarding Grants.gov requirements.	Refer to the General Application Instructions, Section IV, for further information regarding eBRAP requirements.

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

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

- **Extramural Applications Only**

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

- **Extramural and Intramural Applications**

  Attachments:

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

  For all attachments, ensure that the file names are consistent with the guidance. Attachments will be rejected if the file names are longer than 50 characters or have incorrect file names that contain characters other than the following: A-Z, a-z, 0-9, underscore, hyphen, space, and period. In addition, there are file size limits that may apply in some circumstances. Individual attachments may not exceed 20 megabytes (MB), and the file size for the entire full application package may not exceed 200 MB.

  - **Attachment 1: Project Narrative (page limit varies as noted below -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 to expand the Project Narrative and could confer an unfair competitive advantage is prohibited and may result in administrative withdrawal of the application.

    The Project Narrative is NOT the formal clinical trial protocol. Instead, all essential elements of the proposed clinical trial necessary for scientific review must be included as directed in Attachment 1 (the Project Narrative) and Attachments 7–10 described below. Failure to submit these attachments as part of the application package will result in rejection of the entire application

    Describe the proposed project in detail using the outline below.

    Planning Phase, if applicable (eight-page limit):

    - Outline the plan for obtaining IND/IDE status (or other FDA approvals) during the 18-month or less period of performance if an IND or IDE is required. If the product is not currently FDA-approved, -licensed, or -cleared, state the planned indication/use. Indicate whether the product would be classified as a drug, device, biologic, or combination product. Indicate whether the FDA has confirmed the proposed classification. Identify the regulatory sponsor. Include a signed sponsor commitment letter acknowledging the regulatory sponsor's understanding of all sponsor responsibilities, as defined in 21 CFR 312.2 (https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=312.3), and commitment to oversee execution of the study.

    - Describe the overall regulatory strategy and product development plan that will support the planned product indication. Include a description of the numbers and types of studies proposed to reach approval, licensure, or clearance, the types of FDA meetings that will be held/planned, and the submission filing strategy. Include

considerations for compliance with current GMP, Good Laboratory Practice (GLP), and Good Clinical Practice (GCP) guidelines.

- If applicable, describe how the planning phase will enable finalization or completion of Study Procedures and/or Clinical Monitoring Plan.

- If applicable, describe how the planning phase will enable finalization or completion of Study Population, Inclusion/Exclusion Criteria, Recruitment Process, Informed Consent Process, and/or Screening Procedures.

- If applicable, describe how the planning phase will enable finalization or completion of Questionnaires and Other Data Collection Instruments.

- If applicable, describe how the planning phase will enable finalization or completion of Organizational Chart, Study Personnel Description, and/or Study Management Plan.

- If applicable, describe how the planning phase will enable finalization or completion of Data Management and/or Laboratory Evaluations.

- If applicable, describe how the planning phase will enable finalization or completion of the Regulatory Strategy and Product Development Plan to support the planned product indication.

- Describe plans for other administrative approvals (e.g., IRB, DOD HRPO).

Clinical Trial (required for all applications; 20-page limit): If applying for the Planning Phase with Clinical Trial, begin this section on a new page. If the clinical trial includes the planning phase, the total page limit is 28 pages (8 pages for the planning phase plus 20 pages for the clinical trial).

- **Background:** Describe how the proposed project addresses an FY22 PRMRP Topic Area. Additionally, describe how the proposed research project relates to an FY22 PRMRP Strategic Goal. Describe in detail the rationale for the study. Provide a literature review and analysis. Describe the preliminary studies and/or preclinical data that led to the development of the proposed clinical trial. Provide a summary of other relevant ongoing, planned, or completed clinical trials and describe how the proposed study differs. Include a discussion of any current clinical use of the intervention under investigation, and/or details of its study in clinical trials for other indications (as applicable). The background section should clearly support the choice of study variables and should explain the basis for the study questions and/or study hypotheses. This section should establish the relevance of the study and explain the applicability of the proposed findings.

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

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

- **Study Design:** Describe the type of study to be performed (e.g., treatment, prevention, diagnostic), the study phase or class (if applicable), and the study model (e.g., single group, parallel, crossover). Outline the proposed methodology in sufficient detail to show a clear course of action.

  - Identify the intervention to be tested and describe the projected results (refer to Attachment 7, Intervention, for additional details).

  - Define the primary and any secondary or interim endpoints/outcome measures, outline why they were chosen, and describe how and when they will be measured. Include a description of appropriate controls. Outline the timing and procedures planned during the follow-up period.

  - Describe and justify the study population and the inclusion and exclusion criteria that will be used to meet the needs of the proposed clinical trial.

  - Describe the methods that will be used to recruit a sample of human subjects from the accessible population (e.g., convenience, simple random, stratified random; refer to Attachment 8, Human Subject Recruitment and Safety Procedures, for additional details).

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

  - Outline whether subjects, clinicians, data analysts, and/or others will be blinded during the study. Describe any other measures to be taken to reduce bias.

  - If using psychometric measures, describe their reliability and validity.

  - Describe potential problem areas and discuss alternative methods/approaches that may be employed to overcome them. Estimate the potential for subject loss to follow-up, and how such loss will be handled/mitigated.

- **Statistical Plan and Data Analysis:** Describe the statistical model and data analysis plan with respect to the study objectives. Specify the approximate number of human subjects to be enrolled. If multiple study sites are involved, state the approximate number to be enrolled at each site. Include a complete power analysis to demonstrate that the sample size is appropriate to meet the objectives of the study and all proposed correlative studies. 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. Ensure sufficient information is provided to allow thorough evaluation of all statistical calculations during review of the application.

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

  There are no page limits for any of these components unless otherwise noted. Include only those components described below; inclusion of items not requested or viewed as an extension of the Project Narrative will result in the removal of those items or may result in administrative withdrawal of the application.

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

  - **List of Abbreviations, Acronyms, and Symbols:** Provide a list of abbreviations, acronyms, and symbols.

  - **Facilities, Existing Equipment, and Other Resources:** Describe the facilities and equipment available for performance of the proposed project and any additional facilities or equipment proposed for acquisition at no cost to the award. Indicate whether or not government-furnished facilities or equipment are proposed for use. If so, reference should be made to the original or present government award under which the facilities or equipment items are now accountable. There is no form for this information.

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

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

  - **Letters of Collaboration (if applicable):** Provide a signed letter from each collaborating individual or organization that demonstrates that the PI has the support or resources necessary for the proposed work. If an investigator at an intramural organization is named as a collaborator on an application submitted through an extramural organization, the application must include a letter from the collaborator's

Commander or Commanding Officer at the intramural organization that authorizes the collaborator's involvement.

