

# **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: Modified**

**Funding Opportunity Number: W81XWH-21-PRMRP-CTA**

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

## **SUBMISSION AND REVIEW DATES AND TIMES**

- **Pre-Application Submission Deadline:** 5:00 p.m. Eastern time (ET), May 13, 2021
- **Invitation to Submit an Application:** June 2021
- **Application Submission Deadline:** 11:59 p.m. ET, August 26, 2021
- **End of Application Verification Period:** 5:00 p.m. ET, August 31, 2021
- **Peer Review:** October 2021
- **Programmatic Review:** December 2021

*This program announcement must be read in conjunction with the General Application Instructions, version 601. 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 2021 (FY21) Peer Reviewed Medical Research Program (PRMRP) are being solicited for the Defense Health Agency (DHA) J9, Research and Development Directorate, by the U.S. Army Medical Research Acquisition Activity (USAMRAA) using delegated authority provided by United States Code, Title 10, Section 2358 (10 USC 2358). As directed by the Office of the Assistant Secretary of Defense for Health Affairs (OASD[HA]), the DHA manages the Defense Health Program (DHP) Research, Development, Test, and Evaluation (RDT&E) appropriation. The execution management agent for this program announcement is the Congressionally Directed Medical Research Programs (CDMRP). The PRMRP was initiated in 1999 to provide medical research projects of clear scientific merit and direct relevance to military health. Appropriations for the PRMRP from FY99 through FY20 totaled \$2.71 billion. The FY21 appropriation is \$370 million (M).

The vision of the FY21 PRMRP is to improve the health, care, and well-being 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 and direct relevance to military health. The PRMRP challenges the scientific and clinical communities to address the FY21 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 care 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. FY21 PRMRP Topic Areas

***All applications for PRMRP funding must specifically address at least one of the Topic Areas as directed by Congress and must be of clear scientific merit and direct relevance to military health.*** If the proposed research does not specifically address at least one of the FY21 PRMRP Topic Areas, the government will administratively withdraw the application. The government reserves the right to reassign the application's Topic Area if submitted under an inappropriate Topic Area. The FY21 PRMRP Topic Areas are listed below.

- Arthritis
- Burn Pit Exposure
- Cardiomyopathy
- Congenital Heart Disease
- Diabetes
- Dystonia
- Eating Disorders
- Emerging Viral Diseases

- Endometriosis
- Epidermolysis Bullosa
- Familial Hypercholesterolemia
- Fibrous Dysplasia
- Focal Segmental Glomerulosclerosis
- Food Allergies
- Fragile X
- Frontotemporal Degeneration
- Hemorrhage Control
- Hepatitis B
- Hydrocephalus
- Hypertension
- Inflammatory Bowel Diseases
- Malaria
- Metals Toxicology
- Mitochondrial Disease
- Myalgic Encephalomyelitis/Chronic Fatigue Syndrome
- Myotonic Dystrophy
- Non-Opioid Therapy for Pain Management
- Nutrition Optimization
- Pathogen-Inactivated Blood Products
- Peripheral Neuropathy
- Plant-Based Vaccines
- Platelet-Like Cell Production
- Polycystic Kidney Disease
- Pressure Ulcers
- Pulmonary Fibrosis
- Respiratory Health
- Rheumatoid Arthritis
- Sleep Disorders and Restriction
- Suicide Prevention
- Sustained Release Drug Delivery
- Vascular Malformations
- Women's Heart Disease

***Applicants should select the FY21 PRMRP program announcement most appropriate to the stage of the proposed research.*** Areas of Encouragement related to the FY21 PRMRP Topic Areas have been identified by the Department of Defense (DOD), the Department of Veterans Affairs (VA), and other relevant stakeholders ([Appendix 2](#)). Applicants are strongly urged to read and consider these Areas of Encouragement before preparing their applications. ***The information provided is not exhaustive, and applicants are not restricted to submitting applications that address an Area of Encouragement on this list.***

## **II.B. Award Information**

The PRMRP Clinical Trial Award supports the rapid implementation of clinical trials with the potential to have a significant impact on a disease or condition addressed in at least one of the Congressionally directed FY21 PRMRP Topic Areas. 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 feasibility or inform the design of more advanced trials, through large-scale trials to determine efficacy in relevant patient populations.

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. This outcome represents a direct effect on the subject of that intervention or interaction. The term “human subjects” is used in this program announcement to refer to individuals who will be recruited for or who will participate in the proposed clinical trial. For more information, a Human Subject Resource Document is provided at <https://ebrap.org/eBRAP/public/Program.htm>. Applicants seeking funding for a preclinical research project should consider one of the other FY21 PRMRP program announcements being offered.

***Funding from this award mechanism must support a clinical trial and cannot be used for animal studies.***

Two different application categories, based on the phase of planning for the clinical trial, are available under this program announcement (summary available in [Appendix 4](#)):

- 1. 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 at least one of the FY21 PRMRP Topic Areas.
  - ***Within the 18-month period of performance of the Planning Phase, recipients are expected to submit an Investigational New Drug (IND)/Investigation Device Exemption (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.***
  - Important tasks to consider under the Planning Phase with Clinical Trial include, but are not limited to:
    - Planning for appropriate regulatory approvals (for example, Institutional Review Board [IRB] submissions, FDA submissions such as FDA IND/IDE applications, and 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
- Funding under the Planning Phase with Clinical Trial is not an assurance of funding the clinical trial. Exercising the Clinical Trial option will be contingent upon submitting one of the following ***within the 18-month period of performance***, as well as availability of federal funds for the program and topic area; ***the PRMRP will not exercise the option for the initiation of the proposed clinical trial if this milestone is not met.***
  - 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 IRB of record, or the FDA, or the international 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.

**2. Clinical Trial Only:** This is intended to support a clinical trial having either FDA (or other regulatory agency) approval or an exemption; 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.
- Refer to [Attachment 13, 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, 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 13, Regulatory Strategy](#).***
- The following are important aspects of the clinical trial:
  - The proposed clinical trial is expected to begin no later than 9 months after the award date of either the Clinical Trial Only or after exercising the option for the clinical trial in the Planning Phase with Clinical Trial.
  - The proposed intervention(s) to be tested should offer significant potential impact for individuals affected by disease(s)/condition(s).
  - Inclusion of preliminary data relevant to the proposed clinical trial is required.
  - The proposed clinical trial must be based on sound scientific rationale that is established through logical reasoning and critical review and analysis of the relevant literature.
  - Description of the planned indication for the product label, if appropriate, and an outline of the product development plan required to support that indication.
  - Demonstration of availability of, and access to, a suitable patient population that will support a meaningful outcome for the study. A discussion of how accrual goals will be achieved and how standards of care may impact the study population should be included.
  - Demonstration of 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).

- Description of the study team's experience interacting with the FDA, including previous FDA submissions, if applicable.
- The proposed clinical trial design should include clearly defined objectives and appropriate endpoints/outcome measures, and comply with current Good Clinical Practice (GCP) guidelines.
- Inclusion of a clearly articulated statistical analysis plan, appropriate statistical expertise on the research team, and a power analysis reflecting sample size projections that will answer the objectives of the study.
- Inclusion of a clearly articulated data management plan and use of an appropriate database to safeguard and maintain the integrity of the data. If FDA-regulated, the trial must use a 21 CFR 11-compliant database and appropriate data standards. For more on data standards, see <https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/UCM511237.pdf>.
- Inclusion of a clearly articulated safety management plan outlining how safety pharmacovigilance will be conducted, as applicable.
- Inclusion of a clearly articulated clinical monitoring plan outlining how the study will be monitored for GCP compliance.
- Inclusion of 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.
- Inclusion of a Transition Plan (including potential funding and resources) as [Attachment 12](#), showing how the product will progress to the next clinical trial phase and/or delivery to the market after the successful completion of the FY21 PRMRP Clinical Trial Award.
- Clear demonstration of strong institutional support and, if applicable, a commitment to serve as the FDA regulatory sponsor, ensuring all sponsor responsibilities described in 21 CFR 312, Subpart D, are fulfilled.
- Funded trials are required to post a copy of the informed consent form used to enroll subjects on a publicly available federal website in accordance with federal requirements described in 32 CFR 219.
- Funded studies are required to register the study in the National Institutes of Health (NIH) clinical trials registry, [www.clinicaltrials.gov](http://www.clinicaltrials.gov) prior to initiation of the study. Refer to the General Application Instructions, Appendix 1, Section D, 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.

For the Clinical Trial Award – Planning Phase with Clinical Trial, the anticipated direct costs budgeted for the **18-month** period of performance 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 and has a maximum period of performance of **4 years**. The requested budget for the clinical trial must be justified and appropriate to the scope proposed.

Applications to the 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, 2022. For additional information refer to [Section II.F.1, Federal Award Notices](#).

*The CDMRP expects to allot approximately \$45M to fund approximately seven 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 FY21 funding opportunity will be funded with FY21 funds, which will expire for use on September 30, 2027. The clinical trial proposed in the Planning Phase with Clinical Trial will be funded with future fiscal year funds, if the option is exercised.*

**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 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.usammmda.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 FY21 PRMRP Topic Areas can be found in [Appendix 3](#).

**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 U.S. Army Medical Research and Development Command (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 a minimum of 2 to 3 months for HRPO regulatory review and approval processes.*** Refer to the General Application Instructions, Appendix 1, and the Human Subject Resource Document available on the electronic Biomedical Research Application Portal (eBRAP) “Funding Opportunities & Forms” web page (<https://ebrap.org/eBRAP/public/Program.htm>) for additional information. If the proposed research is cooperative (i.e., involving more than one institution), a written plan for single IRB review arrangements must be provided at the time of application submission or award negotiation. The lead institution responsible for developing the master protocol and master consent form should be identified and should be the single point of contact for regulatory submissions and requirements. The written plan for single IRB review arrangements and multi-institutional structure governing the research protocol(s) must be provided in [Attachment 10, Study Personnel and Organization](#) at the time of application submission.

