I. OVERVIEW OF THE FUNDING OPPORTUNITY

Intramural Funding Opportunity Announcement and Application Instructions for the Department of Defense

Defense Health Program

Congressionally Directed Medical Research Programs

Clinical Research Intramural Initiative

Military Performance Optimization Research Award

Funding Opportunity Number: DHA18CRIIMPORA

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-Application Submission Deadline:** 5:00 p.m. Eastern time (ET), April 11, 2018
- **Invitation to Submit an Application:** May 14, 2018
- **Application Submission Deadline:** 11:59 p.m. ET, July 25, 2018
- **End of Application Verification/Approval Period:** 5:00 p.m. ET, July 30, 2018
- **Peer Review:** September 2018
- **Programmatic Review:** November 2018

TABLE OF CONTENTS

II. DETAILED INFORMATION ABOUT THE FUNDING OPPORTUNITY

NOTE: THIS FUNDING OPPORTUNITY IS INTENDED FOR INTRAMURAL INVESTIGATORS ONLY.

- An ***intramural investigator*** is defined as a Department of Defense (DoD) military or civilian employee working within a DoD laboratory or Military Treatment Facility (MTF), or working in a DoD activity embedded within a civilian medical center.

- An ***extramural investigator*** is defined as all those not included in the definition of intramural investigators, above. Submissions from extramural investigators to this Funding Opportunity Announcement will be rejected.

II.A. Program Description

Applications to the Fiscal Year 2018 (FY18) Defense Medical Research and Development Program (DMRDP) Clinical Research Intramural Initiative (CRII) Military Performance Optimization Research Award (MPORA) are being solicited for the Defense Health Agency (DHA) J9, Research and Development Directorate. As directed by the Office of the Assistant Secretary of Defense for Health Affairs (OASD[HA]), the DHA manages and executes the Defense Health Program (DHP) Research, Development, Test, and Evaluation (RDT&E) appropriation. The U.S. Army Medical Research and Materiel Command (USAMRMC) Congressionally Directed Medical Research Programs (CDMRP) is the execution management agent for this Funding Opportunity Announcement.

The CRII was initiated in 2012 to provide support for intramural clinical research in OASD(HA)-directed topic areas. The intent of the CRII is to foster intramural research aimed at protecting, supporting, and advancing the health and welfare of military personnel, families, and communities while supporting the development of military researchers and building Military Health System (MHS) research capabilities. The OASD(HA)-directed topic area for the FY18 CRII is Military Performance Optimization Research.

II.A.1. FY18 CRII Military Performance Optimization Research Award Focus Areas

The FY18 CRII MPORA will support research addressing one or more of the following Focus Areas:

- **Physical Performance Optimization:** Develop and validate strategies and interventions to assess, preserve, and optimize Service member physical performance and resilience.

- **Cognitive Performance Optimization:** Develop and validate strategies and interventions to assess, preserve, and optimize Service member cognitive performance and resilience throughout the military lifecycle.

- **Injury Prevention and Reduction:** Develop and validate injury prevention and reduction strategies and interventions to preserve operational readiness and optimal performance

throughout the military lifecycle with a focus on the development and delivery of prevention/ optimization strategies and interventions for rapid reset and recovery under high operational tempo (OPTEMPO) conditions.

- **Deployment Health Protection:** Develop and validate standards and tools for monitoring health, readiness, and operational effectiveness of Service members exposed to extreme operational environments (e.g., heat, cold, altitude, potentially traumatic events, toxic industrial chemicals and materials) during deployment. Outcomes of health, readiness, and operational effectiveness monitoring should be focused on the development of mitigation strategies.

II.B. Award Information

The FY18 CRII MPORA seeks to support intramural research addressing one or more of the FY18 CRII MPORA Focus Areas toward the following goals:

- Improve the readiness and effectiveness of our military against a broad spectrum of operational threats across the range of military operations[1]

- Build the capacity and enhance the lethality of the Joint Force against high-end, peer, and near-peer competitors

- Optimize Warfighter performance and prevent performance decrements throughout the military lifecycle, including training, deployment, reset, and injury recovery

This Funding Opportunity may support preclinical research, clinical research (i.e., observational studies involving human subjects to include correlative and epidemiological studies), and early phase clinical trials/testing. A clinical trial is defined as a prospective accrual of human subsets where an intervention (e.g., device, drug, biologic, surgical procedure, rehabilitative modality, behavioral intervention, or other) is tested on a human subject for a measurable outcome with respect to safety, effectiveness, and/or efficacy. This outcome represents a direct effect on the human subject of that intervention or interaction. For further definitions, categories, and resource information for human subject research, see "Human Subject Resource Document", available on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) under "Regulatory Information and Forms." This Funding Opportunity does NOT permit Phase II or III clinical trials for U.S. Food and Drug Administration (FDA) licensure of drugs or definitive/pivotal testing for device clearance by the FDA.

The anticipated total costs budgeted for the entire period of performance for an FY18 CRII MPORA will not exceed **$1.25 Million (M)**. Refer to Section II.D.5, Funding Restrictions, for detailed funding information.

[1] Secretary of Defense Memorandum Subject: "Implementation Guidance for Budget Directives in the National Security Presidential Memorandum on Rebuilding the U.S. Armed Forces," 31 January 2017.

Research Resources: Applicants are encouraged to consider leveraging resources available through existing DoD and/or Department of Veterans Affairs (VA) resources, if retrospectively collected human anatomical substances and correlated data are relevant to the proposed research. These resources include:

- **DoD Serum Repository** (https://health.mil/Military-Health-Topics/Health-Readiness/Armed-Forces-Health-Surveillance-Branch/Data-Management-and-Technical-Support/Department-of-Defense-Serum-Repository)**:** The DoD Serum Repository (DoDSR) was established in 1989 as the Army/Navy Serum Repository for storing serum that remained following mandatory HIV testing within the active and reserve components of the Army, Navy, and Marines. Since that time, the mission of the DoDSR has expanded to include the collection and storage of operational deployment specimens as well as Air Force specimens. Specimens contained in the DoDSR are available to researchers and other investigators within the DoD for the purposes of conducting militarily relevant investigations.

- **Millennium Cohort Program** (http://millenniumcohort.org)**:** The Millennium Cohort Study (MCS) and the Millennium Cohort Family Study together make up the Millennium Cohort Program at the Naval Health Research Center, San Diego, CA. The MCS is the largest prospective health study in U.S. military history, with approximately 200,000 participants. The purpose of the MCS is to evaluate the impact of military experiences, including deployment, on long-term health outcomes of Service members, and to provide strategic policy recommendations that inform leadership and guide interventions. The MCS provides the DoD with unique data capabilities to: collect data via survey that is not collected elsewhere; assess temporal sequence of exposures and outcomes or disease; track Service members after they leave military service; and, link survey data with other enterprise data sources. Access to MCS data and biospecimens requires collaboration with one of the MCS investigators and approval of the MCS oversight committee by way of a preproposal/ proposal process.

- **Million Veteran Program** (http://www.research.va.gov/MVP/default.cfm)**:** The VA's Million Veteran Program, with over 445,000 enrolled Veterans, provides a potentially rich clinical database for genetic exploration and analyses.

Use of Military and VA Populations or Resources: If the proposed research plan involves access to active duty military and/or VA patient populations or resources, the Principal Investigator (PI) is responsible for demonstrating such access. If possible, access to target active duty military and/or VA patient population(s)/resource(s) should be confirmed at the time of application submission by inclusion of a letter of support, signed by the lowest-ranking person with approval authority, for studies involving active duty military Service members, Veterans, military and/or VA-controlled study materials, and military and/or VA databases. If access cannot be confirmed at the time of application submission, the Government reserves the right to withdraw or revoke funding until the PI has demonstrated support for and access to the relevant population(s) and/or resource(s). Note that access to a Veteran population for clinical studies may only be obtained by (1) collaboration with a VA investigator where the VA investigator has a substantial role in the research or (2) advertising to the general public.

Research Involving Human Anatomical Substances, Human Subjects, or Human Cadavers: All DoD-funded research involving new and ongoing research with human anatomical substances, human subjects, or human cadavers must be reviewed and approved by the USAMRMC Office of Research Protections (ORP), Human Research Protection Office (HRPO) prior to research implementation. This administrative review requirement is in addition to the local Institutional Review Board (IRB) or Ethics Committee (EC) review. Local IRB/EC approval at the time of submission is ***not*** required. The HRPO is mandated to comply with specific laws and requirements governing all research involving human anatomical substances, human subjects, or human cadavers that is supported by the DoD. These laws and requirements will necessitate information in addition to that supplied to the IRB/EC. ***Allow a minimum of 2 to 3 months for HRPO regulatory review and approval processes***. When possible, protocols should be written for research with human subjects and/or human anatomical substances that are specific to the DoD-supported effort outlined in the submitted application. Submission to HRPO of protocols covering more than the scope of work in the DoD-funded award will require HRPO review of the entire protocol as DoD-supported research and may include extensive modifications to meet DoD human subjects protection requirements. Refer to Appendix 2, Regulatory Requirements, 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.

NOTE: If protocol funding is provided directly from USAMRMC to a DoD MTF or USAMRMC laboratory (through a Military Interdepartmental Purchase Request (MIPR) or Funding Authorization Document (FAD) process), with no non-DoD awardees or collaborators then it is considered intramural research and a HRPO review is not required. If the DoD funding for the protocol is not the scenario just described, HRPO administrative review of the study is required.