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

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

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

- **Data and Research Resources Sharing Plan:** Describe how data and resources generated during the performance of the project will be shared with the research community. Refer to the General Application Instructions, Appendix 2, Section K, for more information about the CDMRP expectations for making data and research resources publicly available.

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

- **Use of VA Resources (if applicable):** Provide a letter of support from the VA Facility Director(s) or individual designated by the VA Facility Director(s), such as the 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. For VA PIs, if the VA non-profit corporation is not identified as the applicant institution for administering the funds, include a letter from the VA ACOS/R&D confirming this arrangement and identifying the institution that will administer the funds associated with the proposed research.

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

  Technical Abstract (one-page limit): Technical abstracts should be written using the outline below. Programmatic reviewers typically do not have access to the full application and rely on the technical abstract for appropriate description of the project's key aspects. Therefore, clarity and completeness within the space limits of the technical abstract are highly important.

  - **Background:** Present the ideas and rationale behind the proposed clinical trial.

- **Relevance to Topic Area(s):** Describe how the proposed research project addresses an FY22 PRMRP Topic Area. Additionally, state the relevance of the project to an FY22 PRMRP Strategic Goal.

- **Hypothesis/Objective(s):** State the hypothesis to be tested and/or objective(s) to be reached.

- **Specific Aims:** State the specific aims of the study.

- **Study Design:** Briefly describe the study design, including appropriate controls.

- **Clinical Impact:** Briefly describe how the proposed project will have an impact on research and patient care in the specified disease(s)/condition(s).

- **Relevance to Military Health:** Describe the study's relevance to military health.

Lay Abstract (one-page limit): Lay abstracts should be written using the outline below. ***Do not duplicate the technical abstract.***

- Clearly describe the objectives and rationale for the proposed study and intervention in a manner readily understood by readers without a background in science or medicine.

- Describe how the proposed research project addresses an FY22 PRMRP Topic Area. Additionally, state the FY22 PRMRP Strategic Goal addressed by the proposed research project.

- Describe the ultimate applicability and impact of the research.

  - What types of patients will it help, and how will it help them?

  - What are the potential clinical applications and benefits?

- **Attachment 4: Statement of Work (no-page limit): Upload as "SOW.pdf".** The suggested SOW format and examples specific to different types of research projects are available on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm). Recommended strategies for assembling the SOW can be found at https://ebrap.org/eBRAP/public/Program.htm. For the FY22 PRMRP CTA mechanism, refer to the "Suggested SOW Strategy Clinical Research" document for guidance on preparing the SOW and use the blank SOW format titled "Suggested SOW Format". The SOW must be in PDF format prior to attaching.

  The SOW should include a list of major tasks that support the proposed specific aims, followed by a series of subtasks related to the major tasks and milestones within the period of performance. ***If applying for the Planning Phase with Clinical Trial, two SOWs should be uploaded as a single attachment: The first should describe the major tasks for the planning phase, and the second, beginning on a new page, should describe the major tasks for the proposed clinical trial.*** The SOW should describe only

the work for which funding is being requested by this application and, as applicable, should also:

- Include the name(s) of the key personnel and contact information for each study site/ subaward site.
- Indicate the number of research subjects and/or human anatomical samples projected or required for each task and at each site. Refer to the General Application Instructions, Appendix 1, for additional information regarding regulatory requirements.
- For studies with prospective accrual of human subjects, indicate quarterly enrollment targets.
- If applicable, indicate timelines required for regulatory approvals relevant to human subjects research (e.g., IND and IDE applications) by the FDA or other government agency.

- **Attachment 5: Impact Statement (two-page limit): Upload as "Impact.pdf".**
  - Describe how the proposed clinical trial will address an FY22 PRMRP Topic Area and an FY22 PRMRP Strategic Goal. Identify the volunteer population(s) that will participate in the proposed intervention, describe how they represent the target population that would benefit from the intervention, and describe the potential impact and anticipated outcomes of the proposed clinical trial on the lives and health of the target population with regard to the FY22 PRMRP Topic Area(s) addressed.
  - ***Describe the short-term impact:*** Detail the anticipated outcomes that will be directly attributed to the results of the proposed clinical trial and how they will provide/ improve short-term benefits for individuals.
  - ***Describe the long-term impact:*** Explain the long-range vision for implementation of the intervention in the clinic or field, and describe the anticipated long-term benefits for the targeted population, including impacts on patient care and/or quality of life.
  - Describe any relevant controversies or treatment issues that will be addressed by the proposed clinical trial.
  - Describe any potential issues that might limit the impact of the proposed clinical trial.
  - Describe how the intervention compares with currently available interventions and/or standards of care.
- **Attachment 6: Relevance to Military Health Statement (one-page limit): Upload as "MilRel.pdf".** Describe how the proposed study is responsive to the healthcare needs of military Service Members, Veterans, and/or beneficiaries. Provide information about the incidence and/or prevalence of the disease or condition in the general population as well as in military Service Members, Veterans, and/or beneficiaries.

- If active-duty military, military families, and/or Veteran population(s) or datasets will be used in the proposed research project, describe the population(s)/dataset(s) and the appropriateness of the population(s)/dataset(s) for the proposed study. If a non-military population will be used for the proposed research project, explain how the population simulates the targeted population (i.e., military Service Members, Veterans, and/or beneficiaries).

- If applicable, show how the proposed research project aligns with DOD and/or VA areas of research interests. 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 7: Intervention (no page limit): Upload as "Intervention.pdf".** The Intervention attachment should include the components listed below.

  - **Description of the Intervention:** Identify the intervention to be tested and describe the particular outcomes. 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. Description of devices should include general concept of design, detailed operational instructions, any potential risks to users, and intended benefits. Other types of interventions should be fully described. Indicate who holds the intellectual property rights to the intervention, if applicable, and how the PI has obtained access to those rights for conduct of the clinical trial.

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

  - **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 GLP and GMP guidelines and other regulatory considerations will be established, monitored, and maintained, as applicable.

  - **Clinical Monitoring Plan:** Describe how the study will be conducted by and monitored for current ICH E6 (International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use) GCP compliance by an independent clinical trial monitor (or clinical research associate).

The monitoring plan should describe the types of monitoring visits to be conducted, the intervals (based on level of risk), how corrective actions will be reported to the Sponsor and PI, and how they will be corrected and prevented by the clinical trial site/PI.

- **Attachment 8: Human Subject Recruitment and Safety Procedures (no page limit): Upload as "HumSubProc.pdf".** The Human Subject Recruitment and Safety Procedures attachment should include the components listed below.