**Multi-Institutional Clinical Trials:** If the proposed clinical trial is multi-institutional, plans for the multi-institutional structure governing the research protocol(s) should be outlined in [Attachment 10, Study Personnel and Organization](#). In accordance with §.114 of the Federal Policy for the Protection of Human Subjects (the Common Rule), any institution located in the United States engaged in cooperative research (i.e., research involving more than one institution) must rely upon approval by a single IRB (sIRB) for the portion of that research that is conducted in the United States (except as specified in §.114(2)(i)). The awardee/offeror must designate a sIRB and include a plan for the sIRB review process in the application submission. Additionally, the application must identify the lead institution responsible for developing the master protocol and informed consent document and that will serve as the single point of contact for regulatory submissions and requirements. Communication and data transfer between/among the collaborating institutions, as well as how specimens and/or products obtained during the study will be handled, should be included in the appropriate sections of the application. A separate intellectual and material property plan agreed upon by all participating institutions is also required for multi-institutional clinical trials.

*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. Funded trials are required to post a copy of the IRB approved informed consent form used to enroll subjects on a publicly available federal website in accordance with federal requirements described in 32 CFR 219.

If the IRB determines that a trial presents greater than minimal risk to human subjects, the DOD requires an independent research monitor with expertise consistent with the nature of risk(s) identified within the research protocol. If applicable, refer to the General Application Instructions, Appendix 1, Section B (Research Monitor Requirement), for more information on study reporting authorities and responsibilities of the research monitor.

## **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 organization 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: 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.***

**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.

There are no limitations on the number of applications for which an investigator may be named 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 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). As an exception, applicants may submit the research project described in their Clinical Trial Award application as part of an application to the FY21 PRMRP Focused Program Award (funding opportunity number W81XWH-21-PRMRP-FPA); however, accepting multiple awards to support the same project will not be allowed.***

### ***Extramural Submission:***

- Pre-application content and forms must be accessed and submitted at [eBRAP.org](http://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](http://eBRAP.org).
- Full application packages must be accessed and submitted at [eBRAP.org](http://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.1. Address to Request Application Package**

eBRAP is a multifunctional web-based system that allows PIs to submit their pre-applications electronically through a secure connection, to view and edit the content of their pre-applications and full applications, to receive communications from the CDMRP, and to submit documentation during award negotiations and period of performance.

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

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

Submission is a two-step process requiring both ***pre-application*** (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 CDMRP Help Desk at [help@eBRAP.org](mailto:help@eBRAP.org) or 301-682-5507 prior to the application submission deadline.

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

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

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

If an error has been made in the selection of extramural versus intramural and the pre-application submission deadline has passed, the PI or Business Official must contact the CDMRP Help Desk at [help@eBRAP.org](mailto: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 CDMRP Help Desk at [help@eBRAP.org](mailto: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 award option (i.e., application category) that is most appropriate for the proposed work (as described in [Section II.B, Award Information](#) or the summary in [Appendix 4](#)).

Select the FY21 PRMRP Topic Area addressed by the proposed research. If the proposed research project is aligned with more than one FY21 PRMRP Topic Area, include all, but select the Topic Area of highest relevance as the required first choice.

- **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.

[FY21 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 CDMRP Help Desk at [help@eBRAP.org](mailto: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:

- **Topic Area:** Describe how the proposed project relates to at least one FY21 PRMRP Topic Area. If applicable, describe how the proposed research project addresses an FY21 PRMRP Area of Encouragement ([Appendix 2](#)).

- **Research Idea:** 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 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 at least one of the FY21 PRMRP Topic Areas. 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 improve patient care in the FY21 PRMRP Topic Area(s) addressed. 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://www.grants.gov/>) for extramural organizations or through eBRAP (<https://ebrap.org/>) for intramural organizations. See Table 1 below for more specific guidelines.

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

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

*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
<b>Application Package Location</b>	
Download application package components for W81XWH-21-PRMRP-CTA from Grants.gov ( <a href="https://www.grants.gov">https://www.grants.gov</a> ) 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-21-PRMRP-CTA from eBRAP ( <a href="https://ebrap.org">https://ebrap.org</a> ).
<b>Full Application Package Components</b>	
<b>SF424 Research &amp; Related Application for Federal Assistance Form:</b> Refer to the General Application Instructions, Section III.A.1, for detailed information.	<p><b>Tab 1 – Summary:</b> Provide a summary of the application information.</p> <p><b>Tab 2 – Application Contacts:</b> This tab will be pre-populated by eBRAP; add Authorized Organizational Representative.</p>

Extramural Submissions	Intramural DOD Submissions
<p>Descriptions of each required file can be found under Full Application Submission Components:</p> <ul style="list-style-type: none"> <li>• <a href="#">Attachments</a></li> <li>• <a href="#">Research &amp; Related Personal Data</a></li> <li>• <a href="#">Research &amp; Related Senior/Key Person Profile (Expanded)</a></li> <li>• <a href="#">Research &amp; Related Budget</a></li> <li>• <a href="#">Project/Performance Site Location(s) Form</a></li> <li>• <a href="#">Research &amp; Related Subaward Budget Attachment(s) Form</a></li> </ul>	<p><b>Tab 3 – Full Application Files:</b> Upload files under each Application Component in eBRAP. Descriptions of each required file can be found under Full Application Submission Components:</p> <ul style="list-style-type: none"> <li>• <a href="#">Attachments</a></li> <li>• <a href="#">Key Personnel</a></li> <li>• <a href="#">Budget</a></li> <li>• <a href="#">Performance Sites</a></li> </ul> <p><b>Tab 4 – Application and Budget Data:</b> Review and edit proposed project start date, proposed end date, and budget data pre-populated from the Budget Form.</p>
<b>Application Package Submission</b>	
<p><b>Create a Grants.gov Workspace.</b> Add participants (investigators and Business Officials) to Workspace, complete all required forms, and check for errors before submission.</p> <p><b>Submit a Grants.gov Workspace Package.</b> 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 <b>at least 24-48 hours prior to the close date</b> to allow time to correct any potential technical issues that may disrupt the application submission.</p> <p><b>Note:</b> If either the Project Narrative or the budget fails eBRAP validation or if the Project Narrative or the budget needs to be modified, an updated Grants.gov application package must be submitted via Grants.gov as a “Changed/Corrected Application” with the previous Grants.gov Tracking ID <i>prior to</i> the application submission deadline. <b><i>Do not password protect any files of the application package, including the Project Narrative.</i></b></p>	<p><b>Submit package components to eBRAP (<a href="https://ebrap.org">https://ebrap.org</a>).</b></p> <p><b>Tab 5 – Submit/Request Approval Full Application:</b> 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. <b><i>Do not password protect any files of the application package, including the Project Narrative.</i></b></p>

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

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

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

- **Extramural Applications Only**

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

- **Extramural and Intramural Applications**

**Attachments:**

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

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

- **Attachment 1: Project Narrative (page limit varies as noted below): Upload as “ProjectNarrative.pdf”.** The page limit of the Project Narrative applies to text and non-text elements (e.g., figures, tables, graphs, photographs, diagrams, chemical structures, drawings) used to describe the project. Inclusion of URLs that provide additional information to expand the Project Narrative and could confer an unfair competitive advantage is prohibited and may result in administrative withdrawal of the application.

**Outline for the Project Narrative:** Describe the proposed project in detail using the outline below. *Funding from this award mechanism must support a clinical trial (and the Planning Phase, if applicable) and cannot be used for animal studies.*

– **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 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 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 Surveys, 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.

***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 7-8 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.

- **Background:** Describe how the proposed project relates to at least one FY21 PRMRP Topic Area. If applicable, describe how the proposed research project addresses an FY21 PRMRP Area of Encouragement ([Appendix 2](#)). Describe in detail the rationale for the study. Provide a literature review and describe the preliminary studies and/or preclinical data that led to the development of the proposed clinical trial. Provide a summary of other relevant ongoing, planned, or completed clinical trials and describe how the proposed study differs. Include a discussion of any current clinical use of the intervention under investigation, and/or details of its study in clinical trials for other indications (as applicable). 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.
  - 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 the study population, criteria for inclusion/exclusion, and the methods used for recruitment/accrual of human subjects, specimens, or human-based resources.
  - Describe the methods that will be used to recruit a sample of human subjects from the accessible population (e.g., convenience, simple random, stratified random).
  - Define each arm/study group of the proposed trial, if applicable. Describe the human subject-to-group assignment process (e.g., randomization, block randomization, stratified randomization, age-matched controls, alternating group, or other procedures). Explain the specific actions to accomplish the group assignment (e.g., computer assignment, use of table of random numbers).
  - Outline whether subjects, clinicians, data analysts, and/or others will be blinded during the study. Describe any other measures to be taken to reduce bias.
  - If using psychometric measures, describe their reliability and validity.
  - If using herbal medicines or nutritional supplements, describe the proposed measures to ensure consistency of dosing of active ingredients.
  - 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 (Clinical Trial Only submission):** Describe the statistical model and data analysis plan with respect to the study objectives. Specify the approximate number of human subjects to be enrolled. If multiple study sites are involved, state the approximate number to be enrolled at each site. Include a complete power analysis to demonstrate that the sample size is appropriate to meet the objectives of the study. If a subpopulation of a recruited sample population will be used for analysis, complete a statistical analysis to ensure appropriate power can be achieved within the subpopulation study. Ensure sufficient information is provided to allow thorough evaluation of all statistical calculations during review of the application.

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

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

- **References Cited:** List the references cited (including URLs, if available) in the Project Narrative using a standard reference format that includes the full citation (i.e., author[s], year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).
- **List of Abbreviations, Acronyms, and Symbols:** Provide a list of abbreviations, acronyms, and symbols.
- **Facilities, Existing Equipment, and Other Resources:** Describe the facilities and equipment available for performance of the proposed project and any additional facilities or equipment proposed for acquisition at no cost to the award. Indicate whether or not government-furnished facilities or equipment are proposed for use. If so, reference should be made to the original or present government award under which the facilities or equipment items are now accountable. There is no form for this information.
- **Publications and/or Patents:** Include a list of relevant publication URLs and/or patent abstracts. If articles are not publicly available, then copies of up to five published manuscripts may be included in Attachment 2. Extra items will not be reviewed.
- **Letters of Organizational Support:** Provide a letter (or letters, if applicable) signed by the Department Chair or appropriate organization official, confirming the laboratory space, equipment, and other resources available for the project. Letters of support not requested in the program announcement, such as those from members of Congress, do not impact application review or funding decisions.
- **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.
- **Letters of Collaboration (if applicable):** Provide a signed letter from each collaborating individual or organization that will demonstrate that the PI has the support or resources necessary for the proposed work. If an investigator at an intramural organization is named as a collaborator on an application submitted

through an extramural organization, the application must include a letter from the collaborator's Commander or Commanding Officer at the intramural organization that authorizes the collaborator's involvement.