Research Involving Animals: All DoD-funded research involving new and ongoing research with animals must be reviewed and approved by the USAMRMC ORP Animal Care and Use Review Office (ACURO), in addition to the local Institutional Animal Care and Use Committee (IACUC) of record. IACUC approval at the time of submission is ***not*** required. Specific documents relating to the use of animals in the proposed research will be requested **if the application is selected for funding**. The ACURO must review and approve all animal use prior to the start of working with animals, including amendments to ongoing projects. PIs must submit the institutional animal use protocol, IACUC approval of that protocol, and a version of the animal use appendix titled "Research Involving Animals." ***Allow at least 2 to 3 months for ACURO regulatory review and approval processes for animal studies.*** Refer to Appendix 2, Regulatory Requirements, for additional information.

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

animal models are required to submit Attachment 9, Animal Research Plan, as part of the application package to describe how these standards will be addressed. Applicants should consult the ARRIVE (Animal Research: Reporting *In Vivo* Experiments) guidelines to ensure relevant aspects of rigorous animal research are adequately planned for and, ultimately, reported. The ARRIVE guidelines can be found at https://www.elsevier.com/__data/promis_misc/622936arrive_guidelines.pdf.

The DHA and CDMRP intend that information, data, and research resources generated under awards funded by this Funding Opportunity Announcement be made available to the research community (which includes both scientific and consumer advocacy communities) and to the public at large. For additional guidance, refer to Appendix 3, Administrative Information.

- Traumatic Brain Injury: If the project includes traumatic brain injury (TBI) research, the PI may be required to make TBI data generated via an award available to the research community by depositing de-identified research data into the Federal Interagency TBI Research (FITBIR) Informatics System (https://fitbir.nih.gov).

- Clinical Trials: If the project includes a clinical trial(s), the PI may be required to register the clinical trial(s) individually on the registry and database ClinicalTrials.gov (https://www.clinicaltrials.gov/).

- Systems Biology: If the project includes systems biology-related research, the PI may be required to make systems biology data, generated via an award, available to the research community by depositing research data into the SysBioCube system (https://sysbiocube-abcc.ncifcrf.gov/).

II.C. Eligibility Information

II.C.1. Eligible Applicants

II.C.1.a. Organization: ONLY intramural DoD organizations are eligible to apply. An **intramural DoD organization** is defined as a DoD laboratory, DoD MTF, or DoD activity embedded within a civilian medical center. Intramural DoD 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.

Extramural (non-DoD) entities are NOT eligible to apply to this Funding Opportunity Announcement, and extramural submissions will be administratively rejected.

Submissions selected for funding will be processed for funding by USAMRMC. Funding is provided to organizations, not individuals.

II.C.1.b. Principal Investigator: Independent intramural investigators are eligible to apply.

An **intramural investigator** is defined as a DoD military or civilian employee working within a DoD laboratory, MTF, or DoD activity embedded within a civilian medical center. **Submissions from extramural (non-DoD) investigators will be rejected.**

PIs are encouraged to participate in a digital identifier initiative through Open Researcher and Contributor ID, Inc. (ORCID) and enter their ORCID identifier in their eBRAP profile. Registration for a unique ORCID identifier can be done online at http://orcid.org/.

II.C.2. Other

It is expected that the work funded through this Funding Opportunity Announcement will be performed within the intramural DoD organization. It is permissible, however, for an extramural investigator to be named as a collaborator in a submission from an intramural investigator. In such cases, the intramural organization will receive all funds and is responsible for executing all necessary awards to collaborating partners through their agency's procedures. Regardless of location, any work that is to be performed by associated non-DoD organizations must be limited to work performed under existing contracts, and resource sharing should be accomplished through Cooperative Research and Development Agreements or Material Transfer Agreements. The Government reserves the right to administratively withdraw any application that does not meet these eligibility criteria. ***Applications that require research to be performed by a non-DoD organization under a new service contract will not be considered for funding.***

Refer to Section II.H.1, 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 Funding Opportunity Announcement.

II.D. Application and Submission Information

II.D.1. Address to Request Application Package

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

Pre-application and full application packages can be accessed at https://eBRAP.org.

Contact information for the eBRAP Help Desk can be found in Section II.G, Agency Contacts.

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

Submission is a two-step process requiring both ***pre-application*** submission and ***full application*** submission through eBRAP (https://eBRAP.org/). The submission process should be started early to avoid missing deadlines. There are no grace periods. It is the applicant's responsibility

to review all application components for accuracy as well as ensure proper ordering as specified in this Funding Opportunity Announcement.

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

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

During the pre-application process, each submission is assigned a unique log number by eBRAP. This unique eBRAP log number will be used to track the application through the submission and review process. In addition, the application title and all information for the PI, Business Official(s), and organization must be consistent throughout the entire pre-application and application submission process. Changes prior to the pre-application deadline can be made by the PI or Business Official by resetting the pre-application to "Draft." If changes need to be made after the pre-application deadline, the PI or Business Official should contact the eBRAP Help Desk at help@eBRAP.org or 301-682-5507 prior to the application deadline.

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.

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. Registration for a unique ORCID identifier can be done online at http://orcid.org/.

The pre-application consists of the following components, which are organized in eBRAP by separate tabs:

- **Tab 1 – Application Information**

  Enter the application information as described in eBRAP before continuing the pre-application. Click on "Save."

- **Tab 2 – Application Contacts**

  Enter contact information for the PI. Enter the organization's Business Official (Resource Manager, Comptroller, Task Area Manager, Sponsored Programs Administrator or equivalent) responsible for sponsored program administration. The Business Official must be either selected from the eBRAP list or invited in order for the pre-application to be submitted. **If the Business Official cannot be found in eBRAP, an invitation must be sent to him/her to register in eBRAP.**

Select the organization submitting on behalf of the PI, 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.

  To preserve the integrity of its peer and programmatic review processes, inclusion of any employee of CDMRP's review contractors with any role in pre-application or application preparation, research, or other duties for submitted pre-applications or applications is strongly discouraged. For FY18, the identities of the peer review contractor and the programmatic review contractor may be found at the CDMRP website (http://cdmrp.army.mil/about/2tierRevProcess). Pre-applications or applications that include names of personnel from either of these companies will be administratively withdrawn unless plans to manage conflicts of interest (COIs) are provided and deemed appropriate by the Program Manager.

- **Tab 4 – Conflicts of Interest**

  To avoid COIs during the screening and review processes, list all individuals other than collaborators and key personnel who may have a COI in the review of the application (including those with whom the PI has a personal or professional relationship). Click on "Save."

- **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 (2-page limit): The Preproposal Narrative page limit applies to text and non-text elements (e.g., figures, tables, graphs, photographs, diagrams, chemical structures, drawings) used to describe the project. Inclusion of URLs that provide additional information to expand the Preproposal Narrative and could confer an unfair competitive advantage is prohibited and may result in administrative withdrawal of the pre-application.

  The Preproposal Narrative should include the following:

  - **Alignment with Focus Areas:** Identify the FY18 CRII MPORA Focus Area(s) that the proposed research addresses. Explain how the proposed research is relevant to the identified Focus Area(s) and the intent of the award mechanism with respect to military performance optimization.

- **Research Plan:** Concisely state the ideas and reasoning on which the proposed work is based. State the project's hypotheses, objectives, and specific aims, and briefly describe the experimental approach.

- **Personnel:** Briefly state the qualifications of the PI and key personnel to perform the described research project.

- **Impact and Military Relevance:** Describe, if successful, the extent to which the study could impact military performance optimization and promote the health, readiness, and performance of Service members and the Joint Force.

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

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

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

  - Key Personnel Biographical Sketches (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.

  - Quad Chart: Complete the Quad Chart template, a one-page PowerPoint file that must be downloaded from eBRAP at https://ebrap.org/eBRAP/public/Program.htm and saved using Adobe Acrobat Reader as a PDF file.

- **Tab 6 – Submit Pre-Application**

  - This tab must be completed for the pre-application to be accepted and processed. Enter eBRAP password and click the "Submit" button. Click the "Confirm Submission" button to complete the pre-application submission. ***This finalizes the pre-application submission process.***

Following completion of pre-application submission, the status of the pre-application in eBRAP will change from "DRAFT" to "SUBMITTED" and a confirmation email will be sent to the PI and named Business Official. ***An applicant with a pre-application in DRAFT status after the pre-application submission deadline is ineligible to submit an application. Check the status of the pre-application. There are no grace periods.***

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 CRII, pre-applications will be screened based on the following criteria:

- **Alignment with Focus Areas:** Whether the proposed research addresses at least one of the FY18 CRII MPORA Focus Areas and meets the intent of the award mechanism with respect to military performance optimization.
- **Research Plan:** How well the rationale, hypotheses, objectives, specific aims, and experimental design support the research idea.
- **Personnel:** How appropriate the qualifications and expertise of the PI and key personnel are for performing the proposed research project.
- **Impact and Military Relevance:** If successful, to what extent the study could impact military performance optimization and promote the health, readiness, and performance of Service members and the Joint Force.

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. The decision to invite an applicant to submit a full application is based on the Pre-Application Screening Criteria, listed above.

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

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

Full application components, which are listed in Table 1, must be submitted by the PI through eBRAP (https://ebrap.org/).