  - **Study Population:** Describe the target population (to whom the study findings will be generalized) and the nature, approximate number, and pertinent demographic characteristics of the accessible population at the study site(s) (population from whom the sample will be recruited/drawn). Provide a table of anticipated enrollment counts at each study site. Demonstrate that the research team has access to the proposed study population at each site, and describe the efforts that will be made to achieve accrual goals. Furthermore, discuss past efforts in recruiting human subjects from the target population for previous clinical trials (if applicable). Address any potential barriers to accrual and plans for addressing unanticipated delays, including a mitigation plan for slow or low enrollment or poor retention. Identify ongoing clinical trials that may compete for the same patient population and how they may impact enrollment progress. Provide justification related to the scientific goals of the proposed study for limiting inclusion of any group by age, race, ethnicity, or sex/gender. ***For clinical trials proposing to include military personnel, refer to the General Application Instructions, Appendix 1, for more information.***

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

  - **Women and Minorities in the Study:** Consistent with the Belmont Report, "Ethical Principles and Guidelines for the Protection of Human Subjects," and congressional legislation, special attention is given to inclusion of women and/or minorities in studies funded or supported by the USAMRDC. This policy is intended to promote equity both in assuming the burdens and in receiving the benefits of human subjects research. Describe the strategy for the inclusion of women and minorities in the clinical 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) with the proposed enrollment distributed on the basis of sex/gender, race, and ethnicity. The Public Health Service (PHS) Inclusion Enrollment Report is a three-page fillable PDF form, which can be downloaded from eBRAP at https://ebrap.org/eBRAP/public/Program.htm.

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

  - Describe the recruitment process in detail. Address who will identify potential human subjects, who will recruit them, and what methods will be used to recruit them.

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

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

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

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

  - 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 trial. If applicable, refer to the General Application Instructions, Appendix 1, for more information.

- ***Assent:*** If minors or other populations that cannot provide informed consent are included in the proposed clinical trial, a plan to obtain assent (agreement) from those with capacity to provide it, or a justification for a waiver of assent, should be provided. PIs should consult with their local IRB to identify the conditions necessary for obtaining assent.

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

– **Risks/Benefits Assessment:**

- **Foreseeable risks:** Clearly identify all study risks, including potential safety concerns and adverse events. Study risks include any risks that the human subject is exposed to as a result of participation in the clinical trial. Consider psychological, legal, social, and economic risks as well as physical risks. Consider how the proposed clinical trial might affect the daily lives of the individual human subjects participating in the study. 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 FDA (if applicable) will be managed and conducted.

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

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

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

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

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

- **Attachment 9: Data Management (no page limit): Upload as "Data_Manage.pdf".** The Data Management attachment should include the components listed below.

  - **Data Management:** Describe all methods used for data collection, including the following:

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

    - **Confidentiality:**

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

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

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

    - **Data capture, verification, and disposition:** Describe how data will be captured and verified. Describe where data (both electronic and hard copy) will be stored, who will keep the data, how the data will be stored, the process for locking the database at study completion, and the length of time data will be stored. Describe the proposed database, how it will be developed and validated, and its capability to safeguard and maintain the integrity of the data. Describe the database lock process. For FDA-regulated studies, compliance with 21 CFR 11 and appropriate data standards (such as those established by the Clinical Data Interchange Standards Consortium) are required.

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

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

- **Laboratory Evaluations:**

  - **Specimens to be collected, schedule, and amount:** All specimens that will be collected for study purposes must be clearly stated. The collection schedule and amount of material collected must also be clearly described.

  - **Evaluations to be made:** Describe all evaluations that will be made for study purposes. Explain how the results of laboratory evaluations will be used to meet the objectives of the study (or to monitor safety of human subjects).

  - **Storage:** Describe specimen storage, including location of storage, how long specimens will be stored, any special conditions required, labeling, and specimen disposition. Outline the plan to store specimens for future use, including considerations for informed consent and providing human subjects with an opportunity to decline participation in the study.

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

- **Attachment 10: Regulatory Strategy (no page limit): If submitting multiple documents, start each document on a new page. Combine and upload as a single file named "Regulatory.pdf".** Answer the following questions and provide supporting documentation as applicable.

  - State the product/intervention name.

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

  - For investigator-sponsored regulatory exemptions (e.g., IND, IDE) provide evidence of institutional support. Provide evidence that the clinical trial does not require regulation by the FDA. If the clinical trial will be conducted at international sites, provide equivalent information relevant to the regulatory requirements of the host country(ies). No further information for this attachment is required.

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

  - State whether the product is FDA-approved, -licensed, or -cleared, and marketed in the 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 FDA-approved, -licensed, or -cleared, state the planned indication/use. Indicate whether the product would be classified as a drug, device, biologic, or combination product. Indicate whether the FDA has confirmed the proposed classification. Identify the regulatory sponsor. Include a signed sponsor commitment letter acknowledging the regulatory sponsor's understanding of all sponsor responsibilities and commitment to oversee execution of the study.

For a Clinical Trial Only submission:

- ***If an IND or IDE is required, the application must be submitted to the FDA prior to the FY22 PRMRP CTA application submission deadline (this includes clinical trials requesting exception from informed consent under 21 CFR 50.24).*** The IND or IDE should be specific for the investigational product (i.e., not a derivative or alternate version of the product) and indication to be tested in the proposed clinical trial. Provide the date of submission, the application number, and a copy of the FDA letter acknowledging the submission. If there are any existing cross-references in place, provide the application number(s) and associated sponsor(s). Provide an explanation of the status of the application (e.g., past the critical 30-day period, pending response to questions raised by the FDA, on clinical hold, on partial clinical hold). If the IND or IDE application has been placed on clinical hold or partial hold, explain the conditions that must be met for release of the hold. Provide a summary of any previous meetings with the FDA on development of this product. A copy of the Agency meeting minutes should be included if available. Provide copies of communications from the FDA relevant to the most recent status of the IND or IDE application.

- If available, provide a copy of the communication from the FDA indicating the IND or IDE application is active/safe to proceed.

- If an active IND or IDE for the investigational product is in effect, but an amendment is needed to include the proposed trial, describe the type and nature of the amendment(s) and the timeline for submission. Indicate whether the amendment increases the risk of the intervention.