- Letters of Commitment (if applicable): If the proposed study involves use of a commercially produced investigational drug, device, or biologic, provide a letter of commitment from the commercial entity indicating availability of the product for the duration of the study, support for the proposed phase of research, and support for the indication to be tested.
- Intellectual Property: Information can be found in 2 CFR 200.315, "Intangible Property."
  - Intellectual and Material Property Plan: Provide a plan for resolving intellectual and material property issues among participating organizations.
- 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.
- o **Attachment 3: Technical and Lay Abstracts (three-page limit): Upload as "Abstract.pdf".** Start each document on a new page. The technical and lay abstracts are used by all reviewers. Abstracts of all funded research projects will be posted publicly on the CDMRP website (<https://cdmrp.army.mil>). **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:** 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 research.
- **Relevance to Topic Area(s):** State the relevance of the project to at least one FY21 PRMRP Topic Area. If applicable, describe how the proposed research project addresses an FY21 PRMRP Area of Encouragement ([Appendix 2](#)).

- **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:** 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.
- State the FY21 PRMRP Topic Area(s) addressed by the proposed research project. If applicable, describe how the proposed research project addresses an FY21 PRMRP Area of Encouragement ([Appendix 2](#)).
- 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 Clinical Trial Award 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 outlined 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”.**
    - 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 of the proposed clinical trial on the lives and health of individuals affected by the specified disease/condition with regard to the FY21 PRMRP Topic Area(s).
    - ***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. 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.
    - **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. Cite evidence showing that the procedures are consistent with sound research design and, when appropriate, that these procedures are already in use for diagnostic or treatment purposes. Clearly delineate research procedures from routine clinical procedures. Discuss how compliance with current GLP guidelines, GMP, and other regulatory considerations will be established, monitored, and maintained, as applicable.
    - **Clinical Monitoring Plan:** Describe how the study will be conducted by and monitored for current ICH E6 (International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use) GCP compliance by an independent clinical trial monitor (or clinical research associate). The safety monitoring and reporting 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, pertinent demographic characteristics of the accessible population at the study site(s) (population from whom the sample will be recruited/drawn), and the prospect of their participation. 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 and retention 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 contingency plans for addressing possible delays, including a mitigation plan for slow or low enrollment and/or attrition. Identify ongoing clinical trials that may compete for the same patient population and how they may impact enrollment progress. Describe how the proposed clinical trial might affect the daily lives of the individual human subjects participating in the study (e.g., medication use, overnight stays). Provide justification related to the scientific goals of the proposed study for limiting inclusion of any group by age, race, ethnicity, or sex/gender. ***For clinical trials proposing to include military personnel, refer to the General Application Instructions, Appendix 1, for more information.***
  - **Inclusion/Exclusion Criteria:** List the inclusion and exclusion criteria for the proposed clinical trial. Inclusion/exclusion criteria should take into consideration the specific risk profile of the studies to be conducted and the standard of care for that patient population. Provide detailed justification for exclusions.

***Inclusion of Women and Minorities in Study.*** Consistent with the Belmont Report, “Ethical Principles and Guidelines for the Protection of Human Subjects,” and Congressional legislation, special attention is given to inclusion of women and/or minorities in studies funded or supported by the USAMRDC. This policy is intended to promote equity both in assuming the burdens and in receiving the benefits of human subjects research. Include a description of the composition of the proposed study population. Describe the strategy for the inclusion of women and minorities in the clinical research appropriate to the objectives of the study, and an accompanying rationale for the selection of subjects to include a justification if women and/or minorities will be excluded from the clinical trial. Provide an anticipated enrollment table(s) in terms of sex/gender, race, and/or ethnicity using the suggested Inclusion Enrollment Report format, Policy on Inclusion of Women and Minorities, and Frequently Asked Questions for the policy may be downloaded from eBRAP under “Resources and Reference Material” 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 or not the potential human subject will be allowed to discuss the study with anyone before making a decision.
  - Consider the need for obtaining ongoing consent or for re-assessing capacity over the course of a long-term study and describe any relevant procedures to assure continued consent.
  - Describe the plan for the consent of the individual's Legally Authorized Representative (LAR) to be obtained prior to the human subject's participation in the study. State law defines who may act as the LAR. The local IRB of record should be consulted for guidance regarding who can serve as LAR for research at the study site. **Note:** In compliance with 10 USC 980 (<https://www.gpo.gov/fdsys/pkg/USCODE-2011-title10/pdf/USCODE-2011-title10-subtitleA-partII-chap49-sec980.pdf>), the application must describe a clear intent to benefit for human subjects who cannot give their own consent to

participate in the proposed clinical trial. If applicable, refer to the General Application Instructions, Appendix 1, for more information.

- **Assent.** If minors or other populations that cannot provide informed consent are included in the proposed clinical trial, a plan to obtain assent (agreement) from those with capacity to provide it, or a justification for a waiver of assent, should be provided. PIs should consult with their local IRB to identify the conditions necessary for obtaining assent.
- **Screening Procedures:** List and describe any evaluations (e.g., laboratory procedures, history, or physical examination) that are required to determine eligibility/suitability for study participation and the diagnostic criteria for entry.  
*Note:* Some screening procedures may require a separate consent or a two-stage consent process.
- **Risks/Benefits Assessment:**
  - **Foreseeable risks:** Clearly identify all study risks, including potential safety concerns and adverse events. Study risks include any risks that the human subject is exposed to as a result of participation in the clinical trial. Consider psychological, legal, social, and economic risks as well as physical risks. If the risks are unknown, this should be stated. If applicable, any potential risk to the study personnel should be identified.
  - **Risk management and emergency response:**
    - ❖ Describe how safety surveillance and reporting to the IRB and FDA (if applicable) will be managed and conducted.
    - ❖ Describe all safety measures to minimize and/or eliminate risks to human subjects and study personnel or to manage unpreventable risks. Describe how the safety monitoring and reporting plan is appropriate for the level of risk. Include safeguards and planned responses such as dose reduction or stopping criteria based on toxicity grading scales or other predetermined alert values.
    - ❖ Discuss the overall plan for provision of emergency care or treatment for an adverse event for study-related injuries, including who will be responsible for the cost of such care.
    - ❖ Address any special precautions to be taken by the human subjects before, during, and after the study (e.g., medication washout periods, dietary restrictions, hydration, fasting, pregnancy prevention).
    - ❖ Describe any special care (e.g., wound dressing assistance, transportation due to side effects of study intervention impairing ability to drive) or equipment (e.g., thermometers, telemedicine equipment) needed for human subjects enrolled in the study.

- ❖ If the IRB determines that a trial presents greater than minimal risk to human subjects, the DOD requires an independent research monitor with expertise consistent with the nature of risk(s) identified within the research protocol. If applicable, refer to the General Application Instructions, Appendix 1, Section B (Research Monitor Requirement), for more information on study reporting authorities and responsibilities of the research monitor.
- **Potential benefits:** Describe known and potential benefits of the study to the human subjects who will participate in the study. Articulate the importance of the knowledge to be gained as a result of the proposed research and if the population selected for participation in the trial stands to benefit from the gained knowledge. 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: Surveys, Questionnaires, and Other Data Collection Instruments, if applicable (no page limit): Upload as “Surveys.pdf”.** The Surveys, Questionnaires, and Other Data Collection Instruments attachment should include a copy of the most recent version of surveys, questionnaires, data collection forms, rating scales, interview guides, or other instruments. For each instrument, describe how the information collected is related to the objectives of the study. Describe how and when the instrument(s) will be administered. Describe how the instrument(s) will be adapted to the subject population, if applicable.
- **Attachment 10: Study Personnel and Organization (no page limit): Start each document on a new page. Combine into one document and upload as “Personnel.pdf”.** The Study Personnel and Organization attachment should include the components listed below. 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.
  - **Organizational Chart:** Provide an organizational chart that identifies key members of the study team and provides an outline of the governing structure for multi-institutional studies. Identify collaborating organizations, centers, and/or departments and name each person’s position on the project. Include any separate laboratory or testing centers. Identify the data and clinical coordinating center(s) and note any involvement from Contract Research Organizations, as appropriate. Identify and provide justification for the inclusion of international sites, as appropriate. If applicable, identify the FDA regulatory sponsor and any external consultants or other experts who will assist with FDA applications. While there is no specified format for this information, a table(s) or diagram is recommended. *Note:* This item may be made available for programmatic review.
  - **Study Personnel Description:** Briefly describe the roles and levels of effort of the individuals listed in the organizational chart on the project. Describe relevant experience and qualifications that demonstrate appropriate expertise for the given

- role, including previous interactions with the FDA, if applicable. An external research monitor (if applicable) and study coordinator(s) should be included.
- **Study Management Plan:** Provide a plan for ensuring the standardization of procedures among staff and across sites (if applicable). If the proposed clinical trial is multi-institutional, clearly describe the multi-institutional structure governing the research protocol(s) across all participating institutions. Provide a regulatory submission plan for the master protocol and master consent form by the lead organization/site; include a single IRB/EC pathway. 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 11: 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 12: 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 to the next phase of development (i.e., next-phase clinical trials, commercialization, delivery to the military or civilian market, incorporation into clinical practice, and/or approval by the FDA).
- Ownership rights/access to the intellectual property necessary for the development and/or commercialization of products or technologies supported with this award, including an intellectual and material property plan among participating organizations (if applicable), and the government’s ability to access such products or technologies in the future.
- A risk analysis for cost, schedule, manufacturability, and sustainability.
- **Attachment 13: Regulatory Strategy (no page limit): If submitting multiple documents, start each document on a new page. Combine and upload as a single file named “Regulatory.pdf”.** Answer the following questions and provide supporting documentation as applicable.
  - State the product/intervention name.

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

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

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

- State whether the product is FDA-approved, -licensed, or -cleared, and marketed in the U.S.