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

Table 1. Full Application Submission Guidelines

Application Package Location
Download application package components for DHA-18-CRII-MPORA from eBRAP (https://ebrap.org).
Full Application Package Components
Tab 1 – Summary: Provide a summary of the application information **Tab 2 – Application Contacts:** This tab will be pre-populated by eBRAP; add Resource Manager/Comptroller or equivalent Business Official.
Full Application Package Components
Tab 3 – Full Application Files: Upload files under each Application Component in eBRAP. Descriptions of each required file can be found under Full Application Submission Components: • Attachments • Key Personnel • Budget • Performance Sites **Tab 4 – Application and Budget Data:** Review and edit proposed project start date, proposed end date, and budget data pre-populated from the Budget Form.
Application Package Submission
Submit package components to eBRAP (https://ebrap.org). **Tab 5 – Submit/Request Approval of Full Application:** After all components are uploaded and prior to the full application submission deadline, enter your password in the space provided next to "Enter Your Password Here" and press the "Submit Full Application" button. eBRAP will validate files against the Funding Opportunity Announcement requirements and discrepancies will be noted. If no discrepancies are noted, press the "Confirm Submission" button to complete the application submission**.** eBRAP will notify your Business Official or equivalent by email to log onto eBRAP to review and approve the submission.
Application Verification/Approval Period
After eBRAP has processed the full application, the organizational Business Official or equivalent and PI(s) will receive an email notification of this status and will be able to view and modify application components in eBRAP. During the application verification/approval period, the full application package, ***with the exception of the Project Narrative and Budget Form,*** may be modified. Only the Business Official or equivalent can modify the application components during the verification/approval period. However, if the Business Official or equivalent selects the "Return to PI" button, the PI can update the application BUT must then resubmit the application for Business Official approval. For the Clinical Research Intramural Initiative Program, your Business Official or equivalent should log into eBRAP to review and approve prior to the application verification/approval deadline. For all other intramural programs, your Business Official or equivalent must log into eBRAP review and approve prior the application and verification/approval deadline.

The organization's Business Official or equivalent should approve/verify the full application submission prior to the application verification/approval deadline.

The Project Narrative and Budget cannot be changed after the application submission deadline. Prior to the application submission deadline, any components of the application package may be modified and re-submitted. Other application components may be changed until the end of the application verification/approval period. After the end of the application verification/approval period, the application cannot be modified.

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

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

For the FY18 CRII MPORA, the eBRAP application package includes the following components, which are organized in eBRAP by separate tabs. **To access these tabs, go to "My Applications" and click on "Start Full Application"** for the log number under which the pre-application was submitted. Page limits are validated as a document is uploaded. ***eBRAP will not allow a file to be uploaded if the number of pages exceeds the limit specified below***.

- **Tab 1 – Summary:** Provides a summary of the application information.
- **Tab 2 – Application Contacts:** This tab will be populated by eBRAP. Edit contact information as applicable.
- **Tab 3 – Full Application Files:** Under each Application Component in eBRAP, upload each as an individual PDF file. Refer to Appendix 4, for detailed formatting guidelines.

    1. **Application Component – 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 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 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 (20-page limit): Upload as "ProjectNarrative.pdf."** The page limit of the Project Narrative applies to text and non-text elements (e.g., figures, tables, graphs, photographs, diagrams, chemical structures, drawings) used to describe the project. Inclusion of URLs that provide additional information to expand the Project Narrative and could confer an unfair competitive advantage is prohibited and may result in administrative withdrawal of the application.

Describe the proposed project in detail using the outline below:

- **Relevance:** Identify the required FY18 CRII MPORA Focus Area(s) to be addressed by the proposed project. Explain the study's relevance to the applicable Focus Area(s) and military performance optimization.

- **Background:** Describe in detail the rationale for the study and include a literature review, preliminary studies, and preliminary data that led to the development of the proposed project. The Background section should clearly explain the basis for the study objectives and/or hypothesis and specific aims.

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

- **Research Design and Methods:**

  - Describe the experimental design, methods, and analyses, including appropriate controls, in sufficient detail for evaluation.

  - If applicable, describe the research objective(s) of the animal study. Explain how and why the animal species, strain, and model(s) being used can address the scientific objectives.

  - Document the availability and accessibility of the samples, data, and/or other materials/resources needed for the proposed research, as applicable.

  - Address potential problem areas and present alternative methods and approaches.

  For applications proposing clinical trials and clinical research involving human subjects:

  - Describe the type of clinical trial (e.g., Phase/Class, prospective, randomized, controlled) or clinical research (i.e., observational studies to include correlative and epidemiological studies) to be performed. Outline the proposed methodology in sufficient detail to show a clear course of action.

  - If applicable, describe the intervention to be studied and the proposed indication. Document the availability and accessibility of the drug/compound, device, or other materials needed for the proposed research, and describe how quality control will be addressed. Include a discussion of any current clinical use of the intervention, and/or details of its study in clinical trials for other indications.

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

        - Describe the study population, criteria for inclusion/exclusion, and the methods that will be used for recruitment/accrual of human subjects and/or samples (i.e., convenience, simple random, stratified random). Specify the approximate number of human subjects that will be accrued. Address any potential barriers to human subjects accrual and plans for addressing potential delays.

        - Describe how the subject-to-group assignments process will be conducted (e.g., randomization, block randomization, stratified randomization, age-matched controls, alternating group, or other procedures), if applicable. Include a discussion of risk/benefit considerations.

    - **Data and Statistical Analysis Plan:** Describe how data will be collected and analyzed in a manner that is consistent with the study objectives.

        - If applicable, include a complete power analysis to demonstrate that the sample size is appropriate to meet the objectives of the study.

        - If applicable, specify the approximate number of human subjects/samples that will be accrued. If multiple study sites are involved, state the approximate number to be enrolled at each site.

        - If applicable, describe how data will be reported and how the PI will assure that the documentation will support a regulatory filing with the FDA.

    - **Study Personnel:** Identify the key members of the study team and describe their roles on the project. For studies involving human subjects, an independent research monitor (external to the study), study coordinator(s), and statistician should be included as applicable.

- **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. Any additional material viewed as an extension of the Project Narrative will be removed or may result in administrative withdrawal of the application.

  There are no page limits for any of these components unless otherwise noted. Include only those components described below; inclusion of items not requested 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. There is no form for this information.

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

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

    - Intangible property acquired, created, or developed by extramural organizations under this award will be subject to all rights and responsibilities established at 2 CFR 200.315.

- 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. If relevant, PIs may be required to report research data to the FITBIR informatics system (http://fitbir.nih.gov/) or to the SysBioCube (https://sysbiocube-abcc.ncifcrf.gov/). Refer to Appendix 3 for more information about the expectations for making data and research resources publicly available.

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

  The technical abstract should be written using the outline below:

  - **Background:** Present the ideas and reasoning behind the proposed work.

  - **Objective/Hypothesis:** State the objectives/hypothesis to be tested. Provide evidence or rationale that supports the objective/hypothesis.

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

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

  - **Impact:** Identify the FY18 CRII MPORA Focus Area(s) to be addressed, and briefly describe how the proposed research will impact military performance optimization and promote the health, readiness, and performance of Service members and the Joint Force.

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

  Lay abstracts should be written using the outline below:

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

  - Identify the FY18 CRII MPORA Focus Area(s) to be addressed and briefly describe how the proposed research will impact military performance optimization and promote the health, readiness, and performance of Service members and the Joint Force.

  - Describe the potential applications, benefits, and risks.

- **Attachment 5: Statement of Work (SOW) (three-page limit): Upload as "SOW.pdf."** The suggested SOW format and examples specific to different types of research projects are available on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm). The SOW must be in PDF format prior to attaching.

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

  - Include the name(s) of the key personnel and contact information for each study site/ subaward site.

  - Indicate the number (and type, if applicable) of research subjects (animal or human) and/or human anatomical samples projected or required for each task and at each site. Refer to Appendix 2 for additional information regarding regulatory requirements.

  - Briefly state the methods to be used.

  - For studies with prospective accrual of human subjects, indicate quarterly enrollment targets.

  - Identify cell line(s) and commercial or organizational source(s) to be used. If human anatomical substances (including cell lines) will be used, specify whether or not identifiable information is accessible to the research team by any means.

  - If applicable, indicate timelines required for regulatory approvals relevant to human subjects research.

- **Attachment 6: Letters of Support (limit each letter to two pages): Combine and upload as a single file named "Letters.pdf."** Start each document on a new page.

  - Resource Manager/Comptroller: Provide a letter of support from the applicant institution's Resource Manager/Comptroller (or appropriate financial point of contact) assuring that the institution will be able to accept and obligate FY18 DHP RDT&E PE 6.3 funds by September 30, 2019, if selected for funding. If funds are to be sent to multiple sites, include a letter from each site.

  - Commander(s): Provide a letter of support from each appropriate Installation Commander, or equivalent Commander/Director, to ensure access to the facility, research population, and other necessary resources. The Commander should be aware of all submissions and should confirm that the proposed work is both feasible, from a technical perspective, and relevant, from a programmatic and command perspective. The letter should provide clear evidence of organizational commitment for the coordinating administrative tasks and for the use of facilities and resources necessary for the proposed work at each participating study site.

  - Partnership/Collaboration (if applicable):

    - If the project includes partnership/collaboration with a non-DoD entity, provide a signed letter from each partner/collaborator that describes his/her contribution to the project and demonstrates support and availability of any resources necessary for the proposed work.

    - If the project involves collaboration with another DoD researcher, provide a letter from the commanding officer or military facility director authorizing his/her participation in the research project.

  - Access to Military or VA Populations and/or Resources (if applicable): If the proposed research plan involves access to active duty military and/or VA populations, patients, data or resources, include letter(s) of support, signed by the lowest-ranking person with approval authority, confirming such access. If access cannot be confirmed at the time of application submission, the Government reserves the right to withhold or revoke funding until the PI has demonstrated support for and access to the relevant population(s) and/or resources.

