

Intramural Program Announcement and

Application Instructions

for the

Department of Defense

Defense Health Program

Congressionally Directed Medical Research Programs

Defense Medical Research and Development Program

Joint Program Committee 6

Combat Casualty Care Research Program

Precision Trauma Care Research Award

Funding Opportunity Number: W81XWH-18-DMRDP-PTCRA

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

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-Application Submission Deadline:** 5:00 p.m. Eastern time (ET), March 17, 2017
- **Invitation to Submit an Application:** April 25, 2017
- **Application Submission Deadline:** 11:59 p.m. ET, June 15, 2017
- **End of Application Verification Period:** 5:00 p.m. ET, June 20, 2017
- **Peer Review:** August 2017
- **Programmatic Review:** September 2017

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I. FUNDING OPPORTUNITY DESCRIPTION

BEFORE APPLYING, NOTE: THIS PROGRAM ANNOUNCEMENT/FUNDING OPPORTUNITY IS INTENDED FOR INTRAMURAL INVESTIGATORS ONLY. EXTRAMURAL INVESTIGATORS ARE REQUIRED TO APPLY TO THE FISCAL YEAR 2018 (FY18) JOINT PROGRAM COMMITTEE 6 (JPC-6)/COMBAT CASUALTY CARE RESEARCH PROGRAM (CCCRP) PRECISION TRAUMA CARE RESEARCH AWARD (PTCRA) EXTRAMURAL ANNOUNCEMENT/FUNDING OPPORTUNITY THROUGH CONGRESSIONALLY DIRECTED MEDICAL RESEARCH PROGRAMS (CDMRP) eBRAP at <https://ebrap.org/eBRAP/public/index.htm>.

- An *intramural investigator* is defined as a Department of Defense (DoD) military or civilian employee working within a DoD laboratory or military treatment facility, 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 intramural investigators to this Program Announcement/Funding Opportunity will be rejected.

A. Program Description

Applications to the Fiscal Year 2018 (FY18) Joint Program Committee 6/Combat Casualty Care Research Program (JPC-6/CCCRP) are being solicited for the Defense Health Agency (DHA), Research and Development Directorate. As directed by the Office of the Assistant Secretary of Defense for Health Affairs (OASD[HA]), the DHA manages the Defense Health Program (DHP) Research, Development, Test, and Evaluation (RDT&E) appropriation. The managing agent for this Program Announcement/Funding Opportunity is the Congressionally Directed Medical Research Programs (CDMRP). The US Army Medical Research and Materiel Command (USAMRMC) CDMRP provides Defense Medical Research and Development Program (DMRDP) execution management support for DHP core research program areas, including the JPC-6/CCCRP. This Program Announcement/Funding Opportunity and subsequent awards will be managed and executed by CDMRP with strategic oversight from the JPC-6/CCCRP.

The JPC-6/CCCRP is one of six major research program areas within the DHP. The JPC-6/CCCRP is a committee of DoD and non-DoD medical and military technical experts in combat casualty care-related program areas. The JPC-6/CCCRP strives to optimize survival and recovery from combat-related or trauma-induced injury in current and future operational scenarios. This is being accomplished through the development of knowledge and materiel products for the acute and early management of combat-related or trauma-induced injury, including point-of-injury, en route, and forward surgical care. Innovations developed by JPC-6/CCCRP-supported research are applied in-theatre and within the clinical facilities of the Military Health System. These solutions not only minimize the morbidity and mortality of combat-related injuries in Service members, they also are often translatable to the civilian healthcare system.

B. Award Information

In support of the Precision Medicine Initiative¹, the OASD(HA) identified “precision medicine” as a top science and technical priority for the FY17 DHP RDT&E funds (this is also applicable to FY18 DHP RDT&E funds) and directed DHA to increase the use of “big data” and interdisciplinary approaches, establish a fundamental understanding of military disease and injury, and advance health status assessment, diagnosis, and treatment tailored to individual Service members and beneficiaries. For this Program Announcement/Funding Opportunity, precision medicine is defined as “an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person.”² Precision medicine pioneers a new model of patient-powered research that aims to accelerate biomedical discoveries and provide clinicians with new tools, knowledge, and approaches to select more accurate treatment and prevention strategies that will work best for individual patients.

The intent of the PTCRA is to support research applying precision medicine concepts to trauma care. In order to improve the care of combat casualties, the JPC-6/CCCRP requires capabilities to more accurately diagnose and treat injuries. In general, the field of trauma care progresses as empirical evidence accumulates. Accumulated evidence supports the reduction of unwarranted practice variability (e.g., protocol-driven care). Reduction in practice variability leads to refinement of protocols through improved diagnostic and prognostic indicators that account for patient-specific variables such as injury pattern, co-morbidities, demographics, and morphometric data. These approaches are further refined by incorporation of near-term patient-specific variables such as injury progression, response to interventions, and theranostic indicators. The result is a precision medicine approach for trauma care that drives application of interventions to improve outcomes following trauma.

The JPC-6/CCCRP seeks to develop precision medicine approaches for trauma care in the most challenging of environments, including point-of-injury care on the battlefield, deployed healthcare facilities such as casualty collection points, forward surgical teams, and combat support hospitals. This challenge of diverse combat environments and medical capabilities also requires research to develop new solutions to include: support for medical providers in the assessment, diagnosis, and treatment of military trauma in out-of-hospital settings (point of injury, austere environment, or en route care) with limited resources through Role 4.³ Proposed research should consider the entire continuum of trauma care and must be focused on enabling patient-specific interventions and improved outcomes rather than “one size fits all” population-based tools and techniques.