- If the product is marketed in the U.S., state the product label indication. State whether the proposed research involves a change to the approved label indication for the route of administration, dosage level, and/or subject population. Indicate whether the proposed research involves a change that increases the risks associated with using the product. State whether the product is being promoted for an off-label use (where promotion involves the sale of a marketed product).
- 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 investigator-sponsored regulatory exemptions (e.g., IND, IDE, [or other international equivalent]), provide evidence of appropriate institutional support, including capabilities to ensure monitoring as required by the FDA or relevant international regulatory agency

For a **Clinical Trial Only** submission:

- ***If an IND or IDE is required, an active IND or IDE, respectively, deemed safe to proceed that covers the proposed trial must be in place by the FY21 PRMRP Clinical Trial Award application submission deadline (this includes clinical trials requesting exception from informed consent under 21 CFR 50.24), and a copy of the FDA or relevant national regulatory agency acknowledgment letter, to include submission date and receipt date, and a statement that the FDA or relevant national regulatory agency did not raise concerns and/or did not place the clinical trial on hold must be included in Attachment 13.*** 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. If there are any existing cross-references in place, provide the application number(s) and associated sponsor(s). 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.
- 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. ***Note: If an amendment is needed to include the proposed trial, then the Planning Phase with Clinical Trial should be used.***
- If the proposed investigational drug/agent/device is exempt or the proposed investigational device qualifies for an abbreviated IDE, provide evidence in writing from the IRB of record, or the FDA, or the international regulatory agency for clinical trials conducted at an international site(s).
- 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).

- GMP Compliance (if applicable): Provide information regarding the resources available to aid in the development of sufficient quantities of the reagent under GMP.
- **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. Include information that describes the PI’s background and expertise. 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”.

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

Applicant organizations and all sub-recipient organizations must have a DUNS number to submit applications to Grants.gov. The applicant organization must also be registered in the Entity Management functional area of the SAM with an “Active” status to submit applications through the Grants.gov portal. Verify the status of the applicant organization’s Entity registration in SAM well in advance of the application submission deadline. Allow several weeks to complete the entire SAM registration process. If an applicant has not fully complied with the requirements at the time the federal awarding agency is ready to make a federal award, the federal awarding agency may determine that the applicant is not qualified to receive a federal award and use that determination as a basis for making a federal award to another applicant. Refer to the General Application Instructions, Section III, for further information regarding Grants.gov requirements.

***Announcement of Transition to SAM-Generated Unique Entity Identifier (UEI):*** Through April 2022, a transition from DUNS to the SAM-generated UEI will occur. Refer to the General Application Instructions, Section III.1, DUNS Number, for more information on the transition and timing.

### **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 for the Planning Phase is **18** months.

The anticipated direct costs budgeted for the entire period of performance of this base award 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 using an indirect cost rate exceeding the organization's negotiated rate.

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. Approval may be dependent on the availability of future year appropriations. ***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 is **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 this award mechanism, direct costs may be requested for (not all inclusive):

- Support for multidisciplinary collaborations, including travel
- 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 two investigators to travel to one scientific/technical meeting per year in addition to the required meeting described above. The intent of travel costs to scientific/technical meeting(s) is to present project information or disseminate project results from the FY21 PRMRP Clinical Trial Award.

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;
  - Surveys, 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:***

- **Research Strategy**

- How well the scientific rationale for clinically testing the intervention is supported by the preliminary data, critical review and analysis of the literature, and/or laboratory/preclinical evidence.

- How well the study aims, hypotheses and/or objective(s), experimental design, methods, data collection procedures, and analyses are designed to answer clearly the clinical objective.
- How well the inclusion criteria and subject-to-group assignment meet the needs of the proposed clinical trial.
- How well the exclusion criteria are justified.
- Whether the strategy for the inclusion of women and minorities and distribution of proposed enrollment are appropriate for the proposed research.
- How well plans to collect specimens and conduct laboratory evaluations are addressed, if applicable.
- To what degree the data collection instruments (e.g., surveys, questionnaires), if applicable, are appropriate to the proposed study.
- **Intervention**
  - Whether there is evidence of support, indicating availability of the intervention from its source, for the duration of the proposed clinical trial (if applicable).
  - To what degree the intervention addresses the clinical need(s) described.
  - How the intervention compares with currently available interventions and/or standards of care.
  - To what degree the PI has provided preclinical and/or clinical evidence to support the safety of the intervention.
  - How well research procedures are clearly delineated from routine clinical procedures.
  - Whether measures are described to ensure the consistency of dosing of active ingredients for nutritional supplements (if applicable).
- **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 contingency plans to resolve them.

- To what extent the proposed clinical trial might affect the daily lives of the individual human subjects participating in the study (e.g., will human subjects still be able to take their regular medications while participating in the clinical trial? Are human subjects required to stay overnight in a hospital?).
- **Clinical Impact**
  - How relevant the anticipated outcomes of the proposed clinical trial are to individuals affected by the specified disease/condition.
  - How well the sample population represents the targeted patient population that might benefit from the proposed intervention.
  - How the potential outcomes of the proposed clinical trial will provide/improve short-term benefits for individuals.
  - How significantly the long-term benefits for implementation of the intervention may impact patient care and/or quality of life.
- **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 FDA or other international agency regulation, or that the IND or IDE application (and/or international equivalent) has been deemed safe to proceed by 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 for providing continuity of development, including proposed development or modification of

clinical practice guidelines and recommendations, provider training materials, patient brochures, and other clinical support tools, scientific journal publications, models, simulations, and applications are established and/or achievable.

- Whether the schedule and milestones for bringing the intervention to the next level of development (next-phase clinical trials, transition to industry, delivery to the market, incorporation into standard practice, and/or approval by the FDA) are achievable.
- Whether the 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.

- **Statistical Plan**

- To what degree the statistical model and data analysis plan are suitable for the planned study objectives.
- How the statistical plan, including sample size projections and power analysis, is adequate to meet the objectives of the study and all proposed correlative studies.
- If applicable, whether the statistical plan compensates for the use of a subpopulation of a recruited sample population to ensure appropriate power can be achieved within the subpopulation study.

- **Ethical Considerations**

- Whether the population selected to participate in the trial stands to benefit from the knowledge gained.
- If applicable, how well the inclusion of international sites is justified.
- How the level of risk to human subjects is minimized and how the safety monitoring and reporting plan is appropriate for the level of risk.
- Whether a research monitor with expertise consistent with the nature of the potential risk(s) is identified, if applicable.
- How well the evidence shows that the procedures are consistent with sound research design and, when appropriate, that these procedures are already in use for diagnostic or treatment purposes.
- To what degree privacy and confidentiality issues are appropriately considered.

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

- **Personnel and Communication**

- Whether the composition of the study team (e.g., study coordinator, statistician) is appropriate.
- To what degree the study team's background and expertise are appropriate to accomplish the proposed work (e.g., statistical expertise, expertise in the disease, and clinical studies).
- How the levels of effort of the study team members are appropriate for successful conduct of the proposed trial.
- How well the logistical aspects of the proposed clinical trial (e.g., communication plan, data transfer and management, standardization of procedures) meet the needs of the proposed clinical trial.
- For multi-site clinical trials, how well the lead site responsibilities and human research protections regulatory coordination are defined and planned for.

- **Budget**

- Whether the budget is appropriate for the proposed research.

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 FY21 PRMRP, as evidenced by the following:
  - Adherence to the intent of the award mechanism
  - Relevance to military health
  - Program portfolio composition
  - Relative clinical impact

### **II.E.2. Application Review and Selection Process**

All applications are evaluated by scientists, clinicians, and consumers in a two-tier review process. The first tier is **peer review**, the evaluation of applications against established criteria to determine technical merit, where each application is assessed for its own merit, independent of other applications. The second tier is **programmatic review**, a comparison-based process in which applications with high scientific and technical merit are further evaluated for programmatic relevance. Final recommendations for funding are made to the Commanding General, USAMRDC, on behalf of the DHA and the OASD(HA). ***The highest-scoring applications from the first tier of review are not automatically recommended for funding. Funding recommendations depend on various factors as described in [Section II.E.1.b, Programmatic Review](#).*** Additional information about the two-tier process used by the CDMRP can be found at <https://cdmrp.army.mil/about/2tierRevProcess>. An information paper describing the funding recommendations and review process for the award mechanisms for the 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 200.88, over the period of performance, the federal awarding agency is required to review and consider any information about the applicant that is available in the Federal Awardee Performance and Integrity Information System (FAPIIS).

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

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

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

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

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

### **II.F. Federal Award Administration Information**

#### **II.F.1. Federal Award Notices**

Awards supported with FY21 funds are anticipated to be made no later than September 30, 2022. 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 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 other 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 or organization will be allowed at the discretion of the USAMRAA 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.

### **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.

Inclusion Enrollment Reporting Requirement: Enrollment on the basis of sex/gender, race, and/or ethnicity will be required with each quarterly, annual, and final technical report. The suggested Inclusion Enrollment Report format is available on the “Funding Opportunities & Forms” web page (<https://ebrap.org/eBRAP/public/Program.htm>) in eBRAP.

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.

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

## **II.G. Federal Awarding Agency Contacts**

### **II.G.1. CDMRP Help Desk**

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

Phone: 301-682-5507

Email: [help@eBRAP.org](mailto:help@eBRAP.org)

### **II.G.2. Grants.gov Contact Center**

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

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

Email: [support@grants.gov](mailto: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 601a. The program announcement numeric version code will match the General Application Instructions version code 601.

### **II.H.2. Administrative Actions**

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

#### **II.H.2.a. Rejection**

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

- Preproposal Narrative is missing.

The following will result in administrative rejection of the application:

- Submission of an application for which a letter of invitation was not received.
- Project Narrative exceeds page limit.
- Project Narrative is missing.
- Budget is missing.
- Submission of the same research project to different Funding Opportunities within the same program and fiscal year. Refer to [Section II.D, Application and Submission Information](#) for exceptions.
- Intervention ([Attachment 7](#)) is missing.
- Human Subject Recruitment and Safety Procedures ([Attachment 8](#)) is missing.
- Data Management ([Attachment 11](#)) is missing.
- Regulatory Strategy ([Attachment 13](#)) 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 FY21 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 FY21 PRMRP Programmatic Panel members can be found at <https://cdmrp.army.mil/prmrp/panels/panels21>.*
- 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 FY21, the identities of the peer review contractor and the programmatic review contractor may be found at the CDMRP website (<https://cdmrp.army.mil/about/2tierRevProcess>). Applications that include names of personnel from either of these companies may be administratively withdrawn.
- Personnel from applicant or collaborating organizations are found to have contacted persons involved in the review or approval process to gain protected evaluation information or to influence the evaluation process.
- Applications from extramural organizations, including non-DOD federal agencies, received through eBRAP may be withdrawn.
- Applications submitted by an intramural DOD organization may be withdrawn if the intramural organization cannot coordinate the use of contractual, assistance, or other appropriate agreements to provide funds to extramural collaborators.
- The proposed research is not a clinical trial.
- The proposed research includes one or more animal research studies.
- 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.
- For clinical trials (Clinical Trial Only) requiring an IND or IDE, documentation that an active IND or IDE deemed safe to proceed that covers the proposed clinical trial is in place is not provided.