- **Attachment 7: Quad Chart: Upload as "Quad.pdf."** Provide an updated Quad Chart for the proposed project. The format for the quad chart is available on eBRAP at https://ebrap.org/eBRAP/public/Program.htm.

- **Attachment 8: Impact and Military Relevance (one-page limit): Upload as "Impact.pdf."** State explicitly how the proposed work will impact military performance optimization. Describe the anticipated short- and/or long-term outcomes of the proposed project on the health, readiness, and performance of Service members and the Joint Force.

- **Attachment 9: Animal Research Plan (if applicable; two-page limit per animal study):** Start each animal study on a new page headed by the name of the PI and title of the animal study**. Combine and upload as a single file named "AnimalResearchPlan.pdf."**

  When the proposed study involves animals, the applicant is required to submit a summary describing the animal research that will be conducted. Applicants should not submit a verbatim replica of the protocol(s) to be submitted to the IACUC as the Animal Research Plan. The Animal Research Plan should address the following points for each proposed animal study:

  - Briefly describe the research objective(s) of the animal study. Explain how and why the animal species, strain, and model(s) being used can address the scientific objectives and, where appropriate, the study's relevance to human biology.

  - Summarize the procedures to be conducted. Describe how the study will be controlled.

  - Describe the randomization and blinding procedures for the study and any other measures to be taken to minimize the effects of subjective bias during animal treatment and assessment of results. If randomization and/or blinding will not be utilized, provide justification.

  - Provide a sample size estimate for each study arm and the method by which it was derived, including power analysis calculations.

  - Describe how data will be handled, including rules for stopping data collection, criteria for inclusion and exclusion of data, how outliers will be defined and handled, statistical methods for data analysis, and identification of the primary endpoint(s).

  - Describe how data will be reported and how the PI will assure that the documentation will support a regulatory filing with the FDA, if applicable.

- **Attachment 10: Human Subject Recruitment and Safety Procedures (if applicable, required for all studies recruiting human subjects; no page limit): Upload as "HumSubProc.pdf."** The Human Subject Recruitment and Safety Procedures attachment should include the components listed below.

  a. Study Population: Describe the target population (to whom the study findings will be generalized) and the nature, approximate number, and pertinent demographic characteristics of the accessible population at the study site(s) (population from whom the sample will be recruited/drawn). Demonstrate that the research team has access to the proposed study population. Furthermore, discuss past efforts in recruiting human subjects from the target population for previous clinical studies (if applicable). Address any potential barriers to accrual and plans for addressing unanticipated delays. Include justification of any age, race, ethnicity, or sex limitations provided. ***For clinical studies proposing to include military personnel as volunteers, refer to*** Appendix 2 ***for more information.***

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

Inclusion of Women and Minorities in Study. Consistent with the Belmont Report, "Ethical Principles and Guidelines for the Protection of Human Subjects," and Congressional legislation, special attention is given to inclusion of women and/or minorities in studies funded or supported by the USAMRMC. This policy is intended to promote equity both in assuming the burdens and in receiving the benefits of human subjects research. Include an appropriate justification if women and/or minorities will be excluded from the clinical study.

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

- Describe the recruitment process in detail. Address who will identify potential human subjects, who will recruit them, and what methods will be used to recruit them.
- Include a detailed description of and justification for the compensation plan if the human subjects will be compensated for participation in the study.
- Describe the recruitment and advertisement materials. The recruitment materials should not be coercive or offer undue inducements and should accurately reflect the study.

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

- 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 study.
- Include information regarding the timing and location of the consent process.
- Address issues relevant to the mental capacity of the potential human subject (e.g., altered capacity due to administration of any mind-altering substances such as tranquilizers, conscious sedation or anesthesia, brain injury, stress/life situations, or human subject age), if applicable.
- Address how privacy and time for decision making will be provided and whether or not the potential human subject will be allowed to discuss the study with anyone before making a decision.

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

- Describe the plan for the consent of the individual's Legally Authorized Representative (LAR) to be obtained prior to the human subject's participation in the study. State law defines who may act as the LAR. The local IRB of record should be consulted for guidance regarding who can serve as LAR for research at the study site. Note: The PI must describe a clear intent to benefit for human subjects who cannot give their own consent to participate in the proposed clinical study to be in compliance with Title 10 United States Code Section 980 (10 USC 980) (https://www.gpo.gov/fdsys/pkg/USCODE-2011-title10/pdf/USCODE-2011-title10-subtitleA-partII-chap49-sec980.pdf).

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

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

f. Risks/Benefits Assessment:

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

- **Risk management and emergency response:**

  - Describe how safety surveillance and reporting to the IRB and FDA (if applicable) will be managed and conducted.

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

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

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

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

- For a study in which the IRB determines there is greater than minimal risk to human subjects, the DoD requires an independent research monitor with expertise consonant with the nature of risk(s) identified within the research protocol. If applicable, refer to Appendix 3 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 subject, a specific community, or society.

- **Attachment 11: Data Management (if applicable; required for studies involving human subjects; no page limit): Upload as "Data_Manage.pdf."** The Data Management attachment should include the components listed below.

  a. Data Management: Describe all methods used for data collection to include 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. For FDA-regulated studies, compliance with 21 CFR 11 is required.

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

b. 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: Include considerations for informed consent and providing human subjects with an opportunity to decline participation in the study.

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

- **Attachment 12: IND/IDE Documentation (if applicable; no page limit): Upload as "IND_IDE.pdf."** Complete the IND/IDE Documentation Form available on eBRAP (https://ebrap.org/eBRAP/public/Program.htm). If submitting multiple documents, combine and upload as a single PDF file.

  The applicant must address the following on the IND/IDE Documentation Form:

  - Documentation of an existing IND or IDE
  - Evidence that an IND or IDE will be filed within 60 days of the award
  - Evidence that an IND or IDE is not required for the proposed study

The Government reserves the right to withdraw funding if the IND or IDE application has not been submitted to the FDA within 60 days of the award date or if the documented status of the IND or IDE has not been obtained within 6 months of the award date.

- **Attachment 13: Intervention (if applicable; required for clinical trials; no page limit): Upload as "Intervention.pdf."** The Intervention attachment should include the components listed below.

  a. Description of the Intervention: Describe the intervention to include the following components, as applicable: Complete name and composition, storage and handling information, source, dose, schedule, administration route, washout period, duration of the intervention, and concomitant medications allowed. Summarize key preclinical pharmacological findings, dosage studies, and other clinical studies (if applicable) that examine the safety of the intervention. Description of devices should include detailed operational instructions, any potential risks to users, and intended benefits. Other types of interventions should be fully described.

  b. Study Procedures: Describe the interaction with the human subject, including the study intervention that he/she will experience. Provide sufficient detail, in chronological order, for a person uninvolved in the study to understand what the human subject will experience. Provide a schedule (e.g., flowchart or diagram) of study evaluations and follow-up procedures. Discuss how compliance with Good Clinical Practices, Good Manufacturing Practices, and other regulatory considerations will be established, monitored, and maintained, as applicable.

- **Attachment 14: Transition Plan and Regulatory Strategy (two-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.

  - Details of the funding strategy to transition to the next level of development and/or commercialization (e.g., partners, internal/external funding opportunities to be applied for). Include description of collaboration 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 (CPGs) 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 (next-phase clinical trials, commercialization, delivery to the military or civilian market, incorporation into clinical practice, and/or approval by the FDA).

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

2. **Application Component – Research & Related Senior/Key Person Profile:** Each of these application components should be included for the PI and each individual identified as Key Personnel. Each attachment must be uploaded as an individual PDF file unless otherwise stated. The Biographical Sketches and the Previous/Current/Pending Support for the PI and Key Personnel may either be attached to the Research & Related Senior/Key Person Profile (Expanded) Form or uploaded as individual files in the "Key Personnel" Application Component.

   - Research & Related Senior/Key Person Profile (Expanded) Form: Upload the completed Research & Related Senior/Key Person Profile (Expanded) Form as "Key Personnel.pdf."

   - 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 National Institutes of Health Biographical Sketch may also be used. All biographical sketches should be submitted in the portable document format (PDF) that is not editable.

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

   - 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."

3. **Application Component – Budget:** Use the DoD Military Budget Form available on the "Funding Opportunities and Forms" page in eBRAP (https://ebrap.org/eBRAP/public/Program.htm). Refer to Appendix 5 for detailed information on completing this form.

   - Upload the DoD Military Budget Form as "Budget_LastName.pdf."

   - Budget Justification (no page limit): Upload as "BudgetJustification.pdf." The budget justification must include a Federal Agency Financial Plan, as described in Appendix 5.

   - Subaward Budget: Include all subaward budgets. Describe in detail funding arrangements with extramural partners (if applicable). Complete a separate detailed budget using the DoD Military Budget Form including a budget justification for each

subaward in accordance with the instructions listed above. Title each individual subaward "Budget" and "Budget Justification," with the name of the subawardee/ subrecipient organization.

4. **Application Component – Project/Performance Site Location(s) Form:** Use the Project/Performance Site Location(s) Form available on the "Funding Opportunities and Forms" page in eBRAP (https://ebrap.org/eBRAP/public/Program.htm). Upload as "Performancesites.pdf."

    - On the Project/Performance Site Location(s) Forms, indicate the primary site where the work will be performed. If a portion of the work will be performed at any other site(s), include the name and address for each collaborating location in the data fields provided. Add more sites as necessary using the "Next Site" button. If more than eight performance site locations are proposed, provide the requested information in a separate file and attach it to this form. Each additional research site requesting funds will require a subaward budget.