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

- Provide the current status for manufacturing development (e.g., manufacturer's name, GMP-compliant lots available, status of stability testing), non-clinical development (e.g., test facility name, status of pivotal GLP toxicology studies to support phase 1 testing, etc.), 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/label. Include a description of the numbers and types of studies proposed to reach approval, licensure, or clearance, the types of FDA meetings that will be held/planned, and the submission filing strategy. Include considerations for compliance with current GMP, GLP, and GCP guidelines.

- **Attachment 11: Study Personnel and Organization (no page limit): Start each document on a new page. Combine into one document and upload as "Personnel.pdf".** The Study Personnel and Organization attachment should include the components listed below.

  If the **Planning Phase** application category is chosen and the **Study Personnel and Organization** are not identified, describe how the planning phase will enable finalization or completion of the components listed below.

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

  - **Study Personnel Description:** Briefly describe the composition of the study team, including roles of the individuals listed in the organizational chart on the project. Study coordinator(s) should be included. Describe how the levels of effort for each individual are appropriate to successfully support the proposed research. Describe relevant background and qualifications that demonstrate appropriate expertise to accomplish the proposed work, including previous interactions with the FDA, if applicable.

  - **Study Management Plan:** Provide a plan for ensuring the standardization of procedures among staff and across sites (if applicable). If the proposed clinical trial is cooperative (i.e., involving more than one institution), clearly describe the multi-institutional structure governing the research protocol(s) across all participating institutions. Provide a regulatory submission plan for the master protocol and master consent form by the lead institution. A single IRB is required for all institutions located in the United States that are engaged in cooperative research. If applicable, describe how communication and data transfer between the collaborating institutions will occur, as well as how data, specimens, and/or imaging products obtained during the study will be handled and shared.

- **Attachment 12: Questionnaires and Other Research Data Collection Instruments, if applicable (no page limit): Upload as "Data_Collection.pdf".** The Questionnaires and Other Research Data Collection Instruments attachment should 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.

- **Attachment 13: Transition Plan (three-page limit): Upload as "Transition.pdf".** Describe/discuss the methods and strategies proposed to move the intervention to the next phase of development (clinical trials, commercialization, and/or delivery to the civilian or military market) after successful completion of the award. Applicants are encouraged to work with their organization's Technology Transfer Office (or equivalent) to develop the transition plan. PIs are encouraged to explore developing relationships with industry and/or other funding agencies to facilitate moving the product into the next phase of development. The post-award transition plan should include the components listed below.

  - Details of the funding strategy to transition to the next level of development and/or commercialization (e.g., specific industry partners, specific funding opportunities to be applied for). Include a description of collaborations and other resources that will be used to provide continuity of development.

  - For knowledge products, a description of collaborations and other resources that will be used to provide continuity of development, including proposed development or modification of clinical practice guidelines and recommendations, provider training materials, patient brochures, and other clinical support tools, scientific journal publications, models, simulations, and applications. (A "knowledge product" is a non-materiel product that addresses an identified need, topic area, or capability gap; is based on current evidence and research; aims to transition into medical practice, training, tools, or to support materiel solutions [systems to develop, acquire, provide, and sustain medical solutions and capabilities]; and educates or impacts behavior throughout the continuum of care, including primary prevention of negative outcomes.)

  - A brief schedule and milestones for transitioning the intervention (e.g., next-phase clinical trials, commercialization, delivery to the military or civilian market, incorporation into clinical practice, and/or approval by the FDA).

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

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

- **Attachment 14: Representations, if applicable (extramural submissions only): Upload as "RequiredReps.pdf".** All extramural applicants must complete and submit the Required Representations template available on eBRAP (https://ebrap.org/eBRAP/public/Program.htm). For more information, see the General Application Instructions, Appendix 5, Section B, Representations.

- **Attachment 15: Suggested Collaborating DOD Military Facility Budget Format, if applicable: Upload as "MFBudget.pdf".** If a military facility (Military Health System facility, research laboratory, medical treatment facility, dental treatment facility, or a DOD activity embedded with a civilian medical center) will be a collaborator in performance of the project, complete a separate budget using "Suggested Collaborating DOD Military Facility Budget Format," available for download on the eBRAP "Funding Opportunities & Forms" web page (https:/ebrap.org/eBRAP/public/Program.htm), including a budget justification, for each military facility as instructed. The costs per year should be included on the Grants.gov Research & Related Budget Form under subaward costs. Refer to the General Application Instructions, Section III.A.8, for detailed information.

- **Extramural and Intramural Applications**

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

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

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

  - PI Biographical Sketch (five-page limit): Upload as "Biosketch_LastName.pdf". The suggested biographical sketch format is available on the "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) in eBRAP. The NIH Biographical Sketch may also be used. All biographical sketches should be submitted in uneditable PDF format.

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

    – For extramural submissions, refer to the General Application Instructions, Section III.A.4, for detailed information.

- For intramural submissions, refer to the General Application Instructions, Section IV.A.3, for detailed information.

- Key Personnel Biographical Sketches (five-page limit each): Upload as "Biosketch_LastName.pdf".

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

  - For extramural submissions, refer to the General Application Instructions, Section III.A.4, for detailed information.

  - For intramural submissions, refer to the General Application Instructions, Section IV.A.3, for detailed information.

Research & Related Budget: For extramural submissions (via Grants.gov), refer to the General Application Instructions, Section III.A.5, and for intramural submissions (via eBRAP), refer to the General Application Instructions, Section IV.A.4, for detailed information.

Budget Justification (no page limit): Upload as "BudgetJustification.pdf". The budget justification for the entire period of performance must be uploaded to the Research & Related Budget after completion of the budget for Period 1.

If applying for the Planning Phase with Clinical Trial, two separate, but related, budget justifications for the planning phase and the clinical trial should be uploaded as a single attachment. The first budget justification should address the costs requested for the Planning Phase, and the second, beginning on a new page, should address the costs requested for the proposed clinical trial.

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

- **Extramural Applications Only**

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

  - **Extramural Subaward:** Complete the Research & Related Subaward Budget Form through Grants.gov. (Refer to the General Application Instructions, Section III.A.7, for detailed information.) Verify subaward budget(s) and budget justification forms are present in eBRAP during the application verification period. If these components are missing, upload them to eBRAP before the end of the application verification period.

  - **Intramural DOD Collaborator(s):** Complete the Suggested Collaborating DOD Military Facility Budget Format and upload to Grants.gov attachment form as

Attachment 15. (Refer to the General Application Instructions, Section IV.A.4, for detailed information.) Each Intramural DOD Collaborator should include costs per year on the Grants.gov Research & Related Budget Form under subaward costs.