- For clinical trials (Clinical Trial Only) requiring an IND or IDE amendment, documentation of the FDA’s concurrence to proposed regulatory approach is not provided.
- For clinical trials (Clinical Trial Only) with international sites, documentation of the relevant regulatory approval from the host country(ies) is not provided.
- The proposed research does not address at least one of the Congressionally directed FY21 PRMRP Topic Areas.
- The PI does not meet the eligibility criteria.
- Submission of the same research project to different funding opportunities within the same program and fiscal year. Refer to [Section II.D, Application and Submission Information](#), for exceptions.

#### **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 ( <b>extramural submissions only</b> )	Complete form as instructed	
Summary (Tab 1) and Application Contacts (Tab 2) ( <b>intramural submissions only</b> )	Complete 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 Abstract: Upload as Attachment 3 with file name "Abstract.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"	
	Surveys, Questionnaires, and Other Data Collection Instruments: Upload as Attachment 9 with file name "Surveys.pdf" if applicable	
	Study Personnel and Organization: Upload as Attachment 10 with file name "Personnel.pdf"	
	Data Management: Upload as Attachment 11 with file name "Data_Manage.pdf"	
	Transition Plan: Upload as Attachment 12 with file name "Transition.pdf"	
	Regulatory Strategy: Upload as Attachment 13 with file name "Regulatory.pdf"	
Representations (extramural submissions only): Upload as Attachment 14 with file name "RequiredReps.pdf" if applicable		

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 ( <b>extramural submissions only</b> )	Complete as instructed. Attach Budget Justification (BudgetJustification.pdf) to the appropriate field	
Budget ( <b>intramural submissions only</b> )	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
ALS	Amyotrophic Lateral Sclerosis
ARDS	Acute Respiratory Distress Syndrome
CDMRP	Congressionally Directed Medical Research Programs
CFR	Code of Federal Regulations
CFS	Chronic Fatigue Syndrome
DHA	Defense Health Agency
DHP	Defense Health Program
DOD	Department of Defense
DODGARs	Department of Defense Grant and Agreement Regulations
DUNS	Data Universal Numbering System
eBRAP	Electronic Biomedical Research Application Portal
EC	Ethics Committee
ET	Eastern Time
FAD	Funding Authorization Document
FAPIIS	Federal Awardee Performance and Integrity Information System
FDA	U.S. Food and Drug Administration
FH	Familial Hypercholesterolemia
FTD	Frontotemporal Degeneration
FXPOI	Fragile X-Associated Primary Ovarian Insufficiency
FXTAS	Fragile X-Associated Tremor/Ataxia Syndrome
FY	Fiscal Year
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
HIV	Human Immunodeficiency Virus
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
ME	Myalgic Encephalomyelitis
MIPR	Military Interdepartmental Purchase Request
NIH	National Institutes of Health

OASD(HA)	Office of the Assistant Secretary of Defense for Health Affairs
ORCID	Open Researcher and Contributor ID, Inc.
ORP	Office of Research Protections
PI	Principal Investigator
PRMRP	Peer Reviewed Medical Research Program
RDT&E	Research, Development, Test, and Evaluation
SAM	System for Award Management
sIRB	Single Inquiry Review Board
SOW	Statement of Work
STEM	Science, Technology, Engineering, and/or Mathematics
UEI	Unique Entity Identifier
URL	Uniform Resource Locator
USAMRAA	U.S. Army Medical Research Acquisition Activity
USAMRDC	U.S. Army Medical Research and Development Command
USC	United States Code
VA	Department of Veterans Affairs

## APPENDIX 2: AREAS OF ENCOURAGEMENT

Applications addressing any of the FY21 PRMRP Topic Areas are of interest to the program. ***Any aspect of research relevant to an FY21 PRMRP Topic Area may be considered for funding.*** Areas of Encouragement related to each FY21 PRMRP Topic Area have been identified by the DOD, VA, and other relevant stakeholders and are listed below under each Topic Area. Applicants are strongly urged to read and consider these Areas of Encouragement before preparing their applications. ***The information provided is not exhaustive, and applicants are not restricted to submitting applications that address an Area of Encouragement on this list.***

### Arthritis (other than [Rheumatoid Arthritis](#), which is a separate Topic Area listed below)

- Research quantifying the impacts of obesity, weight loss, physical fitness (all components, e.g., cardiovascular, strength, flexibility, balance), and dietary factors on the development of or prevention/risk reduction of arthritis.
- Determine factors that lead to accelerated degeneration (post-traumatic osteoarthritis within 3 years) following military-relevant joint injuries.
- Basic and translational research to identify treatments to mitigate and/or reverse osteoarthritis.
- Research to establish activity recommendations for maximal joint life following joint repair, particularly in young patient populations.
- Intra-articular treatments that offer sustained relief of symptoms and/or disease-modifying effects compared to current treatments.
- Research on therapies that target multiple phases of the cellular response pathways that are implicated in the development of arthritis, including cell death, oxidative stress, inflammation, mechanotransduction, matrix changes, and changes in metabolic responses.
- Identification and/or validation of diagnostic biomarkers that can serve as surrogate endpoints.

### Burn Pit Exposure

- Research on the etiology and pathophysiology of adverse health events associated with exposure to airborne hazards and/or open burn pits.
- Development of improved methods for assessing and treating lung injury due to chemical, metal, or smoke inhalation/exposure.
- Toxicological studies to characterize emissions from open air burns, burn boxes, incinerators, and simulated burn pits to ascertain the toxicity and mechanisms of action of such chemicals and airborne environmental dust and mixtures, as well as interactions among pollutants and particulate materials.

- Validation of biomarkers and development of fieldable assays, particularly from the lung microbiome, of exposure to burn pit combustion products, burning biomass and refuse, and geogenic dusts.
- Development and validation of sensors/instruments for assessing (including in real time) area and/or individual levels of exposure to airborne hazards for use in research and for occupational and environmental exposure monitoring.
- Studies exploring the effect of combination traumatic lung injury and burn pit exposure.

### **Cardiomyopathy**

- Development of novel therapeutic approaches for primary and secondary cardiomyopathies.
- Strategies to identify risk factors associated with the development of cardiomyopathy (i.e., genetic, lifestyle, exposure) in the civilian and/or military populations.
- Research to improve the understanding of the pathophysiology of cardiomyopathies.
- Improvement of noninvasive diagnostic techniques for primary and secondary cardiomyopathies.
- Research on the multiple etiologies of cardiomyopathy (e.g., hypertension, ischemia, hemochromatosis, sleep apnea, radiation therapy, medications, smallpox vaccine, infections).

### **Congenital Heart Disease**

- Development of approaches, including regenerative medicine, that provide structural support, restore native activity, allow for tissue growth, and prevent the need for reoperation.
- Population-based or outcomes-based research to assess the health outcomes of individuals with congenital heart disease across their life spans.
- Research to improve understanding of the causes of congenital heart defects, including genomic, proteomic, and metabolomic profiling.
- Research to design and implement improved or novel models (in vitro or in vivo) with an established phenotype to increase the efficacy of discovering drug targets, screening existing drugs, performing cardiotoxicity testing, or uncovering pathogenesis.
- Research both on the risk of neurologic injury and on enhanced neuroprotection before, during, and after surgery for congenital heart disease.

### **Diabetes**

- Identification and/or evaluation of interventions to reduce metabolic dysregulation and the development of diabetes among individuals meeting the clinical criteria for prediabetes.

- Research on interventions to prevent or treat diabetes complications, including diabetic retinopathy, nephropathy, neuropathy, cardiomyopathy, and impaired wound healing.
- Understanding factors/mechanisms responsible for adverse metabolic effects (insulin resistance, beta cell dysfunction, dyslipidemia, nonalcoholic fatty liver disease) of obesity and why some people with obesity are protected from the adverse metabolic effects of excess adiposity.
- Research to understand immunologic contributions to pathophysiology and treatment of adult onset type 1 diabetes, which comprises 25% of all type 1 diabetes cases.
- Research to better understand the heterogeneity of diabetes including the identification of novel biomarkers (especially the metabolomics biomarkers that are common between diabetes and post-traumatic stress disorder).
- Research on the transplantation of allogenic or autologous pancreatic islet cells for long-term natural insulin production, including current good laboratory/clinical/manufacturing practices (as needed) for cell line development.
- Research to design and implement improved or novel models (in vitro or in vivo) to model pancreatic islets to uncover pathogenesis and improve the efficiency of drug discovery.
- Research to improve sensitivity and functionality of biosensor systems to improve quality of life for users.

### **Dystonia**

- Research to improve identification of delayed onset dystonia following traumatic brain injury.
- Research on interventions to prevent, slow the progression of, or treat dystonia.
- Studies into the natural history, genetics, and/or neurobiology of dystonia.
- Research to identify the relationship between specific molecular/genetic changes and circuitry/network alterations in dystonia.
- Identification and development of novel research tools (cellular models, phenotypic models, etc.) to aid dystonia research.

### **Eating Disorders**

- Studies to identify the most effective treatment or preventive strategies for patients with an eating disorder, including those with a comorbid disorder.
- Studies on the pathophysiological consequences of eating disorders, including effects on organ functions and metabolic processes.

- Assessment of patterns of comorbidity between eating disorders and other mental health conditions, including an examination of whether eating disorders are more likely to precede or follow the development of other mental health conditions.
- Research to advance the understanding of the biological, genetic, lifestyle, and/or environmental factors or the effects of social media on eating disorders.
- Investigations into the prevalence, diagnosis, risk factors, and treatment patterns of eating disorders.