- **Tab 4 – Application and Budget Data:**

  Review and edit proposed project start date, proposed end date, and budget data pre-populated from the Budget Form.

- **Tab 5 – Submit/Request Approval of Full Application**

  Once all components have been 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 validate files against the Funding Opportunity Announcement requirements and discrepancies will be noted. If no discrepancies are noted, press the "Confirm Submission" button to complete the application submission**. eBRAP will notify your Business Official or equivalent by email to log into eBRAP to review and to verify and approve the submission prior to the verification/ approval deadline.**

Following submission of the full application, eBRAP will notify the organizational representatives (Business Official or equivalent and Authorized Organizational Representative) by email to log into eBRAP to review, modify, verify, and approve the full application submission. eBRAP will validate submitted files against the specific Funding Opportunity Announcement requirements and discrepancies will be noted in both the email and in the Full Application Files tab in eBRAP. eBRAP does not confirm the accuracy of file content.

Only the Business Official or equivalent can modify the application components during the verification/approval period. If the Business Official or equivalent selects the "Return to PI" button, the PI can update the application BUT must then resubmit the application for Business Official approval. For the Clinical Research Intramural Initiative Program, your Business Official or equivalent should log into eBRAP to review and approve prior to the application verification/approval deadline***. For all other intramural programs, your Business Official or equivalent must log into eBRAP to review and approve prior to the application and verification/approval deadline. NOTE: If either the Project Narrative or the budget fails***

eBRAP validation or needs to be modified, they must be re-submitted prior to the application submission deadline. The Project Narrative and Budget Form cannot be changed after the application submission deadline.

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.

II.D.5. Funding Restrictions

Submissions selected for funding will be processed for funding by the USAMRMC and funds will be transferred to organizations, not individuals. Funding to intramural organizations will be executed through the MIPR or 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 Managers/ Comptrollers.

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

The anticipated total costs budgeted for the entire period of performance will not exceed **$1.25M**. If indirect cost rates have been negotiated, indirect costs are to be budgeted in accordance with the organization's negotiated rate. No budget will be approved by the Government exceeding **$1.25M** total costs or using an indirect cost rate exceeding the organization's negotiated rate.

All direct and indirect costs associated with an intramural or extramural collaboration must be included in the total direct costs of the primary award.

The applicant may request the entire maximum funding amount for a project that may have a period of performance less than the maximum **3** years.

Organizations funded through this Funding Opportunity Announcement must ensure that all FY18 funds will be obligated by September 30, 2019. For this award mechanism, direct costs must be requested for:

- Travel costs for the PI to disseminate project results at one DoD In-Progress Review (IPR) meeting per year. The dates for these meetings will be determined during the performance period. For planning purposes, it should be assumed that the meeting will be held in the National Capital Area. These travel costs are in addition to those allowed for annual scientific/technical meetings.

May be requested for (not all-inclusive):

- Salary, including contract personnel (Federal salaries paid by the parent organization may not be reimbursable)

- Research supplies
- Equipment
- Research-related subject costs
- Clinical research costs
- Support for multidisciplinary collaborations, including travel
- Travel costs for up to one investigator to travel to one scientific/technical meeting per year in addition to the required meeting described above

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 collaborations (if applicable). Refer to Appendix 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 Appendix 5.***

The DHA expects to allot approximately $5.0M of the FY18 DHP RDT&E 6.3 appropriation to fund approximately four Military Performance Optimization Research Award applications, depending on the quality and number of applications received. Funding of applications received in response to this Funding Opportunity Announcement is contingent upon the availability of Federal funds for this program.

II.D.6. Other Submission Requirements

Refer to Appendix 4 for detailed formatting guidelines.

II.E. Application Review Information

II.E.1. Criteria

II.E.1.a. Peer Review

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

- **Research Strategy and Feasibility**
    - The degree to which the scientific rationale supports the project and its feasibility, as demonstrated by a critical review and analysis of the literature, logical reasoning, presentation of background information, and preliminary data.
    - How well the study aims, hypotheses, objectives, experimental design, methods, data collection procedures, and analyses are designed to clearly answer the research objective.
    - Whether the proposed methods, procedures, models, materials, analyses, and other research strategy components are appropriate and indicate a sound research design.

- If applicable, whether the proposed animal model is appropriate.
- If applicable, whether the proposed animal research plan is appropriate.
- How well the PI acknowledges potential problems and addresses alternative approaches.

For clinical trials and clinical research involving human subjects:

- How well the PI describes the population(s) of interest, demonstrates access to these populations, has a viable plan for recruitment, consent, screening, and retention of appropriate subjects, and identifies sampling methods to gain a representative sample from the population(s) of interest.
- How well plans for addressing ethical and regulatory considerations have been developed, including mitigation of risk, consideration of privacy issues, and process for obtaining informed consent.
- If applicable, whether a member of the study team holds the IND/IDE for the indication proposed, or whether the timeline proposed for the IND/IDE application is appropriate.
- If applicable, whether there is evidence demonstrating availability of the device/ intervention from its source for the duration of the proposed study.

- **Data and Statistical Analysis Plan**
  - Whether the statistical analysis plan, including sample size projections and power analysis, is adequate to achieving the study objectives and is appropriate for the proposed study.
  - How well the PI has outlined a plan for management and sharing of research data as appropriate for the study.
  - If applicable, whether there is a clear plan to appropriately report and document data to support a regulatory filing with the FDA.
- **Transition Plan and Regulatory Strategy**
  - Whether the funding strategy described to bring the outcomes(s) to the next level of development (e.g., higher phase clinical trial, transition to industry, delivery to the market, and incorporation into standard practice) is appropriate.
  - For knowledge products, to what degree the transition includes appropriate strategies for further knowledge development, dissemination, and incorporation into clinical care.

- **Personnel**
    - Whether the research team's background and expertise are appropriate to accomplishing the proposed work. Whether the levels of effort by the PI and other key personnel are appropriate to ensuring the successful conduct of the project.
    - If applicable, the extent to which the proposed partnership or collaboration represents a significant contribution to the proposed research project.

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

- **Environment**
    - How appropriate the scientific environment is for the proposed research.
    - How well the research requirements are supported by the availability of and accessibility to facilities and resources (including collaborative arrangements).
    - The quality and extent of institutional support provided.
- **Budget**
    - Whether the budget is appropriate for the proposed research and within the limitations of this Funding Opportunity Announcement.
    - Whether there is a sufficient plan outlining management of funding, including how all FY18 funds will be obligated by September 30, 2019, and how funds for collaborative partnerships will be appropriately distributed (if applicable).
- **Application Presentation**
    - The extent to which 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 the FY18 CRII , as evidenced by the following:
    - Adherence to the intent of the award mechanism
    - Program portfolio composition

- Relevance to military performance optimization and the FY18 CRII MPORA Focus Areas

- Relative military benefit and 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 of applications against established criteria for determining technical merit. Each application is evaluated on its own merit, independent of other applications. The second tier is a programmatic review that makes recommendations for funding to the Commanding General, USAMRMC, on behalf of the DHA and the OASD(HA), based on technical merit, the relevance to the mission of the DHP and CRII, the specific intent of the award mechanism, and to other specified evaluation criteria in this Funding Opportunity Announcement. Programmatic review is a comparison-based process in which applications with scientific and technical merit compete in a common pool. ***The highest-scoring applications from the first tier of review are not automatically recommended for funding. Funding recommendations depend on various factors as described in Section II.E.1.b, Programmatic Review.*** Additional information about the two-tier process used by the CDMRP can be found at http://cdmrp.army.mil/about/fundingprocess.

All review processes are conducted confidentially to maintain the integrity of the merit-based selection process. Panel members sign a statement that application and evaluation information will not be disclosed outside the panel. Violations of confidentiality can result in the dissolving of a panel(s) and other corrective actions. In addition, personnel at the applicant or collaborating organizations are prohibited from contacting persons involved in the review 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 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.4. Anticipated Funding Opportunity Announcement and Funding 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. Funding Administration Information

II.F.1. Funding Notices

Funds will be transferred no later than September 30, 2019.

Funds will be transferred to organizations, not to individual PIs, and will be executed through the MIPR or 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 Managers/Comptrollers.

After email notification of application review results through the eBRAP, and if selected for funding, a Science Officer from CDMRP will contact the PI and authorized business official to begin the award negotiation process.

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

Transfer of funding for this project to a non-DoD institution is not allowed. The PI responsibilities may be transferred to another approved investigator within the same institution. Approval of a PI transfer request will be on a case-by-case basis at the discretion of the FY18 CRII MPORA Program Manager.

II.F.2. Reporting

Refer to Appendix 3, Administrative Information, for general information on reporting requirements.

Quarterly, annual, and final technical progress reports and quad charts will be required. In addition to written progress reports, in-person presentations may be requested.

II.F.3. Site Visits

DHA and CDMRP personnel may, at their discretion, perform site visits during the award period of performance.

II.G. Agency Contacts

II.G.1. eBRAP Help Desk

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

Phone: 301-682-5507

Email: help@eBRAP.org

II.H. Other Information

II.H.1. Administrative Actions

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

II.H.1.a. Rejection

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

- Preproposal Narrative exceeds page limit.
- Preproposal Narrative is missing.
- Preproposal was submitted by an ineligible organization; see Section II.C, Eligibility Information, for details.

The following will result in administrative rejection of the application:

- Submission of an application for which a letter of invitation was not received.
- Project Narrative exceeds page limit.
- Project Narrative is missing.
- Budget is missing.