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/SAM/) and receive confirmation of an "Active" status before submitting an application through Grants.gov. As published in the Federal Register July 10, 2019 (https://www.federalregister.gov/documents/2019/07/10/2019-14665/unique-entity-id-standard-for-awards-management), the UEI for awards management generated through SAM will be used instead of the Data Universal Numbering System (DUNS) number as of April 2022. ***All federal awards including, but not limited to, contracts, grants, and cooperative agreements will use the UEI.*** USAMRDC will transition to use of the UEI beginning with FY22 announcements and utilize the latest SF424, which includes the UEI. The DUNS will no longer be accepted. Applicant organizations will not go to a third-party website to obtain an identifier. During the transition, your SAM registration will automatically be assigned a new UEI displayed in SAM. (For more information, visit the General Services Administration: https://www.gsa.gov/about-us/organization/federal-acquisition-service/office-of-systems-management/integrated-award-environment-iae/iae-information-kit/unique-entity-identifier-update.) Current SAM.gov registrants are assigned their UEI and can view it within SAM.gov. ***Authorized Organizational Representatives with existing eBRAP accounts should update their organizational profile to include the UEI prior to submission of the full application to Grant.gov (see below).*** Refer to the General Application Instructions, Section III, for further information regarding Grants.gov requirements.

II.D.4. Submission Dates and Times

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

Applicant Verification of Full Application Submission in eBRAP

For Both Extramural and Intramural Applicants: eBRAP allows an organization's representatives and PIs to view and modify the full application submissions associated with them. Following retrieval and processing of the full application, eBRAP will notify the organizational representatives and PI by email to log into eBRAP to review, modify, and verify the full application submission. eBRAP will validate full application files against the specific program announcement requirements, and discrepancies will be noted in an email to the PI and in the "Full Application Files" tab in eBRAP. eBRAP does not confirm the accuracy of file content. Application viewing, modification, and verification in eBRAP are strongly recommended, but not required. It is the applicant's responsibility to review all application components and ensure proper ordering as specified in the program announcement. ***If either the Project Narrative or the budget fails eBRAP validation or needs to be modified, an updated full application package must be submitted prior to the application submission deadline. The***

Project Narrative and Research & Related Budget Form cannot be changed after the application submission deadline. Other application components may be changed until the end of the application verification period. Verify that subaward budget(s) and budget justification forms are present in eBRAP during the application verification period. If these components are missing, upload them to eBRAP before the end of the application verification period. After the end of the application verification period, the full application cannot be modified.

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

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

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

II.D.5. Funding Restrictions

For the Clinical Trial Award – Planning Phase with Clinical Trial:

The maximum period of performance is 18 months for the planning phase.

The anticipated direct costs budgeted for the entire period of performance of this base award (i.e., the planning phase) will not exceed **$500,000**. Budget is a scored criterion during peer review. If indirect cost rates have been negotiated, indirect costs are to be budgeted in accordance with the organization's negotiated rate. No budget will be approved by the government exceeding **$500,000** direct costs or using an indirect cost rate exceeding the organization's negotiated rate for the planning phase.

Clinical trial work is considered an optional research effort. Approval of the clinical trial effort will be contingent upon the completion of Planning Phase to include all necessary regulatory approvals under the base award. Additionally, clinical trial efforts will be contingent on PRMRP Programmatic Panel approval and may be dependent on the availability of future year funds. ***The application must include two separate, but related, budgets and SOWs for the planning phase and the clinical trial***. The budget for the clinical trial should be submitted using the Research & Related Subaward Budget Attachment(s) Form.

The clinical trial has a maximum period of performance of **4** years and is not restricted to a predetermined cost limit. The requested budget must be justified and appropriate to the scope of

the clinical trial proposed. Budget is a scored criterion during peer review. If indirect cost rates have been negotiated, indirect costs are to be budgeted in accordance with the organization's negotiated rate. No budget will be approved by the government using an indirect cost rate exceeding the organization's negotiated rate.

For the Clinical Trial Award – Clinical Trial Only:

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

Applications are not restricted to a predetermined cost limit. The requested budget must be justified and appropriate to the scope of the clinical trial proposed. Budget is a scored criterion during peer review. If indirect cost rates have been negotiated, indirect costs are to be budgeted in accordance with the organization's negotiated rate. No budget will be approved by the government using an indirect cost rate exceeding the organization's negotiated rate.

For all applications:

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

For the Clinical Trial Award – Planning Phase with Clinical Trial:

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

- Travel costs for the PI and up to three additional members of the research team to attend a 1-day PRMRP Milestone Meeting to be held in the National Capital Area during the award period of performance. This meeting will be held to present results of the planning phase to the PRMRP Programmatic Panel and may determine the option to fund clinical trial efforts. Costs associated with travel to this meeting should be included in the appropriate year to follow the estimated timeline for Planning Phase completion and no later than year 2. These travel costs are in addition to those allowed for annual scientific/technical and collaborative meetings.

For all applications:

Direct costs may be requested for travel including:

- Travel in support of multidisciplinary collaborations.
- Travel between collaborating organizations
- Travel costs for the PI to disseminate project results at one DOD-sponsored meeting to be specified by the program office during award negotiations (e.g., the Military Health System Research Symposium)
- Travel costs for up to four investigators to travel to one scientific/technical meeting per year in addition to the meeting described above. The intent of travel costs to scientific/ technical meetings is to disseminate project results from the FY22 PRMRP CTA.

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

Refer to the General Application Instructions, Section III.A.5, for budget regulations and instructions for the Research & Related Budget. ***For federal agencies or organizations collaborating with federal agencies, budget restrictions apply as are noted in the General Application Instructions, Section III.A.5***.

II.D.6. Other Submission Requirements

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

II.E. Application Review Information

II.E.1. Criteria

II.E.1.a. Peer Review

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

For the Planning Phase only:

- **Planning Phase**
    - How well the plan is described for obtaining IND/IDE status (or other FDA approvals) during the 18-month or less period of performance if an IND or IDE is required.
    - Whether there is a regulatory sponsor specified and a signed sponsor commitment letter acknowledging the regulatory sponsor's understanding of all sponsor responsibilities and commitment to oversee execution of the study.
    - If applicable, how well the planning phase will enable finalization or completion of:
        - Study Procedures and/or Clinical Monitoring Plan;
        - Study Population, Inclusion/Exclusion Criteria, Recruitment Process, Informed Consent Process, and/or Screening Procedures;
        - Questionnaires and Other Data Collection Instruments;
        - Organizational Chart, Study Personnel Description, and/or Study Management Plan;

- Data Management and/or Laboratory Evaluations; and/or finalization or completion of the Regulatory Strategy.

- To what degree the overall regulatory strategy and product development plan will support the planned product indication.