### **Emerging Viral Diseases**

- Predictive modeling tools that leverage advanced analytics (machine learning, artificial intelligence, etc.) approaches to predict outbreaks and epidemics and support strategies for mitigating the threat of emerging viral diseases as defined by the National Institute of Allergy and Infectious Diseases.<sup>1</sup>
- Rapid prediction of protective antigens/epitopes and testable correlates of protection on emerging or novel pathogens with an emphasis on emerging respiratory viruses with epidemic potential.
- Development of a highly sensitive diagnostic system for use at the point of injury that provides early diagnosis of viral infection prior to the onset of classical symptoms.
- Research, development, and validation of animal models for the study of emerging viral diseases, including novel infections such as the WHO's Disease X,<sup>2</sup> that demonstrate the pathophysiological mechanism of the disease and provide translational data to advance drug products to human clinical trials.
- Development of meaningful and relevant immunological and virological readouts that translate and/or predict human responses to vaccination or infection.
- Development of risk assessment strategies for vector-borne diseases and novel interventions for vector control, including but not limited to novel insecticides, larvicide applications, and barrier methods.

### **Endometriosis**

- Research to elucidate the underlying pathogenesis, evolution, pathophysiology, and progression of endometriosis. (How does it start, why does it start, and why does it get so bad in some women?)
- Improve detection and diagnosis of endometriosis through non-invasive techniques.

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<sup>1</sup> <https://www.niaid.nih.gov/research/emerging-infectious-diseases-pathogens>

<sup>2</sup> <https://www.who.int/activities/prioritizing-diseases-for-research-and-development-in-emergency-contexts>

- Development of novel treatments, including non-opioid pain therapies, or alternative therapies to alleviate symptoms and reduce progression and secondary effects of endometriosis such as pain, scarring, and infertility.
- Research to identify risk factors for subsequent cancer development, such as endometrioid and clear cell ovarian cancer.
- Research to optimize surgical techniques that improve fertility in endometriosis patients and reduce progression and symptoms of disease.

### **Epidermolysis Bullosa**

- Research, including clinical trials, focused on therapeutics (topical or systemic) or dressings that enhance wound healing in inherited epidermolysis bullosa.
- Development of novel therapeutics to reduce epidermolysis bullosa symptoms, improve quality of life, or lead to a cure.
- Research to provide further insight into those cellular pathways that promote the development of squamous cell carcinomas in recessive dystrophic and junctional epidermolysis bullosa.
- Research, including randomized controlled clinical trials, focused on systemic drugs that prevent, delay the onset, or modify the aggressiveness of squamous cell carcinoma in patients with recessive dystrophic and junctional epidermolysis bullosa.

### **Familial Hypercholesterolemia**

- Research to understand the approaches to clinical management to treat familial hypercholesterolemia (FH) patients at higher risk for progressing to clinical atherosclerotic cardiovascular disease.
- Gene editing or gene therapy studies addressing monogenic causes of FH.
- Research to improve early diagnosis of FH and the implementation of diagnostic tools, including in the pediatric population.
- Development of evidence-based approaches for risk stratification to understand FH disease progression and comorbidities (e.g., early onset cardiovascular disease and coronary artery disease), including panomic (genomics, proteomics, metabolomics, transcriptomics, and clinical data) studies to identify and evaluate polygenic risk factors.
- Studies to identify social and/or biological disparities in diagnosis and treatment and how they affect risk.
- Studies to systematically identify individuals at risk for FH using machine learning tools.

## **Fibrous Dysplasia**

- Research to better understand the underlying pathophysiology of fibrous dysplasia, including elucidating any genetic and cellular signaling factors that contribute to pathogenesis.
- Research that explores the prevention of lesion development or expansion in adolescents, or the development of implants that accommodate adolescent growth.
- Research to develop or better characterize animal models of fibrous dysplasia to assist in understanding disease pathogenesis, discover relevant biomarkers, or evaluate therapeutic efficacy.
- Research to discover and explore novel effective therapies for fibrous dysplasia outside of surgical interventions.
- Development of novel diagnostic tools for early and accurate detection of fibrous dysplasia.

## **Focal Segmental Glomerulosclerosis**

- Development of a curative therapy or treatments to delay or halt the progression of focal segmental glomerulosclerosis and/or prevent post-transplantation recurrence.
- Research to improve understanding of the causes of primary and/or secondary focal segmental glomerulosclerosis, including genetic mutations, lifestyle factors, or comorbidities.
- Development of non-invasive methods to diagnose focal segmental glomerulosclerosis and its variants, especially in newborn or pediatric diagnostics for early detection and intervention.
- Research to determine the efficacy of medications used off-label (outside the U.S. Food and Drug Administration [FDA]-approved indication) to treat focal segmental glomerulosclerosis.
- Development of surrogate endpoints to accelerate approval of new treatments.

## **Food Allergies**

- Studies to investigate the role of immunoglobulin E in the development or treatment of food allergies.
- Studies to understand cellular immunologic contributions to development or treatment of food allergies.
- Studies to determine the role of maternal diet on the incidence of food allergies in children.
- Research to understand the impact of environment (urban versus rural) on the incidence and type of food allergy.

- Studies aimed at determining the relationship between gut permeability and food allergies and manipulation of the biome to prevent, mitigate, and treat food allergies.
- Studies to understand the link between the food-processing techniques and food allergies.

### **Fragile X**

- Development and evaluation of gene modification (e.g., gene editing or gene reactivation) therapeutics for the treatment of fragile X syndrome (including fragile X-associated tremor/ataxia syndrome [FXTAS] and fragile X-associated primary ovarian insufficiency [FXPOI]).
- Identification and validation of functional measures of the manifestations of fragile X syndrome (including FXTAS and FXPOI) across the life span.
- Research to advance the understanding of the pathophysiology/natural history or life course of fragile X syndrome (including FXTAS and FXPOI).
- Identification of novel targets and/or testing novel or existing therapeutics (e.g., repurposing drugs) for fragile X syndrome (including FXTAS and FXPOI).
- Research to establish the benefits of early diagnosis/early treatment of fragile X syndrome in patients and progeny.
- Development of a preclinical model that is representative of human fragile X syndrome.
- Development and testing of behavioral interventions to improve symptoms of fragile X syndrome.

### **Frontotemporal Degeneration**

- Basic research to establish in vivo and in vitro models or research tools for disease pathology, behavioral/cognitive symptoms, or the frontotemporal degeneration/amyotrophic lateral sclerosis (FTD/ALS) spectrum.
- Research to understand the neurological basis of deficits in social cognition and emotional regulation.
- Research to improve diagnostics of and/or prognostics for frontotemporal degeneration and related proteinopathies.
- Research to identify risk factors (e.g., gene or epigenetic networks, environmental factors, and family history of neurodegeneration or linked to FTD/ALS gene mutations).
- Development/advancement of evidence-based treatments (including pharmacological and non-pharmacological) for FTD and associated disorders.

## **Hemorrhage Control**

- Development of new and innovative capabilities to stop non-compressible intracavitary hemorrhage as well as improved technologies to stop junctional and pelvic bleeding in pre-hospital environments.
- Development of battlefield hemostatic wound solutions or dressings with integrated antimicrobial and/or analgesic effects. Hemostatic effects should arrest major hemorrhage within 3 minutes of placement.
- Development of innovative damage control resuscitation and damage control surgical and non-surgical capabilities, especially interventions to be used in an austere environment by physician or non-physician providers.
- Research on strategies (e.g., innovative technologies, wearable devices, analyte indicators) for early (e.g., pre-hospital) detection (especially internal bleeding) and treatment for hemorrhage, coagulopathy of trauma, and hemodynamic decompensation/hypovolemic shock.
- Research on novel or engineered blood products that offer physiological, logistical, or cost advantages over current products. Hemoglobin-based oxygen carrier research should address nitric oxide scavenging.
- Research on adjunctive pharmacological solutions for hemorrhage, shock, coagulopathy, transfusion, and/or the stabilization of polytrauma, with attention to the impact on potential traumatic brain injury.
- Research to evaluate the effects of current combat blood product transfusion guidelines on immunological status and clinical outcomes.
- Research on treatment of mitochondrial dysfunction during hemorrhagic shock.

## **Hepatitis B**

- Impact of co-infection with hepatitis C or human immunodeficiency virus (HIV) on hepatitis B pathogenesis.
- Research on strategies to reduce vertical (mother-to-child) transmission of hepatitis B.
- Development of strategies for reliable, non-invasive, early detection of hepatitis-related liver disease and hepatocellular carcinoma.
- Research on strategies to promote reversal of liver fibrosis and/or assess the associated clinical and pathological outcomes.
- Clinical studies to evaluate combination or curative therapies for treatment of hepatitis B infection.

- Basic/translational research leading to new therapies for viral hepatitis and hepatocellular carcinoma.

### **Hydrocephalus**

- Research on the etiology, prevention, diagnosis, and treatment of post-traumatic hydrocephalus.
- Discovery or validation of novel and/or innovative therapies and therapeutic targets for the treatment of hydrocephalus and its sequelae, including therapies directed at myelin regeneration and repair.
- Development or validation of biomarkers and imaging techniques, particularly multimodal approaches, to aid in diagnosis, prognosis, and monitoring of therapeutic efficacy.
- Research on the prevention of shunt failure or the development of novel shunt technologies.
- Development or validation of improved hydrocephalus model systems.

### **Hypertension**

- Studies that leverage digital phenotyping, genomic, metabolomic, microbiomic, immunological, and/or other systems approaches to identify objective markers of increased risk of hypertension, including hypertension associated with post-traumatic stress, acute stress disorder, and/or other stress-related psychological conditions and diagnoses.
- Research on the etiology, prevalence, and trends of hypertension in children and adolescents.
- Research on the vascular structure changes in pre-hypertensive individuals, especially in children and adolescents.
- Research to develop inexpensive and effective tools to detect secondary hypertension and its causes at an early stage (e.g., diagnostic algorithms).
- Research to understand ethnic/racial differences in the pathophysiology of hypertension and the response to treatments.
- Research to elucidate the impact of hypertension on the heart, brain, arteries, and other target organs across a patient's life span.

### **Inflammatory Bowel Diseases**

- Studies directed toward understanding how acute enteric infections may trigger chronic inflammatory bowel diseases, including studies aimed at elucidating the interactions between chronic/post-traumatic stress and infection that may provoke inflammatory bowel disease.
- Studies that leverage genomic, metabolomic, microbiomic, immunological, and systems biology approaches to prevent or treat inflammatory bowel disease (especially inflammatory bowel diseases associated with acute enteric infection).