II.H.1.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.1.c. Withdrawal

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

- The pre-application or application fails to conform to this Funding Opportunity Announcement description to the extent that appropriate review cannot be conducted.
- 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).
- The PI does not meet the eligibility criteria.
- Letters of support are missing.
- To preserve the integrity of its peer and programmatic review processes, the CDMRP discourages inclusion of any employee of its review contractors having any role in the preparation, research or other duties for submitted applications. For FY18, the identities of the peer review contractor and the programmatic review contractor may be found at the CDMRP website (http://cdmrp.army.mil/about/2tierRevProcess). Applications that include

names of personnel from either of these companies will be administratively withdrawn unless plans to manage COIs are provided and deemed appropriate by the Program Manager. Refer to Appendix 3 for detailed information.

- Personnel from applicant or collaborating organizations are found to have contacted persons involved in the review process to gain protected evaluation information or to influence the evaluation process.

- 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.

II.H.1.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 CDMRP for a determination of the final disposition of the application.

II.H.2. Application Submission Checklist

Application Components	Action	Completed
Summary (Tab 1) and Application Contacts (Tab 2)	Complete these tabs as instructed.	
Attachments	Project Narrative: Upload as Attachment 1 with file name "ProjectNarrative.pdf."	
	Supporting Documentation: Upload as Attachment 2 with file name "Support.pdf."	
	Technical Abstract: Upload as Attachment 3 with file name "TechAbs.pdf."	
	Lay Abstract: Upload as Attachment 4 with file name "LayAbs.pdf."	
	Statement of Work: Upload as Attachment 5 with file name "SOW.pdf."	
	Letters of Support: Upload as Attachment 6 with file name "Letters.pdf."	
	Quad Chart: Upload as Attachment 7 with file name "Quad.pdf."	
	Impact and Military Relevance: Upload as Attachment 8 with file name "Impact.pdf."	
	Animal Research Plan (if applicable): Upload as Attachment 9 with file name "AnimalResearchPlan.pdf."	
	Human Subject Recruitment and Safety Procedures: Upload as Attachment 10 with file name "HumSubProc.pdf" (if applicable; required for all studies recruiting human subjects).	
	Data Management (if applicable): Upload as Attachment 11 with file name "Data_Manage.pdf."	
	IND/IDE Documentation (if applicable): Upload as Attachment 12 with file name "IND_IDE.pdf."	
	Intervention (if applicable): Upload as Attachment 13 with file name "Intervention.pdf."	
	Transition Plan and Regulatory Strategy: Upload as Attachment 14 with file name "Transition.pdf."	
Research & Related Senior/Key Person Profile (Expanded)	Research & Related Senior/Key Person Profile (Expanded): Upload as "Key Personnel.pdf."	
	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.	

Application Components	Action	Completed
Budget	Complete the DoD Military Budget Form and justification. Upload Budget (Budget_LastName.pdf) and Budget Justification (BudgetJustification_LastName.pdf), and Subaward Budgets and Budget Justifications, as applicable.	
Project/Performance Site Location(s) Form	Complete form as instructed.	

APPENDIX 1: ACRONYMS LIST

ACURO	Animal Care and Use Review Office
CDMRP	Congressionally Directed Medical Research Programs
CFR	Code of Federal Regulations
CRII	Clinical Research Intramural Initiative
DHA	Defense Health Agency
DHP	Defense Health Program
DoD	Department of Defense
eBRAP	Electronic Biomedical Research Application Portal
EC	Ethics Committee
FAD	Funding Authorization Document
FDA	Food and Drug Administration
FY	Fiscal Year
HRPO	Human Research Protection Office
IACUC	Institutional Animal Care and Use Committee
IRB	Institutional Review Board
MCS	Millennium Cohort Study
MHS	Military Health System
MIPR	Military Interdepartmental Purchase Request
MPORA	Military Performance Optimization Research Award
MTF	Military Treatment Facility
OASD(HA)	Office of the Assistant Secretary of Defense for Health Affairs
ORP	Office of Research Protections
PI	Principal Investigator
RDT&E	Research, Development, Test, and Evaluation
SOW	Statement of Work
USAMRMC	U.S. Army Medical Research and Materiel Command
USC	United States Code
VA	Department of Veterans Affairs

APPENDIX 2: REGULATORY REQUIREMENTS

A. Research Protections Review Requirements – Use of Human Subjects, Human Anatomical Substances, Human Data, Human Cadavers, and Animals

The USAMRMC Office of Research Protections (ORP) ensures that research conducted, contracted, sponsored, supported, or managed by the USAMRMC and involving human subjects, human anatomical substances, human data, human cadavers, and animals are conducted in accordance with Federal, DoD, Army, USAMRMC, and international regulatory requirements.

Principal Investigators (PIs) and applicant organizations **may not commence performance** of research involving the above, **or expend funding** on such efforts, until and unless regulatory documents are submitted and approved by the USAMRMC ORP to ensure that DoD regulations are met. All expectations described below are consistent with the DoD Instruction (DoDI) 3216.01, "Use of Animals in DoD Programs," as issued 13 September 2010, available at https://mrmc.amedd.army.mil/index.cfm?pageid=research_protections.acuro_regulations and DoDI 3216.02, "Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research," as issued on 8 November 2011, and available at http://www.dtic.mil/whs/directives/corres/pdf/321602p.pdf.

The ORP Animal Care and Use Review Office (ACURO) is responsible for administrative review, approval, and oversight of all animal research protocols, including all changes made during the life of the protocol.

The ORP Human Research Protection Office (HRPO) is responsible for administrative review, approval, and oversight of USAMRMC-supported research involving human subjects, human anatomical substances or data, and use of human cadavers.

NOTE: If protocol funding is provided directly from USAMRMC to a DoD MTF or USAMRMC laboratory (through a MIPR or FAD process), with no non-DoD awardees or collaborators, then it is considered intramural research and a HRPO review is not required. ***Research involving use of human data and/or specimens that is anticipated to be exempt from human subjects protections regulations requires a determination from the PI's institution as well as the ORP HRPO at USAMRMC.*** A timeframe for submission of the appropriate protocols and required approvals will be established during negotiations.

1. Research Involving Animal Use

Specific documents relating to the use of animals in the proposed research will be requested if the application is selected for funding. The ACURO, a component of the USAMRMC ORP, must review and approve all animal use prior to the start of working with animals. PIs must submit the institutional animal use protocol, IACUC approval of that protocol, and a version of the Animal Use Appendix titled "Research Involving Animals." For guidance on which version of the appendix to use, as well as links to both, visit the ACURO website at: https://mrmc.amedd.army.mil/index.cfm?pageid=Research_Protections.acuro_Animalappendix. ***Allow at least 2 to 3 months for regulatory review and approval processes for animal studies.***

For additional information, send questions via email to ACURO (usarmy.detrick.medcom-usamrmc.other.acuro@mail.mil).

2. Use of Human Cadavers or Human Anatomical Substances Obtained from Human Cadavers

Research, development, test and evaluation (RDT&E), education or training activities involving human cadavers shall not begin until approval is granted in accordance with the Army Policy for Use of Human Cadavers for RDT&E, Education, or Training, 20 April 2012 (https://mrmc.amedd.army.mil/index.cfm?pageid=research_ protections.overview). The USAMRMC ORP is the Action Office (usarmy.detrick.medcom-usamrmc.other.hrpo @mail.mil) for this policy. Award recipients must coordinate with the supporting/funding Army organization to ensure that proper approvals are obtained. Written approvals to begin the activity will be issued under separate notification to the recipient. Questions regarding submission of cadaver research for USAMRMC ORP review and approval should be directed to the ORP at usarmy.detrick.medcom-usamrmc.other.hrpo@mail.mil.

3. Research Involving Human Subjects, Human Subjects Data, or Human Anatomical Substances

In addition to local Institutional Review Board (IRB) review, investigators must submit all USAMRMC-funded research protocols involving human subjects and human anatomical substances for review and approval by the USAMRMC ORP HRPO prior to implementation of the research. The focus of this review is to validate IRB review as appropriate and ensure that DoD, Army, and USAMRMC regulatory requirements have been met.

Human subject research definitions, categories, and resource information may be found in the Human Subject Resource Document on the eBRAP website (https://ebrap.org/eBRAP/public/Program.htm). This information is a guide only; it is not intended to be a source for human subjects protection regulations. Questions regarding applicable human subjects protection regulations, policies, and guidance should be directed to the local IRB, the ORP HRPO (usarmy.detrick.medcom-usamrmc.other.hrpo@mail.mil), and/or the U.S. Food and Drug Administration (FDA) as appropriate. For in-depth information and to access HRPO protocol submission forms, refer to the ORP HRPO website (https://mrmc.amedd.army.mil/index.cfm?pageid=Research_Protections.hrpo).

ORP HRPO-required language must be inserted into the consent form, and compliance with DoD regulations may require additional information be included in the protocol.

The ORP HRPO ensures that DoD-supported and/or -conducted research complies with specific DoD laws and requirements governing research involving human subjects. These laws and requirements may require information in addition to that supplied to the local IRB.

During the regulatory review process for research involving human subjects, the ORP HRPO requirements must be addressed, and any changes to the already approved protocol must be approved as an amendment by the local IRB. It is strongly recommended that

investigators carefully read the "Information for Investigators" found at https://mrmc.amedd.army.mil/index.cfm?pageid=Research_Protections.acuro_Animalappendix. The time to approval depends greatly on adherence to the requirements described within. If the protocol has not been submitted to the local IRB at the time of award negotiation, these guidelines should be considered before submission.