C. FY18 DMRDP JPC-6/CCCRP PTCRA Focus Areas

The JPC-6/CCCRP has identified four overarching Focus Areas for funding under this Program Announcement/Funding Opportunity. To meet the intent of the award mechanism, applications

¹<https://www.whitehouse.gov/precision-medicine>

² <https://ghr.nlm.nih.gov/primer/precisionmedicine/definition>

³ See <http://www.cs.amedd.army.mil/FileDownloadpublic.aspx?docid=1a73495d-1176-4638-9011-9e7f3c6017d8> for a description of DoD roles of medical care.

MUST propose research that specifically addresses at least one of the four FY18 JPC-6/CCCRP PTCRA Focus Areas. Research not aligned to at least one of these Focus Areas will not be considered for funding.

Neurotrauma

For studies proposing animal research, only proposals collecting data from gyrencephalic animal models of traumatic brain injury (TBI) will be considered for funding.

Focus Area 1: Improving the Characterization of TBI

- Identification and/or characterization of TBI biomarkers that are specific to TBI alone and/or TBI with concomitant injuries (e.g., burn, hemorrhage) and identification of biomarker profile specific to TBI pathology and treatment effectiveness
- Development of targeted therapies, devices, or clinical guidelines to improve diagnosis/stabilization/treatment of TBI casualties with and without concomitant polytrauma based upon the precise characterization and individualized assessment of affected domains
- Improve TBI treatment decision capabilities based upon the precise characterization and individualized assessment of TBI pathology (e.g., contusion, diffuse axonal injury, subdural hematoma, epidural hematoma)
- Improve the understanding of risk factors and outcomes associated with specific brain pathology (e.g., contusions, diffuse axonal injury, hematomas) with the end state goal of improving prognosis and optimizing recovery
- Improve the understanding of the role of genetic factors and/or physiology status on short- and long-term consequences of combat-related TBI

Focus Area 2: Understanding the factors that influence and/or inform patient responsiveness to TBI therapeutic interventions

- Pharmacodynamic characterization of therapeutics with respect to patients responsive to treatment
- Targeting therapeutics to the blood-brain barrier in response to specific brain injuries (e.g., contusions, diffuse axonal injury, subdural hematoma, epidural hematoma)
- Understanding the impact of sex-associated differences on the efficacy of TBI treatments
- Understanding the potential role of genetics and sex-associated differences in TBI treatment decisions and TBI treatment response
- Identification of biomarkers of TBI that inform treatment effectiveness and stage of recovery
- Identify the impact of environmental factors (such as altitude, vibration, and/or temperature) that negatively affect TBI outcomes. Identify potential treatments and/or interventions to mitigate these effects

Forward Surgical, En Route, and Critical Care

Focus Area 3: Understanding the role of environmental and physiological factors impacting injury outcomes:

- Environmental, physiological, and physical factors that govern an individual's predisposition to various responses to trauma
- Physiological, genetic, or physical factors that govern the individual's response to blood loss (ability to compensate for blood loss)
- Impact of vascular disruption, repair, extremity ischemia, and reperfusion, and its relationship to long-term limb recovery and function
- Determination of more effective and efficient ways to diagnose and manage vascular disruption (with or without hemorrhagic shock) in forward surgical and limited-resource critical care environments

Focus Area 4: Developing materiel and knowledge products to assist medical and non-medical care providers in administering individualized combat-related or trauma-induced injury care such as:

- Standardized, clinically relevant decision support model for severely mangled extremities (i.e., decisions regarding primary amputation vs. pursuit of limb salvage, optimal amputation level to support future treatment (i.e., transplant, prosthetic, etc.)
- Computational algorithms and predictive tools for physiological status monitoring that use available information and can predict necessary statuses in an expedient manner
- Evidence-based clinical decision support tools/protocols for the prehospital environment and throughout the continuum of care to include en route care (patient medical transport) and timing of transport (particularly for strategic air movement) for post-surgical patients
- Non-invasive physiological monitoring for compartment syndrome
- Innovative patient-centered technologies to maintain physiological equilibrium (homeostasis) such as dynamically responsive closed-loop technologies for oxygenation, core temperature maintenance, and medication delivery in the prehospital environment and throughout the continuum of care, to include en route care (patient medical transport)

For this Program Announcement/Funding Opportunity, a knowledge product is defined as a non-materiel product that addresses an identified need, research area, or capability gap in the continuum of trauma care. Knowledge products provide information, awareness, and procedures to support clinical practice, training recommendations, and the application of existing materiel products (e.g., drugs, medical devices, equipment).

This Program Announcement/Funding Opportunity may support preclinical research, clinical research, and early clinical trials/testing. A clinical trial is defined as a prospective accrual of human subjects 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, efficacy, and/or exploratory

information. 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 the Human Subject Resource Document available on the eBRAP “Funding Opportunities and Forms” web page (<https://ebrap.org/eBRAP/public/Program.htm>). ***Phase II and Phase III clinical trials for US Food and Drug Administration (FDA) licensure of drugs and definitive/pivotal testing for device clearance by the FDA will NOT be permitted under this Program Announcement/Funding Opportunity.***

Research Involving an FDA-Regulated Drug, Biologic, or Device: If the study proposed involves the use of a drug or biologic that has not been approved by the FDA for the proposed investigational use, evidence that an Investigational New Drug (IND) exemption application that meets all requirements under the Code of Federal Regulations, Title 21, Part 312 (21 CFR 312) ***has been submitted or will be submitted to the FDA within 60 days of award*** is required. If the investigational product is a device, evidence that an Investigational Device Exemption (IDE) application that meets all requirements under 21 CFR 812 has been reviewed and approved by the FDA ***has been submitted or will be submitted to the FDA within 60 days of award*** is required. 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 DoD award date or if the documented application status of the IND or IDE has not been obtained within 12 months of the award date.

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.*** Refer to the General Application Instructions, [Appendix 3](#), and the Human Subject Resource Document available on the eBRAP “Funding Opportunities & Forms” web page (<https://ebrap.org/eBRAP/public/Program.htm>) for additional information.