- How well the plans for other administrative approvals (e.g., IRB, DOD HRPO) are outlined.

For all clinical trials:

- **Clinical Impact**

  - How impactful the anticipated outcomes of the proposed clinical trial would be to the target population with regard to the FY22 PRMRP Topic Area and FY22 PRMRP Strategic Goal addressed.

  - How well the sample population represents the targeted patient population that might benefit from the proposed intervention.

  - How the anticipated outcomes of the proposed clinical trial will provide/improve short-term benefits for individuals.

  - How significantly the long-term benefits for implementation of the intervention may impact patient care and/or quality of life.

- **Research Strategy and Feasibility**

  - How well the scientific rationale for the proposed clinical trial is supported by the preliminary data, critical review and analysis of the literature, relevant ongoing, planned, or complete clinical trials, and/or laboratory/preclinical evidence.

  - How well the study questions, specific aims, hypotheses and/or objective(s), experimental design, methods, data collection procedures, and analyses are designed to answer clearly the clinical objective and purpose.

  - How well the inclusion/exclusion criteria and group assignment process meet the needs of the proposed clinical trial.

  - How well plans to collect specimens and conduct laboratory evaluations are addressed, if applicable.

  - To what degree the data collection instruments, if applicable, are appropriate to the proposed study.

- **Intervention**

  - Whether there is evidence of support, indicating availability of the intervention from its source, for the duration of the proposed clinical trial (if applicable).

- To what degree the intervention addresses the clinical need(s) described.
- How the intervention compares with currently available interventions and/or standards of care.
- To what degree the application includes preclinical and/or clinical evidence 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).

- **Regulatory Strategy and Transition Plan**
  - How the regulatory strategy and development plan to support the product indication or product label change, if applicable, are appropriate and well-described.
  - ***For the Planning Phase:*** How well the documentation provided supports the feasibility of acquiring an active IND or IDE (and/or international equivalent) covering the proposed trial, if applicable.
  - ***For the Clinical Trial:*** Whether the application includes documentation that the study is exempt from the FDA (or other international agency) regulation, or that the IND or IDE application (and/or international equivalent) has been submitted to the FDA (and/or relevant international regulatory agency), as appropriate.
  - For investigator-sponsored regulatory exemptions (e.g., IND, IDE, or other international equivalent), whether there is evidence of appropriate institutional support, including capabilities to ensure monitoring as required by the FDA or relevant international regulatory agency.
  - Whether plans to comply with GMP, GLP, and GCP guidelines are appropriate.
  - Whether the identified next level of development and/or commercialization is realistic.
  - Whether the funding strategy described to bring the intervention to the next level of development (e.g., specific industry partners, specific funding opportunities to be applied for) is reasonable and achievable.
  - For knowledge products, whether the proposed collaborations and other resources are achievable to provide continuity of development.
  - Whether the schedule and milestones for bringing the intervention to the next level of development (next-phase clinical trials, transition to industry, delivery to the market, incorporation into clinical practice, and/or approval by the FDA) 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, demonstrates the appropriate access to all intellectual property rights necessary for development and commercialization, describes an appropriate intellectual and material property plan among participating organizations (if applicable), and addresses any impact of intellectual property issues on product development and subsequent government access to products supported by this program announcement.

- **Recruitment, Accrual, and Feasibility**

  - How well the application addresses the availability of human subjects for the clinical trial and the prospect of their participation.

  - Whether the application demonstrates access to the proposed human subject population.

  - The degree to which the recruitment, informed consent, screening, and retention processes for human subjects will meet the needs of the proposed clinical trial.

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

  - To what extent the proposed clinical trial might affect the daily lives of the individual human subjects participating in the study.

  - Whether the strategy for the inclusion of women and minorities is appropriate to the objectives of the study.

  - Whether the distribution of the proposed enrollment on the basis of sex/gender, race, and/or ethnicity is appropriate for the proposed research.

- **Statistical Plan and Data Analysis**

  - To what degree the statistical model and data analysis plan are suitable for the planned study.

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

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

  - 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.

- **Ethical Considerations**
    - Whether the population selected to participate in the trial stands to benefit from the knowledge gained.
    - If applicable, how well the inclusion of international sites is justified.
    - How the level of risk to human subjects is minimized and how the safety monitoring and reporting plan is appropriate for the level of risk.
    - How well the evidence shows that the procedures are consistent with sound research design and, when appropriate, that these procedures are already in use for diagnostic or treatment purposes.
    - To what degree privacy and confidentiality issues are appropriately considered.
    - To what degree the process for seeking informed consent is appropriate and whether safeguards are in place for vulnerable populations.
- **Personnel and Communication**
    - Whether the composition of the study team is appropriate.
    - To what degree the study team's background and expertise are appropriate to accomplish the proposed work.
    - How the levels of effort of the study team members are appropriate for successful conduct of the proposed trial.
    - How well the logistical aspects of the proposed clinical trial (e.g., communication plan, data transfer and management, standardization of procedures) meet the needs of the proposed clinical trial.
    - For clinical trials that are cooperative (i.e., involving more than one institution), to what degree the multi-institutional structure governing the research protocol(s) across all participating institutions and regulatory submission plan are described and appropriate.
- **Budget**
    - Whether the budget is appropriate for the proposed research.
    - ***For the Planning Phase:*** Whether the **direct** costs exceed the allowable direct costs as published in the program announcement, if applicable.

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

- **Environment**
    - To what degree the scientific environment, clinical setting, and the accessibility of institutional resources support the clinical trial at each participating center or institution (including collaborative arrangements).
    - Whether there is evidence for appropriate institutional commitment from each participating institution.
- **Application Presentation**
    - To what extent the writing, clarity, and presentation of the application components influence the review.

II.E.1.b. Programmatic Review

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

- Ratings and evaluations of the peer reviewers
- Relevance to the mission of the DHP and FY22 PRMRP, as evidenced by the following:
    - Adherence to the intent of the award mechanism
    - Relative clinical impact
    - Relevance to the FY22 PRMRP Topic Areas
    - Relevance to the FY22 PRMRP Strategic Goals
    - Relevance to military health
    - Program portfolio composition

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.army.mil/about/2tierRevProcess. An information paper describing the funding

recommendations and review process for the award mechanisms for the FY22 PRMRP will be provided to the PI and posted on the CDMRP website.