Documents related to the use of human subjects or human anatomical substances will be requested if the application is recommended for funding. ***Allow at least 2 to 3 months for regulatory review and approval processes for studies involving human subjects.***

Specific requirements for research involving human subjects or human anatomical substances can be found at https://mrmc.amedd.army.mil/index.cfm?pageid=research_protections.hrpo.

a. Assurance of Compliance: Each institution engaged in non-exempt human subjects research must have a current Department of Health and Human Services Office for Human Research Protection (OHRP) Federal-wide Assurance (FWA) or DoD Assurance.

b. Training: Personnel involved in human subjects research must have appropriate instruction in the protection of human subjects. Documentation confirming completion of appropriate instruction may be required during the regulatory review process.

c. Informed Consent Form: The following must appear in the consent form:

- A statement that the U.S. Department of Defense is providing funding for the study.
- A statement that representatives of the DoD are authorized to review research records.
- In the event that a Health Insurance Portability and Accountability Act (HIPAA) authorization is required, the DoD must be listed as one of the parties to whom private health information may be disclosed.

d. Intent to Benefit: The requirements of Title 10 of the United States Code Section 980 (10 USC 980), which are applicable to DoD-sponsored research, must be considered. 10 USC 980 requires that "Funds appropriated to the Department of Defense may not be used for research involving a human being as an *experimental subject* unless (1) the informed consent of the subject is obtained ***in advance***; or (2) in the case of research intended to be beneficial to the subject, the informed consent may be obtained from a legal representative of the subject."

An individual not legally competent to provide informed consent (e.g., incapacitated individuals, cognitively impaired, minors) may not be enrolled as an ***experimental subject*** in a DoD-supported study unless the research is intended to benefit each subject enrolled in the study, to include subjects enrolled in study placebo arms. Studies designed in a manner that permits all subjects to potentially benefit directly from medical treatment or enhanced surveillance beyond the standard of care can meet the 10 USC 980 requirements. Note that the definition of ***experimental subject*** as defined

in the DoDI 3216.02 has a much narrower definition than ***human subject***. Research with experimental subjects must involve an intervention or interaction where the primary purpose of the research is to collect data regarding the effects of the intervention or interaction.

10 USC 980 is only applicable to certain intervention studies. It does not apply to retrospective studies, observational studies, studies that involve only blood draws, and tissue collections. Contact the HRPO at usarmy.detrick.medcom-usamrmc.other.hrpo@mail.mil if further clarification regarding applicability of 10 USC 980 to the proposed research project is required.

4. **Research Monitor Requirement:** ***For research determined to be greater than minimal risk, DoDI 3216.02 requires that the IRB approve, by name, an independent research monitor with expertise consonant with the nature of risk(s) identified within the research protocol.*** The IRB must approve a written summary of the monitor's duties, authorities, and responsibilities.

The research monitor's duties should be based on specific risks or concerns about the research. The research monitor may perform oversight functions and report his/her observations and findings to the IRB or a designated official. The research monitor may be identified from within or outside the PI's institution. Research monitor functions may include:

- Observing recruitment and enrollment procedures and the consent process for individuals, groups or units;
- Overseeing study interventions and interactions;
- Reviewing monitoring plans and Unanticipated Problems Involving Risk to Subjects or Others (UPIRTSO) reports; and/or
- Overseeing data matching, data collection, and analysis.

There may be more than one research monitor (e.g., if different skills or experiences are necessary). The monitor may be an ombudsman or a member of the data safety monitoring board. At a minimum, the research monitor:

- May discuss the research protocol with the investigators, interview human subjects, and consult with others outside of the study about the research;
- Shall have authority to stop a research protocol in progress, remove individual human subjects from a research protocol, and take whatever steps are necessary to protect the safety and well-being of human subjects until the IRB can assess the monitor's report; and,
- Shall have the responsibility for promptly reporting his or her observations and findings to the IRB or other designated official and the HRPO.

A curriculum vitae or biographical sketch and human subjects protection training for the research monitor must be provided. There should be no apparent conflict of interest, and the research monitor cannot be under the supervision of the PI, other investigators, or research staff associated with the proposed research project. If the duties of the research monitor could require disclosure of subjects' Protected Health Information outside a covered entity (i.e., the research monitor is not an agent of the covered entity), the PI's institution may require the identity and location of the research monitor to be described in the study HIPAA authorization. It is acceptable to provide appropriate compensation to the research monitor for his or her services.

5. **Military Personnel Volunteers:** The following is important information for research projects proposing to include military personnel as volunteers.

- **Recruitment of Military Personnel:** Civilian investigators attempting to access military volunteer pools are advised to seek collaboration with a military investigator familiar with service-specific requirements.

  A letter of support from Commanders of military units in which recruitment will occur or the study will be conducted will be requested by the HRPO. Some military sites may also require that each volunteer seek written permission from their supervisor prior to participation in research studies.

  Special consideration must be given to the recruitment process for military personnel. The Chain of Command must not be involved in the recruitment of military personnel and cannot encourage or order Service members to participate in a research study.

  For greater than minimal risk research, an ombudsman must be employed when conducting group briefings with active duty personnel to ensure that volunteers understand that participation is voluntary; this ombudsman may be recommended in other situations as well, especially when young enlisted Service members, who by virtue of their age and enlistment status are trained to follow orders, are being recruited. Service members are trained to act as a unit, so peer pressure should also be considered and minimized, if possible.

- **Payment to Federal Employees and Military Personnel:** Under 24 USC 30, payment to Federal employees and active duty military personnel for participation in research while on duty is limited to blood donation and may not exceed $50 per blood draw. These individuals may not receive any other payment or non-monetary compensation for participation in a research study unless they are off duty or on leave during the time they are participating in the protocol.

- **Confidentiality for Military Personnel:** Confidentiality risk assessment for military personnel requires serious consideration of the potential to affect the military career. Medical and psychological diagnoses can lead to limitation of duties and/or discharge from active duty. Information regarding alcohol or drug abuse, drunk driving, and sexual or spousal abuse can lead to actions under the Uniform Code of Military Justice, including incarceration and dishonorable discharge.

6. **Site Visits:** The USAMRMC ORP HRPO conducts site visits as part of its responsibility for compliance oversight.

   Accurate and complete study records must be maintained and made available to representatives of the USAMRMC as a part of their responsibility to protect human subjects in research. Research records must be stored in a confidential manner so as to protect the confidentiality of subject information.

   Additional information pertaining to the human subjects regulatory review process, guidelines for developing protocols, and suggested language for specific issues can be found at: https://mrmc.amedd.army.mil/index.cfm?pageid=research_protections.hrpo.

7. **Protocol Submission Format:** The ORP HRPO accepts protocol submissions in the format required by the local IRB. The IRB protocol application, if separate from the protocol itself, should be included with protocol submissions. A HRPO protocol submission form should be completed and submitted with each protocol.

   If the project includes a clinical trial(s), the PI may be required to register the clinical trial(s) individually on the registry and database ClinicalTrials.gov (https://www.clinicaltrials.gov/).

APPENDIX 3: ADMINISTRATIVE INFORMATION

A. Reporting Requirements

Reporting requirements and deliverables will be determined prior to funding and may vary depending on the research being conducted. Anticipated reporting requirements and deliverables may include the following:

Progress Reports: Quarterly, annual, and final reports will be required. These reports will present a detailed summary of scientific issues and accomplishments. A final report will be submitted within 30 days of the end of the performance period and will detail the findings, their potential impact to the military population, and other issues for the entire project. The format for the progress reports is available on eBRAP at https://ebrap.org/eBRAP/public/Program.htm.

Quad Charts: Quad Charts that outline the specific aims, approach, timeline and costs, and goals/milestones will be required with every quarterly report. The format for the quad chart is available on eBRAP at https://ebrap.org/eBRAP/public/Program.htm.

B. Publication, Acknowledgement, and Public Release

Publication of Findings: Publication of findings is a requirement of this submission. It is expected that at study completion researchers will submit their findings to an appropriate peer-reviewed journal for publication. Copies of all scientific publications, presentations, and reports resulting from this funding mechanism shall be submitted to CDMRP when published or completed even if beyond the period of performance to allow reporting to the DHP and Congress on the accomplishments of the program.

Acknowledgment: The recipient agrees that in the release of information relating to this funding such release shall include the statements below, as applicable. "Information" includes, but is not limited to, news releases, articles, manuscripts, brochures, advertisements, still and motion pictures, speeches, trade association meetings, and symposia.

- "This work was supported by the Office of the Assistant Secretary of Defense for Health Affairs and the Defense Health Agency J9, Research and Development Directorate through the Clinical Research Intramural Initiative. Opinions, interpretations, conclusions and recommendations are those of the author and are not necessarily endorsed by the Department of Defense."

- "In conducting research using animals, the investigator(s) adheres to the laws of the United States and regulations of the Department of Agriculture." Include required assurances, approvals, documents and information specified on the Animal Care and Use Review Office (ACURO) website (http://mrmc.amedd.army.mil/index.cfm?pageid=research_protections.acuro).

- "In the conduct of research utilizing recombinant DNA, the investigator adhered to NIH Guidelines for research involving recombinant DNA molecules." (http://www.nih.gov)

- "In the conduct of research involving hazardous organisms or toxins, the investigator adhered to the CDC-NIH Guide for Biosafety in Microbiological and Biomedical Laboratories." (http://www.cdc.gov/biosafety)

C. Sharing of Data and Research Resources

It is the intent of the Department of Defense that data and research resources generated by this funded research be made available to the research community (which includes both scientific and consumer advocacy communities) and to the public at large.