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. Principal Investigators (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 3](#) 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 8, 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.

Military Relevance: Although the research outcomes are expected to benefit both the military and the general public, relevance to the healthcare needs of military Service members and other beneficiaries is a key requirement of this award. Investigators are encouraged to consider the following characteristics as examples of how a project may demonstrate relevance to the mission of the DHP, JPC-6/CCCRP, and the military:

- Explanation of how the project has direct relevance to DoD healthcare personnel, recipients, and other beneficiaries
- Use of military populations or data in the proposed research
- Collaboration with DoD investigators
- Involvement of military consultants (Army, Air Force) or specialty leaders (Navy, Marine Corps) to the Surgeons General in a relevant specialty area

Principal Investigators are encouraged to integrate and/or align their research projects with DoD and/or Department of Veterans Affairs (VA) research laboratories and programs. Collaboration with DoD or VA investigators is also encouraged. The following websites may be useful in identifying information about ongoing DoD and VA areas of research interest:

Air Force Research Laboratory
<http://www.wpafb.af.mil/afrl>

Combat Casualty Care Research Program
<https://ccc.amedd.army.mil>

Armed Forces Institute of Regenerative
Medicine
<http://www.afirm.mil>

Congressionally Directed Medical Research
Programs
<http://cdmrp.army.mil>

Center for Neuroscience and Regenerative
Medicine
<http://www.usuhs.mil/cnrm/>

Defense Advanced Research Projects
Agency
<http://www.darpa.mil>

Clinical and Rehabilitative Medicine Research
Program
<https://crmrp.amedd.army.mil>

Defense Medical Research and
Development Program
<http://cdmrp.army.mil/dmrdp/default>

Defense Technical Information Center

<http://www.dtic.mil>

Military Infectious Diseases Research Program

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

Military Operational Medicine Research Program

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

National Center for Telehealth and Technology

<http://t2health.org/>

National Museum of Health and Medicine

<http://www.medicalmuseum.mil/index.cfm>

Naval Health Research Center

<http://www.med.navy.mil/sites/nhrc>

Navy and Marine Corps Public Health Center

<http://www.med.navy.mil/sites/nmcphe>

Office of Naval Research

<http://www.med.navy.mil>

Office of the Under Secretary of Defense for
Acquisition, Technology and Logistics

<http://www.acq.osd.mil/>

US Army Medical Research Acquisition
Activity

<https://www.usamraa.army.mil/>

US Army Medical Research and Materiel
Command

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

US Army Research Laboratory

<http://www.arl.army.mil>

US DoD Blast Injury Research Program

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

US Naval Research Laboratory

<https://www.nrl.navy.mil>

US Department of Veterans Affairs, Office
of Research and Development

<http://www.research.va.gov>

Walter Reed Army Institute of Research

<http://www.wrair.army.mil>

Use of Military and VA Populations or Resources: If the proposed research involves access to military and/or VA population(s) and/or resource(s), the PI is responsible for establishing access. Access to target military and/or VA patient population(s) should be confirmed at the time of application submission. A letter of support, signed by the lowest-ranking person with approval authority, should be included for studies involving military Service members, Veterans, military and/or VA-controlled study materials, and military and/or VA databases. Use Attachment 2 to provide this documentation (see [Section II.C., Full Application Submission Content, Attachment 2, Supporting Documentation](#)). 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. 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.

Federal Interagency TBI Research (FITBIR) Informatics System: For studies that will enroll TBI subjects, the DoD requires that the awardees make data available to the TBI research community by depositing de-identified research data into the FITBIR Informatics System on a quarterly basis. The FITBIR Informatics System is a free resource to the TBI community designed to accelerate comparative effectiveness research on brain injury diagnosis and treatment. Data reporting to FITBIR is an opportunity for investigators to facilitate their own research and collaborate with others performing similar research. While use of the informatics system presents no direct cost to the user, a *project estimation tool* (<https://fitbir.nih.gov/jsp/>

[contribute/fitbir-costs.jsp](#)) is available to help estimate indirect cost and manpower needs associated with data submission.

- In order to facilitate FITBIR compliance, it is recommended that investigators contact the FITBIR Operations Center (FITBIR-ops@mail.nih.gov) during the application development phase to discuss submission requirements and potential IRB submission modifications.
- All reasonable efforts should be made to ensure that data elements are reported using the National Institute of Neurological Disorders and Stroke (NINDS) TBI Common Data Elements (CDEs), which are housed within the FITBIR data dictionary (<https://fitbir.nih.gov/content/data-dictionary>). Use of these TBI CDEs, as published, is required to facilitate data sharing and collaboration through the usage of standard definitions across studies. *If the proposed research data cannot be entered in CDE format, the investigators must supply a proposal for an alternative data submission or data sharing vehicle and justification for its use.* FITBIR Operations can provide assistance in mapping study variables to specific CDEs. If necessary, FITBIR Operations will work with researchers to create new, unique data elements when suitable data elements are not available in the FITBIR data dictionary.

Additional information, including the advantages of FITBIR use to the researcher, is detailed at the FITBIR website (<http://fitbir.nih.gov/>).

The JPC-6/CCCRP and CDMRP intends that information, data, and research resources generated under awards funded by this Program Announcement/Funding Opportunity 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 2, Administrative Information](#).

D. Eligibility Information

This Program Announcement/Funding Opportunity is intended for intramural investigators only. Extramural investigators are required to apply to the FY18 JPC-6/CCCRP Precision Trauma Care Research Award (PTCRA) Announcement/Funding Opportunity through CDMRP eBRAP at <https://eBRAP.org>.