- Studies to elucidate pathological processes involved in inflammatory bowel disease-related complications, such as strictures or primary sclerosing cholangitis, or progression to cancer with the goal of prevention or treatment.
- Research on the role of diet in the development and progression of inflammatory bowel diseases.
- Research on treatment strategies for patients with inflammatory bowel diseases to include, but not limited to, microbiome-related and those that target epithelial health and function strategies, including those who are refractory to standard care.

### **Malaria**

- Investigation of mechanisms of drug resistance in malaria, to include host, pathogen, and region-specific resistance against drugs used for treatment and prophylaxis.
- Studies to determine the levels of naturally occurring resistance to currently used prophylactic drugs in endemic regions of the world.
- Development of long-lasting (6 months) passive immunization approaches for the management of malaria.
- Identification of novel and/or innovative malaria drug targets for blood and liver stage malaria parasites.
- Studies evaluating co-infections with malaria, including host susceptibility and changes in risk.

### **Metals Toxicology**

- Validation of biomarkers and development of fieldable assays to evaluate acute exposure to toxic metals by inhalation and/or ingestion (e.g., drinking water).
- Development of microsurgical techniques to remove embedded toxic metals.
- Understanding the effects of embedded metals as a confounder on medical treatment of trauma injury and patient outcomes.
- Evaluating the long-term effects of exposure to nano/micro/airborne/aerosolized or non-removable embedded toxic metals.
- Studies exploring the effect of combination traumatic injury and exposure to toxic metals.
- Retrospective studies to evaluate risks and exposure to toxic metals among workers at industrial facilities.

## **Mitochondrial Disease**

- Research on novel and/or innovative treatments to alleviate symptoms or slow down the progression of mitochondrial diseases.
- Development of tools and methodologies to assess mitochondrial heteroplasmy on a cellular, tissue, and organ level.
- Identification and testing of non-invasive techniques and biomarkers to monitor mitochondrial function, aid in clinical diagnosis, and/or evaluate therapeutic efficacy.
- Development of improved tools and animal models to study primary mitochondrial diseases and evaluate therapeutics.
- Development of tools to distinguish whether mitochondrial dysfunction is inherited or acquired.
- Research to better understand the progression of mitochondrial diseases.

## **Myalgic Encephalomyelitis/Chronic Fatigue Syndrome**

- Development and testing of treatments or preventive measures for myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS).
- Research to understand the mechanisms underlying ME/CFS.
- Epidemiological research to understand the link between medical history and ME/CFS.
- Research to identify biomarkers to diagnose and test potential therapeutics for ME/CFS.

## **Myotonic Dystrophy**

- Research on the role of epigenetic factors in the onset, progression, and/or severity of myotonic dystrophy in relevant animal models or patients.
- Research into the mechanisms of expanded CTG or CCTG repeat instability in somatic or germ line cells in myotonic dystrophy.
- Identification of biomarkers that can be detected through minimally invasive means to signal early changes in the progression of myotonic dystrophy, especially in myotonic dystrophy type 2.
- Development and/or testing of novel and/or innovative treatments, including those utilizing gene editing or silencing.
- Clinical research into the natural history of myotonic dystrophy in order to understand disease progression and develop/validate clinical trial endpoint measures across the multiple organ systems involved in the disease.

## **Non-Opioid Therapy for Pain Management**

- Development of non-opioid, non-addictive pain management therapies, including non-pharmacological interventions and those that do not affect the cardiorespiratory system.
- Research to identify and address biopsychosocial aspects of pain to reduce or eliminate the use of opioid pain medication(s).
- Research to identify and reduce disparities in opioid prescribing practices for pain management.
- Research on non-opioid, non-addictive pain management strategies for patients with limited access to skilled providers and resources, including battlefield and resource-limited environments.

## **Nutrition Optimization**

- Research into nutrition-based strategies to prevent or reduce the impact of disease.
- Determining therapeutic effects and mechanisms of selected diets (Mediterranean, plant-based low-fat, low-carb, etc.) in people with obesity and other metabolic diseases.
- Development or validation of nutrition-based strategies that mitigate the consequences of environmental and/or physiological stressors.
- Development of prolonged nutrition care using oral and/or intravenous approaches including precision nutrition care following injury or illness.
- Research on the impact of the use of nutrition strategies or dietary supplements on physical or cognitive performance.
- Development or validation of improved nutrition strategies to enhance and sustain performance in operational environments, extreme climates/weather, or resource-limited settings.
- Research to develop strategies to apply metabolomics to optimize individual nutrition and the development of tools or devices to monitor nutritional intake at an individual level.
- Research to study how diet or changes to the gut microbiome impact brain health.
- Investigation into treatment strategies for obesity and weight management therapies, especially in the VA Health Care System.

## **Pathogen-Inactivated Blood Products**

- Development and validation of next-generation technologies and/or devices to reduce the production time, increase portability, decrease weight, or develop unpowered technologies for pathogen reduction/inactivation in whole blood.

- Research on lyophilization of pathogen-reduced/-inactivated blood products and derivatives (platelets, plasma, red cells, cryoprecipitate, coagulation factors, etc.).
- Development and advancement of technologies to improve the safety of blood products to include pathogen reduction/inactivation in whole blood for military/civilian blood donor centers and blood banks that meet the requirements for FDA licensure in support of domestic and global contingency/combat operations.
- Expansion and validation of the library of blood-borne pathogens that are reduced/inactivated to include emerging pathogens, genetically modified pathogens, and pathogens designed for biological warfare.
- Advancement in pathogen reduction technology to further improve the log-kill reduction for known blood-borne pathogens (e.g., hepatitis B, hepatitis C, cytomegalovirus, Korean hemorrhagic fever virus, Bunyaviruses, HIV, Rift Valley fever virus, malaria, *Trypanosoma cruzi* and *T. brucei*, Ebola virus, West Nile virus, dengue virus, chikungunya virus, Zika virus).
- Research studies, including clinical trials, to further characterize the effects of pathogen reduction technologies in blood products (e.g., whole blood, platelets, plasma, cryoprecipitate).

### **Peripheral Neuropathy**

- Research on the role of intense physical training, especially in a military setting, in the rapid onset and progression of hereditary neuropathy with liability to pressure palsies.
- Research on treatment strategies for patients with hereditary peripheral neuropathy.
- Research on the etiology and/or progression of idiopathic neuropathy with a focus on clinical description and clinical studies.
- Mechanistic studies to inform the treatment development for diabetic neuropathy or chemo-induced neuropathy.
- Research to discover and develop novel effective non-pharmacological therapies for idiopathic neuropathy or other peripheral neuropathy such as those induced by diabetes or chemotherapy.
- Regenerative medicine based solutions for peripheral nerve injury, such as gene therapy.
- Research on the etiology and progression of peripheral neuropathies associated with autoimmune diseases.
- Refinement of existing or development of new model systems (in vivo and in vitro) that better represent a neuropathy disease state and progression of the particular neuropathy.

- Addition of new sites to the consortium supporting the Peripheral Neuropathy Research Registry biobank housing DNA sample, plasma and serum, and associated data such as demographics, medical history of patient and family, lab and clinical tests from peripheral neuropathy patients (<https://www.foundationforpn.org/research/research-registry>).

### **Plant-Based Vaccines**

- Optimize expression and purification systems for plant-based vaccine production.
- Research to demonstrate safety and efficacy of plant-based vaccines, including oral administration of non-purified forms, such as food or feed product.

### **Platelet-Like Cell Production**

- Development of a lyophilized or manufactured platelet-like cell product that reduces hemorrhage or dilutional coagulopathy with a safety and efficacy profile that demonstrates compatibility with licensed blood products or derivatives (red blood cells, plasma – liquid or dried, platelets, cryoprecipitate, fibrinogen, albumin, etc.).
- Development of a lyophilized platelet-like product that provides universal compatibility, a shelf life of 2-3 years, and immediate reconstitution with sterile water/buffered solution and that is pathogen-reduced and a pooled product (e.g., 10 donors).
- Research toward early-stage animal model studies (safety) and first-in-human efficacy in clinical trials.

### **Polycystic Kidney Disease**

- Development of improved treatment strategies for polycystic kidney disease, including approaches to identify and monitor patients at higher risk for progressing to end-stage renal disease.
- Research on the underlying pathobiology and molecular mechanisms of polycystic kidney disease, including studies of genetic factors, cyst formation and growth, the role of cilia, and factors that modify disease progression and/or severity.
- Research on the lifestyle factors or comorbidities that may modify the progression of polycystic kidney disease.
- Development of surrogate endpoints to accelerate approval of new treatments.

### **Pressure Ulcers**

- Strategies to prevent or reduce the formation of pressure ulcers during prolonged immobilization of casualties in a pre-hospital environment (e.g., spinal cord injuries) or long-range transport/aeromedical evacuation.

- Development of (novel) point-of-care diagnostics or tools, such as artificial intelligence or algorithms using structured or unstructured data, for detecting early formation of pressure ulcers.
- Novel strategies for the treatment of pressure ulcers, including the mitigation of progression to advanced stages.
- Research on novel synthetic production, delivery, and adhesion methodologies leading to permanent closing of pressure ulcers. Methodologies might encompass synthetic fibers, novel tissue culture methodologies, growth factors, dermal printing, artificial skin, skin graft substitutes, regenerative medicine, etc.
- Development of novel wound healing and infection prevention strategies that are easy to administer and will prevent bacterial colonization, biofilm formation, and sepsis with extended activity (e.g., up to 72 hours) once placed.

### **Pulmonary Fibrosis**

- Development and/or testing of novel and/or innovative treatments, including precision medicine approaches, to delay or modify the progression of pulmonary fibrosis.
- Development and/or validation of improved in vitro and in vivo models (excluding mice) to study pulmonary fibrosis and evaluate therapeutics.
- Identification of biomarkers of pulmonary injury or early predictors of interstitial lung disease.
- Research into the pathobiology and molecular mechanisms underlying the development and progression of pulmonary fibrosis.
- Retrospective studies to determine the risk and incidence of pulmonary fibrosis among military Service Members and/or Veterans.

### **Respiratory Health (excluding lung cancer and mesothelioma)**

- Development and/or testing of novel and/or innovative treatments including precision medicine approaches, to prevent, or delay the progression of, acute lung injury (ALI)/acute respiratory distress syndrome (ARDS).
- Research on the etiology and prevention of ARDS caused by host responses to trauma, transfusion, mechanical ventilation, burns, infection, hemorrhagic shock, inhalation, and/or oxygen exposure.
- Development of improved methods for assessing and treating lung injury due to inhalation burn or high-dose radiation exposure.