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 panel. Violations of confidentiality can result in the dissolving of a panel(s) and other corrective actions. In addition, personnel at the applicant or collaborating organizations are prohibited from contacting persons involved in the review and approval process to gain protected evaluation information or to influence the evaluation process. Violations of these prohibitions will result in the administrative withdrawal of the organization's application. Violations by panel members or applicants that compromise the confidentiality of the review and approval process may also result in suspension or debarment from federal awards. Furthermore, the unauthorized disclosure of confidential information of one party to another third party is a crime in accordance with 18 USC 1905.

II.E.3. Integrity and Performance Information

Prior to making an assistance agreement award where the federal share is expected to exceed the simplified acquisition threshold, as defined in 2 CFR 200.1, over the period of performance, the federal awarding agency is required to review and consider any information about the applicant that is available in the Federal Awardee Performance and Integrity Information System (FAPIIS).

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

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

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

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

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

II.F. Federal Award Administration Information

II.F.1. Federal Award Notices

Awards supported with FY22 funds are anticipated to be made no later than September 30, 2023. Refer to the General Application Instructions, Appendix 2, for additional award administration information.

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

Pre-Award Costs: An institution of higher education, hospital, or non-profit 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. Refer to the General Application Instructions, Section III.A.5.

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

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

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

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

An organizational transfer of an award will not be allowed in the last year of the (original) period of performance or any extension thereof.

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

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

II.F.2. Administrative and National Policy Requirements

Applicable requirements in the DoDGARs found in 32 CFR, Chapter 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 2, for general information regarding administrative requirements.

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

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

New Requirement: Certification Regarding Disclosure of Funding Sources. The proposing entity must comply with Section 223(a) of the William M. (Mac) Thornberry National Defense Authorization Act for Fiscal Year 2021, which requires that the PI, Partnering PIs (if applicable), and all key personnel:

- Certify that the current and pending support provided on the application is current, accurate, and complete;
- Agree to update such disclosure at the request of the agency prior to the award of support and at any subsequent time the agency determines appropriate during the term of the award; and
- Have been made aware of the requirements under Section 223(a)(1) of this Act.

False, fictitious, or fraudulent statements or claims may result in criminal, civil, or administrative penalties (218 USC 1001).

II.F.3. Reporting

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

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

Quarterly progress reports will be required for the clinical trial.

The Award Terms and Conditions will specify if more frequent reporting is required.

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 if 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 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.

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 $10M are required to provide information to FAPIIS about certain civil, criminal, and administrative proceedings that reached final disposition within the most recent 5-year period and that were connected with performance of a federal award. 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 5, Section B).

II.G. Federal Awarding Agency Contacts

II.G.1. eBRAP Help Desk

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

Phone: 301-682-5507

Email: help@eBRAP.org

II.G.2. Grants.gov Contact Center

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

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

Email: support@grants.gov

Sign up on Grants.gov for "send me change notification emails" by following the link on the "Synopsis" page for the program announcement or by responding to the prompt provided by Grants.gov when first downloading the Grants.gov application package. If the Grants.gov application package is updated or changed, the original version of the application package may not be accepted by Grants.gov.

II.H. Other Information

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

Questions related to this program announcement should refer to the program name, the program announcement name, and the program announcement version code 701Tb. The program announcement numeric version code will match the General Application Instructions version code 701.

II.H.2. Administrative Actions

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

II.H.2.a. Rejection

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

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

The following will result in administrative rejection of the application:

- Submission of an application for which a letter of invitation was not received.
- Project Narrative exceeds page limit.
- Project Narrative is missing.
- Budget is missing.
- Intervention (Attachment 7) is missing.
- Human Subject Recruitment and Safety Procedures (Attachment 8) is missing.
- Data Management (Attachment 9) is missing.
- Regulatory Strategy (Attachment 10) is missing.

II.H.2.b. Modification

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

II.H.2.c. Withdrawal

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

- An FY22 PRMRP Programmatic Panel member is named as being involved in the research proposed or is found to have assisted in the pre-application or application processes including, but not limited to, concept design, application development, budget preparation, and the development of any supporting documentation. ***A list of the FY22 PRMRP Programmatic Panel members can be found at https://cdmrp.army.mil/prmrp/panels/panels22***.
- The application fails to conform to this program announcement description.
- Inclusion of URLs, with the exception of links in References Cited and Publication and/or Patent Abstract sections.
- Page size is larger than 8.5 inches x 11.0 inches (approximately 21.59 cm x 27.94 cm).
- To preserve the integrity of its peer and programmatic review processes, the CDMRP discourages inclusion of any employee of its review contractors having any role in the preparation, research or other duties for submitted applications. For FY22, the identities of the peer review contractor and the programmatic review contractor may be found at the CDMRP website (https://cdmrp.army.mil/about/2tierRevProcess). Applications that include names of personnel from either of these companies may be administratively withdrawn.
- Personnel from applicant or collaborating organizations are found to have contacted persons involved in the review or approval process to gain protected evaluation information or to influence the evaluation process.
- Applications from extramural organizations, including non-DOD federal agencies, received through eBRAP may be withdrawn.
- Applications submitted by an intramural DOD organization may be withdrawn if the intramural organization cannot coordinate the use of contractual, assistance, or other appropriate agreements to provide funds to extramural collaborators.
- Submission of the same research project to different funding opportunities within the same program and fiscal year.
- The proposed research is not a clinical trial.

- For clinical trials (Clinical Trial Only) in which an IND or an IDE is not required/exempt, evidence in the form of formal communication from the FDA or the IRB of record to that effect is not provided.
- The invited application proposes a different research project than that described in the pre-application.
- The PI does not meet the eligibility criteria.
- The proposed project includes preclinical research.
- The application fails to address one of the congressionally directed FY22 PRMRP Topic Areas.
- The application fails to address one of the FY22 PRMRP Strategic Goals.
- The investigator is named as PI on more than one application submitted to the FY22 PRMRP CTA mechanism.