- Independent investigators at all academic levels (or equivalent) are eligible to submit applications.
- Cost sharing/matching is not an eligibility requirement.
- Submissions from extramural (non-DOD) investigators will be rejected. 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 existing contractual or assistance funding awards to collaborating partners through their agency's procedures.
- It is expected that the majority of work funded through this Program Announcement/Funding Opportunity will be performed within a DoD laboratory or military treatment

facility. Regardless of the location, any work that is to be performed by associated non-DoD organizations must be limited to work performed under existing service contracts or under Cooperative Agreements or Materiel Transfer Agreements. The Government reserves the right to administratively withdraw any application that does not meeting these eligibility. ***Applications that require research to be performed completely by a non-DoD organization under a new service contract will not be considered for funding***

E. Funding

Research supported under this Program Announcement/Funding Opportunity will be funded in three phases, Phase 1 Base, Phase 2 Option.I, and Phase 3 Option.II. Each Phase must be a distinct research effort with a non-overlapping period of performance, research outcomes/milestones, and budget. Research products from a previous Phase shall be leveraged in subsequent Phase(s) if planned. However, proposal of subsequent Option Phases is not required.

- Each Phase has a maximum period of performance of **12 months**. The maximum period of performance for all Phases is **36 months**.
- Transition from Phase 1 to subsequent Phase(s) will be based on the following criteria:
 - Completion of the research within the 12-month period of performance
 - Documented progress in making data available to the research community
 - Timely submission of quarterly and annual progress reports and quad charts
 - Availability of funds
 - Presentation of research at a minimum of one national research or military relevant conference (for Phase 2 to Phase 3 transition)
 - One or more documented publication submissions (for Phase 2 to Phase 3 transition)
- The anticipated total costs (direct and indirect) budgeted for each Phase will not exceed **\$1.5 million (M)**. The maximum anticipated total costs (direct and indirect) for all Phases are **\$4.5M**. Indirect costs are to be budgeted in accordance with the organization's negotiated rate. No budget will be approved by the Government exceeding the total cost limitations or using an indirect rate exceeding the organization's negotiated rate.
- All direct and indirect costs of any subaward must be included in the total direct costs of the primary award.

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

- Travel costs for the PI(s) to disseminate project results at one DoD-related meeting to be determined at the discretion of the Government during the award performance period. Costs associated with travel to this meeting should be included in the budget. For planning purposes, it should be assumed that the 2-day 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
- Research-related subject costs
- Clinical research costs
- Equipment
- Research supplies
- Support for multidisciplinary collaborations
- Travel between collaborating organizations
- Travel costs for up to four investigators to travel to one scientific/technical meeting per year in addition to the required meeting described above

Submissions selected for funding will be processed for award by USAMRMC. Awards are made to organizations, not individuals. Awards to intramural organizations will be executed through the Military Interdepartmental Purchase Request (MIPR) or Funding Authorization Document (FAD) process. Transfer of funds is contingent upon appropriate safety and administrative approvals. Intramural applicants and collaborators are reminded to coordinate receipt and commitment of funds through their respective resource managers. ***It is permissible, however, for an extramural investigator to be named as a collaborator in an application submitted by an intramural investigator.*** In such cases, the intramural organization will receive all funds and is responsible for executing all necessary contractual or assistance funding awards to collaborating partners through their agency's procedures.

The JPC-6/CCCRP expects to allot approximately \$9.5M of the FY18, \$9.5M of the FY19, and \$10.2M of the FY20 DHP RDT&E appropriations to fund approximately six (6) intramural and extramural FY18 JPC-6/CCCRP Precision Trauma Care Research Award applications, depending on the quality and number of applications received. Funding of applications received in response to this Program Announcement/Funding Opportunity is contingent upon the availability of Federal funds for this program. As of the release date of this Program Announcement/Funding Opportunity, the FY18, FY19, or FY20 Defense Appropriations Bills have not been passed and there is no guarantee that any funds will be made available to support this program. The funding estimated for this Program Announcement/Funding Opportunity is approximate and subject to realignment.

NOTE: Applications received under this mechanism will compete with applications received under the FY18 JPC-6/CCCRP Precision Trauma Care Research Award Extramural Program Announcement/Funding Opportunity found at <https://eBRAP.org>.

II. SUBMISSION INFORMATION

Submission is a two-step process requiring both (1) pre-application submission and (2) application submission through the electronic Biomedical Research Application Portal (eBRAP) (<https://eBRAP.org/>).

All submission dates and times are indicated on the [title page](#) of this Program Announcement/Funding Opportunity. Pre-application and application submissions are required. Failure to meet either of these deadlines will result in application rejection.

Start the submission process early. eBRAP has a number of required steps that must be completed before submissions will be accepted. Be sure to allow adequate time for completion of all pre-application and application steps by their respective deadlines.

eBRAP is a multifunctional web-based system that allows PIs to submit their pre-applications electronically through a secure connection, to view and edit the content of their pre-applications and full applications, to receive communications from the CDMRP, and to submit documentation during award negotiations and period of performance. It is the applicant's responsibility to review all application components for accuracy as well as ensure proper ordering as specified in this Program Announcement/Funding Opportunity.

A. Pre-Application Submission Content

The pre-application process should be started early to avoid missing deadlines. There are no grace periods. During the pre-application process, each submission is assigned a unique log number by eBRAP.

All pre-application components must be submitted by the indicated deadline by the PI through eBRAP (<https://eBRAP.org/>). Material submitted after the deadline, unless specifically requested by the Government, will not be forwarded for processing.

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

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.
- **Tab 2 – Application Contacts**
 - Enter contact information for the PI. Enter the organization's Resource Manager/Comptroller or equivalent Business Official and Authorized Business Official or equivalent responsible for sponsored program administration. The Business

Official must either be selected from the eBRAP list or invited in order for the pre-application to be submitted.