- Strategies to stabilize and support the safe transport of patients with ARDS in order to optimize therapeutic interventions, particularly in operational scenarios requiring prolonged or extended care and/or longer transport times prior to definitive care.
- Studies to identify the prevalence and associated morbidity and mortality of blast overpressure, including combined overpressure and burn/lung injury.
- Research on the causes, treatment, and prevention of obstructive pulmonary diseases (e.g., chronic obstructive pulmonary disease and bronchiectasis), including identification and validation of biomarkers and disease phenotypes, as well as employing personalized medicine in clinical research and disease management.
- Development of biomarker metrics to associate the long-term health outcomes of ARDS with degradation of physiological and physical performance.
- Research on airborne chemical and pollution hazards that affect lung function associated with specific acute health outcomes for first responders or deployed Service Members.
- Research focused on acute and chronic lung injury/disorders due to viral infections, such as SARS-CoV-2.

### **Rheumatoid Arthritis**

- Research to better understand the relationship between genetic risk, environmental exposures, and triggers in developing rheumatoid arthritis.
- Studies that identify or validate biomarkers or personalized medicine strategies that allow for individualized medication choice based on the patient's underlying biology or disease state.
- Research on the long-term use of immunosuppressive and other therapies in patients with rheumatoid arthritis.
- Research to better characterize and understand the preclinical disease stage of rheumatoid arthritis for early diagnosis and treatment.
- Research on management of comorbidities, including biopsychosocial outcomes, for patients with rheumatoid arthritis.
- Research to establish activity recommendations following joint replacement for maximal joint life.

### **Sleep Disorders and Restriction**

- Research on the effects of disrupted normal sleep and circadian rhythms on the physical and psychological health, safety, performance, and productivity, including sex differences.
- Research on the physiology or treatment of sleep alterations in critically ill and injured patients.

- Research on the prevention and/or mitigation of sleep disorders and sleep restriction.
- Development and/or testing of non-pharmacological treatments for sleep disorders associated with long-term exposure to limited daylight or enclosed environments (e.g., aircraft, submarines, and/or tanks).
- Research on the objective screening and triage, precision diagnosis, management, and/or treatment (including non-pharmacological treatments such as cognitive behavioral interventions) of sleep disorders, especially following traumatic brain injury and/or related to post-traumatic stress disorder.
- Research to examine the impact of cognitive behavioral interventions, or other non-pharmacological interventions among Service Members post-deployment for preventing chronic sleep disruption.

### **Suicide Prevention**

- Research on treatment strategies to prevent suicidality.
- Research to examine effectiveness of public health interventions, including which interventions or combinations of interventions are most helpful, and under what specific circumstances are interventions most helpful.
- Determining strategies for an efficacy of lethal means safety and restriction methods, especially in military populations.
- Determination of risk factors and prevention strategies for suicide in those that have recovered from critical illness, polytrauma, and/or traumatic brain injury.
- Research on effective public messaging, tools, policies and practices for communications and public awareness to reduce suicide risk and rates in the population (e.g., reducing barriers to help-seeking while avoiding risks of normalizing suicidal behavior, safe messaging, encouraging help-seeking, normalizing lethal means safety practices).

### **Sustained Release Drug Delivery**

- Development of technology platforms or formulations for long-term sustained-release delivery of drugs, especially for radiation pre-exposure prophylaxis, post-traumatic stress disorder, substance use or abuse, suicidality, pain control, allergies, attention deficit/hyperactivity disorder, and chemoprophylaxis for any condition.
- Development of a sustained drug delivery system for pre-hospital trauma and pain medications for up to 24 hours prior to definitive care, including passive slow release or closed loop feedback delivery solutions, particularly in far-forward military operational environments.

- Development of a delivery system (including novel Good Manufacturing Practice (GMP)-grade biomaterials) that could accurately deliver prescription and non-prescription medications.
- Development of novel and/or innovative approaches for bioavailable and sustained-release oral formulations of existing broad-spectrum fungicidal, antimicrobial, antiparasitic, and antiviral medications.
- Research into techniques to provide sustained release of drugs in tissue repair applications, such as bone or nerve regeneration or vision restoration.

### **Vascular Malformations**

- Studies into the natural history, genetics, and pathogenesis of vascular malformations, including, but not limited to, lymphatic, capillary, venous, and arteriovenous and hemangiomas.
- Research to develop or improve methods to diagnose and manage vascular malformations, including, but not limited to, lymphatic, capillary, venous, and arteriovenous and hemangiomas.
- Research to discover or develop novel and/or innovative therapeutic targets and treatments to regress or prevent vascular malformations (both hereditary and acquired) including, but not limited to, lymphatic, capillary, venous, and arteriovenous and hemangiomas.
- Development of non-invasive or minimally invasive technologies or approaches for the control of internal bleeding, including cerebral arteriovenous malformations, associated with vascular malformations.
- Development of in vivo or in vitro models of vascular malformations for the purpose of identifying novel and/or innovative drug targets, screening existing drugs, and/or elucidating the pathogenesis of the disease.
- Research to understand and diagnose high-risk vascular malformations to prevent severe adverse events.

### **Women's Heart Disease**

- Identification of sex- and/or gender-specific approaches, as appropriate, to develop novel diagnostics, treatments, or artificial intelligence/machine learning using structured and/or unstructured data, or to increase the effectiveness of current practice to improve clinical care using these tools.
- Research on factors to predict and prevent the long-term impacts of the endocrine system, gestational diabetes, gestational hypertension, menopause, or preeclampsia on the cardiovascular health of women.
- Research on trauma-induced cardiac arrest secondary to hemorrhage and polytrauma.

- Research focused on elucidating the potential relationship between post-traumatic stress disorder and women's heart disease.
- Studies to determine the risk and incidence of heart disease among female Service Members operating extreme environments (e.g., hot, cold, altitude, subterranean).
- Research investigating drug-induced arrhythmias.

### APPENDIX 3: 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 FY21 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://www.usuhs.edu/afri/>

Combat Casualty Care Research Program

<https://ccc.amedd.army.mil>

Congressionally Directed Medical Research Programs

<https://cdmrp.army.mil>

Defense Advanced Research Projects Agency

<https://www.darpa.mil/>

Defense 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/>

Military Infectious Diseases Research Program

<https://midrp.amedd.army.mil>

Military Operational Medicine Research Program

<https://momrp.amedd.army.mil>

Naval Health Research Center

<https://www.med.navy.mil/sites/nmrc/nhrc/>

Navy and Marine Corps Public Health Center

<https://www.med.navy.mil/sites/nmcphc/>

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. Army Institute of Surgical Research

<https://usaisr.amedd.army.mil>

U.S. Army Medical Materiel Development Activity

<https://www.usamma.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. 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 4: APPLICATION CATEGORY SUMMARY

	<b>Planning Phase with Clinical Trial</b>	<b>Clinical Trial Only</b>
<b>Award Information</b>	<ul style="list-style-type: none"> <li>• Supports the final phase of regulatory activity necessary to initiate a clinical trial</li> <li>• Includes planning for regulatory/administrative approvals, developing the clinical protocol, establishing access to patients, and other preparatory activities</li> <li>• 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</li> <li>• Not an assurance of funding for the proposed clinical trial</li> <li>• Includes option for clinical trial if regulatory submissions are achieved, federal funds are available, and the topic area is supported at that time</li> </ul>	<ul style="list-style-type: none"> <li>• Supports a clinical trial having either FDA (or equivalent agency) approval or exemption in place prior to the application submission deadline</li> </ul>
<b>Budget</b>	<ul style="list-style-type: none"> <li>• Up to \$500,000 for the Planning Phase</li> <li>• No predetermined cost limit for the proposed clinical trial</li> </ul>	<ul style="list-style-type: none"> <li>• No predetermined cost limit</li> </ul>
<b>Period of Performance</b>	<ul style="list-style-type: none"> <li>• Up to 18 months for the Planning Phase</li> <li>• Up to 4 years for the proposed clinical trial</li> </ul>	<ul style="list-style-type: none"> <li>• Up to 4 years</li> </ul>
<b>Pre-Application Components</b>	<ul style="list-style-type: none"> <li>• Preproposal Narrative <ul style="list-style-type: none"> <li>◦ Describes the proposed clinical trial</li> </ul> </li> <li>• Pre-Application Supporting Documents <ul style="list-style-type: none"> <li>◦ Includes an estimated budget for the Planning Phase and the proposed clinical trial</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Preproposal Narrative <ul style="list-style-type: none"> <li>◦ Describes the clinical trial</li> </ul> </li> <li>• Pre-Application Supporting Documents <ul style="list-style-type: none"> <li>◦ Includes an estimated budget for the clinical trial</li> </ul> </li> </ul>
<b>Full Application Components</b>	<ul style="list-style-type: none"> <li>• Project Narrative <ul style="list-style-type: none"> <li>◦ 8-page limit for the Planning Phase</li> <li>◦ 20-page limit for the proposed clinical trial</li> </ul> </li> <li>• Statement of Work <ul style="list-style-type: none"> <li>◦ Includes two SOWs: one for the Planning Phase and one for the proposed clinical trial</li> <li>◦ Uploaded as one attachment; starts statement for the proposed clinical trial on a new page</li> <li>◦ No page limit</li> </ul> </li> <li>• Human Subject Recruitment and Safety Procedures; Surveys, Questionnaires, and Other Data Collection Instruments; Study Personnel and Organization; Data Management; Regulatory Strategy <ul style="list-style-type: none"> <li>◦ Describes any missing or applicable aspects to be addressed during the Planning Phase</li> <li>◦ Requires resubmission if changed/finalized when/if option for the proposed clinical trial is exercised</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Project Narrative <ul style="list-style-type: none"> <li>◦ 20-page limit</li> </ul> </li> <li>• Statement of Work <ul style="list-style-type: none"> <li>◦ No page limit</li> </ul> </li> <li>• Human Subject Recruitment and Safety Procedures; Surveys, Questionnaires, and Other Data Collection Instruments; Study Personnel and Organization; Data Management; Regulatory Strategy <ul style="list-style-type: none"> <li>◦ Requires submission in full</li> </ul> </li> </ul>