II.H.2.d. Withhold

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

II.H.3. Application Submission Checklist

Application Components	Action	Completed
SF424 Research & Related Application for Federal Assistance **(extramural submissions only)**	Complete form as instructed.	
Summary (Tab 1) and Application Contacts (Tab 2) **(intramural submissions only)**	Complete these tabs as instructed.	
Attachments	Project Narrative: Upload as Attachment 1 with file name "ProjectNarrative.pdf"	
	Supporting Documentation: Upload as Attachment 2 with file name "Support.pdf"	
	Technical and Lay Abstracts: Upload as Attachment 3 with file name "Abs.pdf"	
	Statement of Work: Upload as Attachment 4 with file name "SOW.pdf"	
	Impact Statement: Upload as Attachment 5 with file name "Impact.pdf"	
	Relevance to Military Health Statement: Upload as Attachment 6 with file name "MilRel.pdf"	
	Intervention: Upload as Attachment 7 with file name "Intervention.pdf"	
	Human Subject Recruitment and Safety Procedures: Upload as Attachment 8 with file name "HumSubProc.pdf"	
	Data Management: Upload as Attachment 9 with file name "Data_Manage.pdf"	
	Regulatory Strategy: Upload as Attachment 10 with the file name "Regulatory.pdf"	
	Study Personnel and Organization: Upload as Attachment 11 with file name "Personnel.pdf"	
	Questionnaires and Other Research Data Collection Instruments: Upload as Attachment 12 with file name "Data_Collection.pdf" if applicable	
	Transition Plan: Upload as Attachment 13 with file name "Transition.pdf"	
	Representations (extramural submissions only): Upload as Attachment 14 with file name "RequiredReps.pdf"	

Application Components	Action	Completed
	Suggested Collaborating DOD Military Facility Budget Format: Upload as Attachment 15 with file name "MFBudget.pdf" if applicable	
Research & Related Personal Data	Complete form as instructed.	
Research & Related Senior/Key Person Profile (Expanded)	Attach PI Biographical Sketch (Biosketch_LastName.pdf) to the appropriate field.	
	Attach PI Previous/Current/Pending Support (Support_LastName.pdf) to the appropriate field.	
	Attach Biographical Sketch (Biosketch_LastName.pdf) for each senior/key person to the appropriate field.	
	Attach Previous/Current/Pending (Support_LastName.pdf) for each senior/key person to the appropriate field.	
Research & Related Budget **(extramural submissions only)**	Complete as instructed. Attach Budget Justification (BudgetJustification.pdf) to the appropriate field.	
Budget **(intramural submissions only)**	Complete the Suggested DOD Military Budget Format, including justification.	
Project/Performance Site Location(s) Form	Complete form as instructed	
Research & Related Subaward Budget Attachment(s) Form, if applicable	Complete form as instructed	

APPENDIX 1: ACRONYM LIST

ACOS/R&D	Associate Chief of Staff for Research and Development
ACURO	Animal Care and Use Review Office
CDMRP	Congressionally Directed Medical Research Programs
CFR	Code of Federal Regulations
CTA	Clinical Trial Award
DHP	Defense Health Program
DOD	Department of Defense
DoDGARs	Department of Defense Grant and Agreement Regulations
DUNS	Data Universal Numbering System
eBRAP	Electronic Biomedical Research Application Portal
EC	Ethics Committee
ET	Eastern Time
FAD	Funding Authorization Document
FAPIIS	Federal Awardee Performance and Integrity Information System
FDA	U.S. Department of Food and Drug Administration
FY	Fiscal Year
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
HRPO	Human Research Protection Office
ICH E6	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
IDE	Investigational Device Exemption
IND	Investigational New Drug
IRB	Institutional Review Board
LAR	Legally Authorized Representative
M	Million
MB	Megabytes
ME/CFS	Myalgic Encephalomyelitis/Chronic Fatigue Syndrome
MIPR	Military Interdepartmental Purchase Request
NIH	National Institutes of Health
ORCID	Open Researcher and Contributor ID, Inc.
ORP	Office of Research Protections

PDF	Portable Document Format
PHS	Public Health Service
PI	Principal Investigator
PRMRP	Peer Reviewed Medical Research Program
SAM	System for Award Management
SOW	Statement of Work
STEM	Science, Technology, Engineering, and/or Mathematics
UEI	Unique Entity Identifier
URL	Uniform Resource Locator
USAMMDA	U.S. Army Medical Materiel Development Activity
USAMRAA	U.S. Army Medical Research Acquisition Activity
USAMRDC	U.S. Army Medical Research and Development Command
USC	United States Code
VA	Department of Veterans Affairs

APPENDIX 2: DOD AND VA WEBSITES

PIs are encouraged to integrate and/or align their research projects with DOD and/or VA research laboratories and programs. Collaboration with DOD 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 within the FY22 PRMRP Topic Areas.

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://ccc.amedd.army.mil/Pages/default.aspx

Congressionally Directed Medical Research Programs
https://cdmrp.army.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.amedd.army.mil/SitePages/Home.aspx

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

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

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

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

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

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

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/research

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

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

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

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

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

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

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

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

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

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

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

APPENDIX 3: APPLICATION CATEGORY SUMMARY

	Planning Phase with Clinical Trial	Clinical Trial Only
Award Information	• Supports the final phase of regulatory activity necessary to initiate a clinical trial • Includes planning for regulatory/administrative approvals, developing the clinical protocol, establishing access to patients, and other preparatory activities • Expectation that recipients will submit an IND/IDE application to the FDA (or equivalent agency) and receive an acknowledgement letter (or equivalent communication) during period of performance • Not an assurance of funding for the proposed clinical trial • Includes option for clinical trial if regulatory submissions are achieved, federal funds are available, and the topic area is supported at that time	• Supports a clinical trial having either FDA (or equivalent agency) approval or exemption in place prior to the application submission deadline
Budget	• Up to $500,000 for the planning phase • No predetermined cost limit for the proposed clinical trial	• No predetermined cost limit
Period of Performance	• Up to 18 months for the planning phase • Up to 4 years for the proposed clinical trial	• Up to 4 years
Pre-Application Components	• Preproposal Narrative ○ Describes the proposed clinical trial • Pre-Application Supporting Documents ○ Includes an estimated budget for the planning phase and the proposed clinical trial	• Preproposal Narrative ○ Describes the clinical trial • Pre-Application Supporting Documents ○ Includes an estimated budget for the clinical trial
Full Application Components	• Project Narrative ○ 8-page limit for the planning phase ○ 20-page limit for the proposed clinical trial • Statement of Work ○ Includes two SOWs: one for the planning phase and one for the proposed clinical trial ○ Uploaded as one attachment; starts statement for the proposed clinical trial on a new page ○ No page limit • Budget ○ Includes two budgets: one for the planning phase and one for the proposed clinical trial • Human Subject Recruitment and Safety Procedures; Questionnaires and Other Data Collection Instruments; Study Personnel and Organization; Data Management; Regulatory Strategy ○ Describes any missing or applicable aspects to be addressed during the Planning Phase ○ Requires resubmission if changed/finalized when/if option for the proposed clinical trial is exercised	• Project Narrative ○ 20-page limit • Statement of Work ○ No page limit • Human Subject Recruitment and Safety Procedures; Questionnaires and Other Data Collection Instruments; Study Personnel and Organization; Data Management; Regulatory Strategy ○ Requires submission in full