- Select the performing organization (site at which the PI will perform the proposed work) and the contracting organization (organization submitting on behalf of the PI), and click on “*Add Organizations to this Pre-application.*” The organization(s) must either be selected from the eBRAP drop-down list or invited in order for the pre-application to be submitted.

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

- Enter the name, organization, and role of all collaborators and key personnel associated with the application.
- It is recommended that PIs identify an Alternate Submitter in the event that assistance with pre-application submission is needed.
- FY18 JPC-6/CCCRP Precision Trauma Care Research Award Programmatic Panel members should not be involved in any pre-application or application including, but not limited to, concept design, application development, budget preparation, and the development of any supporting documentation. A list of the FY18 JPC-6/CCCRP Precision Trauma Care Research Award Programmatic Panel members can be found at http://cdmrp.army.mil/dmrdp/panels/18jpc_6. For questions related to Panel members and pre-applications or applications, refer to [Section IV.C., Withdrawal](#), or contact the CDMRP Help Desk at help@eBRAP.org or 301-682-5507.
- To preserve the integrity of its peer and programmatic review processes, the CDMRP discourages inclusion of any employee of its review contractors having any role in application preparation, research, or other duties for submitted applications. 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 Government.

- **Tab 4 – Conflicts of Interest**

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

- **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, etc.) used to describe the project. Inclusion of URLs

that provide additional information to expand the Preproposal Narrative and could confer an unfair competitive advantage is prohibited and may result in administrative withdrawal of the pre-application.

The Preproposal Narrative should include the following:

- **Research 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. Organize the research plan according to the Phase 1 Base, Phase 2 Option.I, and Phase 3 Option.II periods, as applicable. Each Phase should be a distinct research effort with a non-overlapping period of performance and research outcomes/milestones.
- **Personnel:** Briefly state the qualifications of the PI and key personnel to perform the described research project.
- **Impact and Military Benefit:** State explicitly how the proposed work will impact the development of precision medicine approaches for trauma care. Describe how the proposed work will directly or indirectly benefit military Service members and other beneficiaries.
- **Alignment with Focus Areas:** Identify and explain how the proposed work aligns with the intent of the PTCRA and addresses at least one of the [FY18 JPC-6/CCCRP PTCRA Focus Areas](#).

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:

- 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, 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 used in the Preproposal Narrative.
 - Key Personnel Biographical Sketches (six-page limit per individual). *All biographical sketches should be uploaded as a single combined file.* Biographical sketches should be used to demonstrate background and expertise through education, positions, publications, and previous work accomplished.
 - Quad Chart: Complete the Quad Chart template, a one-page PowerPoint file that must be downloaded from the CDMRP eBRAP System at <https://ebrap.org/eBRAP/public/Program.htm>, and save, 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.

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 JPC-6/CCCRP, pre-applications will be screened based on the following criteria:

- **Research Plan:** How well the rationale, hypotheses, objectives, specific aims, experimental design, and proposed research Phase(s) support the research idea.
- **Personnel:** To what extent the qualifications and expertise of the PI and key personnel are appropriate to perform the proposed research project.
- **Impact and Military Benefit:** If successful, to what extent the study could impact the development of precision medicine approaches and improve trauma patient care. How well the proposed study will directly or indirectly benefit military Service members and other beneficiaries.
- **Alignment with Focus Areas:** How well the projects address at least one of the [FY18 JPC-6/CCCRP PTCRA Focus Areas](#).

- **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 on the [title page](#) of this Program Announcement/Funding Opportunity. Invitations to submit a full application are based on the Pre-Application Screening Criteria as published above.

B. Full Application Submission Content

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

The pre-application process in eBRAP must be completed before the application can be submitted. After pre-application submission, go to “My Applications” and click on “Start Full Application” for the log number under which the pre-application was submitted.

The application process should be started early to avoid missing deadlines. There are no grace periods.

All application components must be submitted by the indicated deadline by the PI through eBRAP (<https://eBRAP.org/>). Material submitted after the deadline, unless specifically requested by the Government, will not be forwarded for processing. ***The organization’s Business Official or Authorized Organization Representative (or Resource Manager/Comptroller) must approve/verify the full application submission prior to the verification/approval deadline.***

eBRAP application package components: For the FY18 JPC-6/CCCRP Precision Trauma Care Research Award, 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.

- **Tab 1 – Summary:** Provides a summary of the application information.
- **Tab 2 – Application Contacts:** This tab will be populated by eBRAP. Add Authorized Organization Representative.
- **Tab 3 – Full Application Files:** Under each Application Component in eBRAP, upload each as an individual PDF file. Refer to [Appendix 1](#), for detailed formatting guidelines.

1. Application Component: Attachments: Each attachment must be uploaded as an individual PDF file unless otherwise stated.

- **Attachment 1: Project Narrative (15-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, etc.) 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.

- **Background:** Describe in detail the rationale for the study and include a literature review, preliminary studies, and/or preclinical data that led to the development of the proposed project. The background section should clearly support the choice of study variables and should explain the basis for the study questions and/or study hypotheses. Establish the relevance and applicability of the proposed study and findings to the intent of the mechanism and at least one of the [FY18 JPC-6/CCCRP PTCRA Focus Areas](#).
- **Objectives/Specific Aims/Hypothesis:** Provide a description of the purpose and objectives of the study with detailed specific aims and hypotheses. Clearly communicate the objectives/specific aims of the Phase 1 Base and each Option, and their performance periods, as applicable. Each Phase should reflect a distinct research effort with a non-overlapping period of performance and research outcomes/milestones.
- **Research Design and Methods:** Describe the experimental design, methods, and analyses including appropriate controls in sufficient detail for analysis. Applications that include research on animal models are also required to submit [Attachment 8, Animal Research Plan](#).