Expectations for sharing of data and research resources apply to all basic research, clinical studies, surveys, and other types of research funded through this award. This includes all data and research resources generated during the project's period of performance through grants, cooperative agreements, or contracts. It is critically important to share unique data and research resources that cannot be readily replicated, including but not limited to the following:

- **Unique Data**[2] are defined as data that cannot be readily replicated. Examples of unique data include large surveys that are expensive to replicate; studies of unique populations, such as patients to whom access is not widely available; studies conducted at unique times, such as during military conflict; studies of rare phenomena, such as rare diseases.

- **Final Research Data**[2] are defined as recorded factual material commonly accepted in the scientific community as necessary to document and support research findings. These are not the summary statistics or tables; rather, final research data are the data on which summary statistics and tables are based. Final research data do not include laboratory notes or notebooks, partial datasets, preliminary analyses, drafts of scientific papers, plans for future research, peer review reports, communications with colleagues, or physical objects, such as gels or laboratory specimens.

- **Research Resources**[3] include, but are not limited to, the full range of tools that scientists and technicians use in the laboratory, such as cell lines, antibodies, reagents, growth factors, combinatorial chemistry, DNA libraries, clones and cloning tools (such as PCR), methods, laboratory equipment and machines.

Data and research resources generated from this funded research should be made as widely available as possible while safeguarding the privacy of participants, and protecting confidential and proprietary data, and third-party intellectual property. By sharing and leveraging data and research resources, duplication of very expensive and time-consuming efforts can be avoided, allowing for the support of more investigators with Federal funds. Such sharing allows for a more expeditious translation of research results into knowledge, products, and procedures to improve human health.

[2] Adapted from https://grants.nih.gov/grants/policy/data_sharing/data_sharing_guidance.htm
[3] Adapted from http://www.gpo.gov/fdsys/pkg/FR-1999-12-23/pdf/99-33292.pdf

The PI may be required to participate in the following:

- Traumatic Brain Injury: If the project includes traumatic brain injury (TBI) research, the PI may be required to make TBI data generated via an award available to the research community by depositing de-identified research data into the Federal Interagency TBI Research (FITBIR) informatics System (https://fitbir.nih.gov).

- Systems Biology: If the project includes systems biology-related research, the PI may be required to make systems biology data, generated via an award, available to the research community by depositing research data into the SysBioCube system (https://sysbiocube-abcc.ncifcrf.gov/).

For additional information on data-sharing, refer to the document titled "Congressionally Directed Medical Research Programs: Policy on Sharing Data and Research Resources," available on eBRAP under Resources and Reference Material at https://ebrap.org/eBRAP/public/Program.htm.

APPENDIX 4: FORMATTING GUIDELINES

All pre-application and application documents must be legible and should conform to the formatting guidelines described below. The font size, spacing, page size, and margins may differ between the word processing, PDF, and printed versions. These guidelines apply to the document properties of the electronic version of the PDF file(s) as viewed on a computer screen.

Document Format: All attachments must be in PDF.

Font Size: 12 point, 10 pitch.

Font Type: Times New Roman.

Spacing: Single space or no more than six lines of type within a vertical inch (2.54 cm).

Page Size: No larger than 8.5 inches x 11.0 inches (21.59 cm x 27.94 cm).

Margins: At least 0.5 inch (1.27 cm) in all directions.

Print Area: 7.5 inches x 10.0 inches (19.05 cm x 25.40 cm).

Color, High-Resolution, and Multimedia Objects: Project narratives and pre-application files may include color, high-resolution, or multimedia objects (e.g., MPEG, WAV, or AVI files) embedded in the PDF files; however, these objects should not exceed 15 seconds in length and a size of 10 MB. Photographs and illustrations must be submitted in JPEG format; bit map or TIFF formats are not allowed.

Scanning Resolution: 100 to 150 dots per inch.

Internet URLs: URLs directing reviewers to websites that contain additional information about the proposed research are not allowed in the application or its components. Inclusion of such URLs may be perceived as an attempt to gain an unfair competitive advantage. However, links to publications referenced in the application are encouraged.

Language: All documents must be submitted in English, unless otherwise specified in the Funding Opportunity Announcement (e.g., foreign transcripts submitted with English translations).

Headers and Footers: Should not be used. Pre-existing headers and footers on required forms are allowed.

Page Numbering: Should not be used.

Recommended Component Size: Each attachment should not exceed 20 MB.

APPENDIX 5: BUDGET FORM INSTRUCTIONS

An estimate of the total proposed research project cost, with a breakdown of all cost categories for each year, must be submitted on the DoD Military Budget Form and Justification form. For limits on funding amounts, types of costs, and period of performance, refer to the Funding Opportunity Announcement. No budget will be approved by the Government exceeding the cost limit stated in the specific Funding Opportunity Announcement. The budget and budget justification should include sufficient detail for the Government to determine whether the proposed costs are allowable, allocable, and reasonable for the proposed research.

The PI name, eBRAP log number, and period of performance fields should be entered at the top of the DoD Military Budget Form.

DoD Civilian and Military Personnel: Personnel involved in the project should be listed in this section; however, this award is not intended to provide salary support for any Federal employee, as those costs were to have been included in infrastructure costs. If salary support is requested, sufficient justification must be provided in the budget justification section.

- **Name:** Beginning with the PI, list all participants who will be involved in the project during the initial budget period, whether or not salaries are requested. Include all collaborating investigators, research associates, individuals in training, mentor (if applicable), and support staff.

- **Role on Project:** Identify the role of each personnel listed. Describe his/her specific functions in the proposed research in the budget justification.

- **Type of Appointment (Months):** List the number of months per year reflected in an individual's contractual appointment with the applicant organization. The Government assumes that appointments at the applicant organization are full time for each individual. If an appointment is less than full time (e.g., 50%), note this with an asterisk (*) and provide a full explanation in the budget justification. Individuals may have split appointments (e.g., for an academic period and a summer period). For each type of appointment, identify and enter the number of months on separate lines.

- **Annual Base Salary:** Enter the annual organizational base salary (based on a full-time appointment) for each individual listed for the project.

- **Effort on Project:** List the percentage of each appointment to be spent on this project for all staff members including unpaid personnel.

- **Salary Requested:** Enter the salary for each position for which funds are requested. This is calculated automatically from the data provided. If you do not wish this to be calculated for you, uncheck the small "Calculate Salary" checkbox in the bottom of the field. Calculate the salary request by multiplying an individual's organizational base salary by the percentage of effort on the project.

- **Fringe Benefits:** Enter the fringe benefits requested for each individual in accordance with organizational guidelines.

- **Totals:** Calculated automatically from the data provided.

- **Major Equipment:** Provide an itemized list of proposed equipment, showing the cost of each item. Equipment is any article of nonexpendable tangible property having a useful life of more than 1 year and an acquisition cost of $5,000 or more per unit.

- **Materials, Supplies, and Consumables:** The budget justification for supporting material and supply (consumable) costs should include a general description of expendable materials and supplies.

- **Travel Costs:** PIs are responsible for budgeting for all costs associated with travel, including airfare, hotel, etc., associated with the trip. Anticipated travel costs should be built into the budget at current or projected DoD per-diem rates. Travel costs must include:

    - Travel costs for the PI to attend one DoD-related meeting to be determined at the discretion of the Government during the award performance period.

  Travel costs may include:

    - Travel costs for one investigator to travel to one scientific/technical meeting during the period of performance.

    - Travel costs between collaborating organizations.

- **Research-Related Subject Costs:** Include itemized costs of subject participation in the proposed research. These costs are strictly limited to expenses specifically associated with the proposed research.

- **Other Direct Costs:** Itemize other anticipated direct costs such as publication and report costs, equipment rental (provide hours and rates), communication costs, and organizationally provided services. Unusual or expensive items should be fully explained and justified. Estimate the costs of publishing and reporting research results, including direct charges for clerical preparation, illustrations, reprints, and distribution. Organizationally provided services should be supported by the organization's current cost/rate schedule. These items should be described in detail and clearly justified.

- **Subcontract Costs (Partnership/Collaboration Costs):** Should an intramural organization propose collaboration with an extramural entity for part of the research effort, the intramural organization will receive all funds and is responsible for executing all necessary contractual or assistance funding awards to collaborating partners through the agency's procedures. **All direct and indirect costs of any partnership/collaboration costs must be included in the total direct costs of the primary award**. The nature of the partnership/collaboration should be described in the Budget Justification section.

- **Total Direct Costs:** Calculated automatically from the data provided for the initial budget period on page F-2 and for the entire proposed period of support on page F-3.

- **Total Indirect Costs:** If funds for indirect costs are requested, sufficient justification must be provided in the budget justification section. The Government reserves the right to disallow any indirect costs not sufficiently justified. All direct and indirect costs of any proposed collaborator must be included in the total direct costs of the primary award. (See Section II.D.5, Funding Restrictions.)

- **Total Costs:** This section is calculated automatically from the data provided.

- **Fee:** A profit or fixed fee is not allowable on awards or on subawards.

  ***Budget Justification Instructions*:** Provide a clear budget justification for each item in the budget over the entire period of performance in the Justification section of the DoD Military Budget Form. Itemize direct costs within each budget category for additional years of support requested beyond Year 1.

- **Federal Agency Financial Plan (required):** Provide a detailed Federal Agency Financial Plan after the budget justification information in the DoD Military Budget Form. The plan delineates how all FY18 funding will be obligated by **September 30, 2019**. The plan must include the funding mechanism(s) or contractual arrangements that will be used to carry over funds between fiscal years, if applicable. Any FY18 funding not obligated by September 30, 2019 may be withdrawn by the issuing Comptroller.