For clinical trials and research involving human subjects:

- 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 laboratory analyses to be conducted and how they relate to the objectives of the study and the anticipated research outcomes.
- Describe the methods that will be used to recruit a sample of human subjects from the accessible population (e.g., convenience, simple random, stratified random).
- Describe the human subject-to-group assignment process (e.g., randomization, block randomization, stratified randomization, age-matched controls, alternating group, or other procedures), if applicable. Explain the specific actions to accomplish the group assignment (e.g., computer assignment, use of table of random numbers).
- Specify the approximate number of human subjects that will be enrolled. If multiple study sites are involved, state the approximate number to be enrolled at each site. Include a complete power analysis to demonstrate that the sample size is appropriate to meet the objectives of the study. If a subpopulation of a recruited sample population will be used for analysis, complete a statistical analysis to ensure appropriate power can be achieved within the subpopulation study.

For clinical trials:

As appropriate, identify and describe the intervention to be tested and describe the projected outcomes.

- Summarize key preclinical 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, as applicable.
- Describe the interaction with the human subject to include 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., flow chart or diagram) of study evaluations and follow-up procedures.
- Discuss how compliance with Good Laboratory Practices, Good Manufacturing Practices, and other regulatory considerations will be established, monitored, and maintained, as applicable. Demonstrate that the research team has access to the proposed intervention, from its source for the proposed indication, for the duration of the proposed study.

- **Technical Risks:** Identify and describe potential problem areas in the proposed approach and alternative methods and approaches that will be employed to mitigate any risks that are identified.
- **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 applicable, describe the plan to make data available to the TBI research community through the FITBIR Informatics System. If an alternative data sharing vehicle will be employed, provide a justification for its use.
 - Refer to [Appendix 2, Administrative Information, Section E](#), for more information about the CDMRP expectations for making data and research resources publicly available.
- **Attachment 2: Supporting Documentation.** Start each document on a new page. Combine and upload as a single file named “Support.pdf.” If documents are scanned to pdf, the lowest resolution (100 to 150 dpi) should be used. *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. Indicate whether or not Government-furnished facilities or equipment are proposed for use. If so, reference should be made to the original or present Government award under which the facilities or equipment items are now accountable. There is no form for this information.
 - **Publications and/or Patents:** Include a list of relevant publication URLs and/or patent abstracts. If publications are not publicly available, then copies of up to five published manuscripts may be included in Attachment 2. Extra items will not be reviewed.
 - **Letters of Organizational Support:** Provide a letter (or letters, if applicable), signed by the Department Chair or appropriate organization official, confirming the laboratory space, equipment, and other resources available for the project. Letters of support not requested in the Program

Announcement/Funding Opportunity, such as those from members of Congress, do not impact application review or funding decisions.

- **Letters of Collaboration (if applicable):** Provide a signed letter from each collaborating individual or organization that will demonstrate that the PI has the support or resources necessary for the proposed work, to include:
 - Availability of and access to research resources (to include proprietary material for the purpose/duration of the proposed research), and/or
 - Availability of and access to appropriate populations (and/or access to available samples/data or databases), if applicable
 - For applications that include an intramural (DoD) collaborator, include a letter from the collaborator's Commander or Commanding Officer at the intramural organization that authorizes the collaborator's involvement in the proposed research.
- **Letter(s) of Support for Use of Military and VA Populations or Resources (if applicable):** If the proposed research plan involves access to active duty military and/or VA patient populations or resources, include a 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.
- **Joint Sponsorship (if applicable):** Describe present or prospective joint sponsorship of any portion of the program outlined in the application. In the absence of agreements among sponsors for joint support, the application should be structured so that the research can be carried out without the resources of any other sponsor. If, however, it is desirable to request partial support from another agency, the proposed plan should be stated and the reasons documented. If the plan cannot be formulated at the time the application is submitted, information should be sent later as an addendum to the application. Prior approval from both agencies must be secured for research to be undertaken under joint sponsorship. Provide letters of support related to recruitment, subject access, and data access plans.
- **Intellectual Property:** Refer to [Appendix 2](#), for additional information. Provide the following.
 - Intangible property acquired, created or developed under this award will be subject to all rights and responsibilities established at 2 CFR 200.315. Should the applicant intend to use, in the performance of this program, pre-existing, legally protected and perfected intangible property and for which no Federal funds had been used in the development of said property, the applicant must:

- Clearly identify all such property;
 - Identify the cost to the Federal Government for use or license of such property, if applicable; or
 - Provide a statement that no property meeting this definition will be used on this project.
- Intellectual and Material Property Plan (if applicable): Provide a plan for resolving intellectual and material property issues among participating organizations.
 - **Current Quad Chart:** Provide a current Quad Chart in the same format as in the pre-application. If no changes have been made to the project, the same Quad Chart submitted with the pre-application may be used.
- **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 is used by all reviewers and should be clear and concise and written using the outline below.

- **Background:** Present the ideas and reasoning behind the proposed work..
 - **Objective/Hypothesis:** State the objective/hypothesis to be tested. Provide evidence or rationale that supports the objective/hypothesis.
 - **Specific Aims:** State the specific aims of the study. Denote which aims will be accomplished during each performance phase of the project.
 - **Study Design:** Briefly describe the study design including appropriate controls. For studies enrolling human subjects, describe the population and enrollment targets. For animal studies, include a description of the animal model.
 - **Impact:** Identify the FY18 JPC-6/CCCRP PTCRA Focus Area(s) to be addressed and briefly describe how the proposed research will impact the field of precision medicine research for trauma care.
- **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.

The lay abstract should not duplicate the technical abstract. The lay abstract should be written using the outline below:

- Describe the objectives and rationale for the research in a manner that will be readily understood by readers without a science or medical background.
 - Identify the FY18 JPC-6/CCCRP PTCRA Focus Area(s) to be addressed.
 - Describe the types of patients that will be helped by the research and how it will help them. Include currently available statistics to the related injury/condition, if applicable.
 - Describe the potential clinical applications, benefits, and risks.
 - Describe the projected timeline to achieve the expected patient-related outcome.
 - Describe how the proposed project will benefit Service members, Veterans, and/or their family members.
- **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>). For the FY18 JPC-6/CCCRP PTCRA mechanism, use the SOW format example titled “SOW (Statement of Work) Generic Format.” The SOW should clearly delineate the tasks that will be performed during each performance phase. The SOW must be in PDF format prior to attaching.
 - **Attachment 6: Impact and Military Benefit (two-page limit): Upload as “Impact.pdf.”** Explain the proposed research project’s potential impact and military benefit as follows:
 - **Short-Term Impact:** Describe the anticipated short-term outcome(s) that will be directly attributed to the results of the proposed research. Describe how the proposed work will impact the development of precision medicine for trauma care.
 - **Long-Term Impact:** Describe the anticipated long-term vision for implementation of the proposed materiel or knowledge product in trauma care. Describe how the research will contribute to the development or validation of evidence-based policy or guidelines for patient evaluation and care. Compare the proposed materiel or knowledge product to currently available pharmacologic agents, devices, or clinical guidance, if applicable.
 - **Military Benefit:** Clearly articulate how the proposed research can optimize survival and recovery from combat-related or trauma-induced injury.
 - **Public Purpose:** Concisely describe how this research can benefit the general public.
 - **Challenges:** Describe potential issues that might limit the impact of the proposed research.

- **Attachment 7: Transition Plan (one-page limit): Upload as “Transition.pdf.”** Provide information on the methods and strategies proposed to move the anticipated research outcomes to the next phase of research or delivery to the military or civilian market/clinical practice after successful completion of the award. The transition plan should include the components listed below.
 - Details of the funding strategy that will be used to bring the outcomes to the next level (e.g., specific potential industry partners, specific funding opportunities to be pursued).
 - A description of collaborations and other resources that will be used to provide continuity of development.
 - A brief schedule and milestones for bringing the outcome(s) to the next level of research and development. Include identification of the FDA regulatory strategy (if appropriate).
 - The involvement of appropriate intellectual property, licensing, and/or business professionals.
 - A risk analysis for cost, schedule, manufacturability, and sustainability, if applicable.
- **Attachment 8: Animal Research Plan (if applicable; required for all studies utilizing animals; three-page limit per animal study): Upload as “AnimRschPln.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 it will be assured that the documentation will support a regulatory filing with the FDA, if applicable.
- **Attachment 9: IND/IDE Documentation (if applicable): Upload as “IND-IDE.pdf.”** If submitting multiple documents, start each document on a new page. Combine and upload as a single file named “IND-IDE.pdf.”
 - **Complete the IND/IDE Documentation Form**, which is available for download on the Full Announcement page for this Program Announcement/ Funding Opportunity on Grants.gov, and provide one of the following:
 - Evidence that an IND or IDE application has been submitted and includes an explanation of the current status (e.g., past the critical 30-day review period, pending response to questions raised by the Agency, on clinical hold). Inclusion of copies of any Agency meeting minutes or other relevant correspondence (e.g., submission documents, email) is encouraged but not required to support this explanation.
 - Evidence that an IND or IDE application will be submitted and include a description of the submission plan. If applicable, indicate time required for submission and/or approval of IND or IDE applications to the FDA, or appropriate regional regulatory authority if the study will be conducted outside of the United States.
 - If the proposed study has been previously exempted by the FDA from IND or IDE regulation (or international equivalent thereof), provide evidence in the form of formal communication (e.g., letterhead correspondence) from the FDA or regional regulatory authority to that effect.
 - The Government reserves the right to withdraw funding if the IND/IDE application has not been submitted **within 60 days of the DoD award date** or if the documented application status of the IND/IDE has not been obtained within **12 months of the award date**.
- **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 (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, refer to the regulatory requirements in [Appendix 3](#) for additional 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, healthcare provider identification).
- Describe the recruitment process in detail. Address who will identify potential human subjects, who will recruit them, and what methods will be used to recruit them.
 - Include a detailed description of and justification for the compensation plan if the human subjects will be compensated for participation in the study.
 - Describe the recruitment and advertisement materials. The recruitment materials should not be coercive or offer undue inducements and should accurately reflect the study.
- d. Description of the Informed Consent Process:** Specifically describe the plan for obtaining informed consent from human subjects.
- ***For the proposed study, provide a draft, in English, of the Informed Consent Form.***
 - Identify who is responsible for explaining the study, answering questions, and obtaining informed consent. Include a plan for ensuring that human subjects’ questions will be addressed during the consent process and throughout the 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 brain injury, stress/life situations, or

human subject age or administration of any mind-altering substances such as tranquilizers, conscious sedation or anesthesia), 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 trial to be in compliance with Title 10 United States Code Section 980 (10 USC 980) (<http://www.gpo.gov/fdsys/pkg/USCODE-2011-title10/pdf/USCODE-2011-title10-subtitleA-partII-chap49-sec980.pdf>). If applicable, refer to the Regulatory Requirements, [Appendix 3](#), for more information.
 - **Assent for minors or other populations that cannot provide informed consent:** If these populations are included in the proposed clinical trial, describe a plan to obtain assent (agreement) from those with capacity to provide it, or a justification for a waiver of assent, should be provided. PIs should consult with their local IRB to identify the conditions necessary for obtaining assent.
- e. **Screening Procedures:** List and describe any evaluations (e.g., laboratory procedures, history, or physical examination) that are required to determine eligibility/suitability for study participation and the diagnostic criteria for entry. Note that some screening procedures may require a separate consent or a two-stage consent process. Informed consent must be obtained prior to initiation of any procedures for the purpose of determining eligibility.
- f. **Risks/Benefits Assessment:**
- **Foreseeable risks:** Clearly identify all study risks. Study risks include any risks that the human subject is subjected to as a result of participation in the proposed research. Consider psychological, legal, social, and economic risks as well as physical risks. If the risks are unknown, this should be stated. If applicable, any potential risk to the study personnel should be identified.
 - **Risk management and emergency response:**
 - Describe all safety measures to minimize and/or eliminate risks to human subjects and study personnel or to manage unpreventable risks. Include safeguards and planned responses such as dose

reduction or stopping criteria based on toxicity grading scales or other predetermined alert values.

- Discuss the overall plan for provision of emergency care or treatment for an adverse event for study-related injuries, to include who will be responsible for the cost of such care.
 - Address any special precautions to be taken by the human subjects before, during, and after the study (e.g., medication washout periods, dietary restrictions, hydration, fasting, pregnancy prevention).
 - Describe any special care (e.g., wound dressing assistance, transportation due to side effects of study intervention impairing ability to drive) or equipment (e.g., thermometers, telemedicine equipment) needed for human subjects enrolled in the study.
 - **Potential benefits:** Describe known and potential benefits of the study to the human subject, a specific community, or society.
- **Attachment 11: Data Management (required for all studies recruiting 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, to include 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 to include considerations for informed consent and providing human subjects with an opportunity to decline participation in the study.
- **Labs performing evaluations and special precautions:** Identify the laboratory performing each evaluation, as well as any special precautions that should be taken in handling the samples. Special precautions that should be taken by the human subject before, during, or after the laboratory procedure should be clearly defined. If transport of samples is required, describe provisions for ensuring proper storage during transport.

2. Application Component: 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 (six-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.

Biographical Sketches should be used to demonstrate background and expertise through education, positions, publications, and previous work accomplished.

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

For all previous (award period of performance ending within the past 5 years), current, and pending research support, include the title, time commitments, supporting agency, name and address of the funding agency’s procuring Contracting/Grants Officer, period of performance, level of funding, brief description of the project’s goals, and list of the specific aims. If applicable, identify where the proposed project overlaps with other existing and pending research projects. Clearly state if there is no overlap.

- **Key Personnel Biographical Sketches** (six-page limit each): Upload as “Biosketch_LastName.pdf.”
- **Key Personnel Previous/Current/Pending Support** (no page limit): Upload as “Support_LastName.pdf.”

3. Application Component: Budget: Use the DoD Military Budget Form available on the “Funding Opportunity and Forms” page in eBRAP (<https://ebrap.org/eBRAP/public/Program.htm>). Refer to [Appendix 4](#) 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_LastName.pdf.” The budget justification must include a Federal Agency Financial Plan as described in [Appendix 4](#).
- Subaward Budget: Include all Subaward budgets. Complete a separate detailed Budget using the DoD Military Budget Form including a budget justification for each subaward (subgrant or subcontract) 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 Opportunity and Forms” page in eBRAP (<https://ebrap.org/eBRAP/public/Program.htm>). Upload as “Performancesites.pdf.”

- On the Project/Performance Site Location(s) Form, 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 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 Program Announcement/Funding Opportunity 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 Resource Manager/Comptroller or equivalent Business Official by email to log into eBRAP to review and to approve prior to the Approval deadline.**

C. Submission Dates and Times

All submission dates and times are indicated on the [title page](#) of this Program Announcement/Funding Opportunity. Pre-application and application submissions are required. Failure to meet either of these deadlines will result in submission rejection.

III. APPLICATION REVIEW INFORMATION

A. Application Review and Selection Process

All applications are evaluated by scientists, clinicians, and consumers in a two-tier review process. The first tier is peer review of applications against established criteria for determining technical merit. Each application is evaluated for its own merit, independent of other applications. The second tier is a programmatic review that makes recommendations for funding to the DHA and the Commanding General, USAMRMC, based on technical merit, the relevance to the mission of the DHP and JPC-6/CCCRP, the specific intent of the award mechanism, and to other specified evaluation criteria in the Program Announcement/Funding Opportunity. 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 III.B.2., Programmatic Review](#).*** Additional information about the two-tier process used by the CDMRP can be found at <http://cdmrp.army.mil/about/fundingprocess.shtml>.

All CDMRP review processes are conducted confidentially to maintain the integrity of the merit-based selection process. Panel members sign a statement that application and evaluation information will not be disclosed outside the panel. Violations of confidentiality can result in the dissolving of a panel(s) and other corrective actions. In addition, personnel at the applicant or collaborating organizations are prohibited from contacting persons involved in the review 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 Title 18 United States Code 1905.

Extramural and Intramural applications will be reviewed by the same panels and evaluated with the same criteria.

B. Application Review Process

1. 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**
 - How well the preliminary data and scientific rationale supports the research project.
 - How relevant and applicable the proposed research and findings are to at least one of the FY18 JPC-6/CCCRP PTCRA Focus Areas.
 - How well the hypotheses or objectives, aims, experimental design, methods, and analyses are developed and integrated into the project.
 - How consistent the methods and procedures are with a sound research design.
 - How well the study is designed to achieve the research objectives, including the choice of model (if applicable) and endpoints/outcome measures to be used, and generate reproducible and rigorous results.
 - How well the PI acknowledges potential problems and addresses alternative approaches.
 - Whether the research can be completed within the proposed period of performance (including Base and Option Phases, as applicable).
 - How well the PI has outlined a plan for management and sharing of research data as appropriate for the type of study.
 - If applicable, whether data will be appropriately reported and documented to support a regulatory filing with the FDA.
 - For clinical trials and research involving human subjects:
 - How well the PI describes the population(s) of interest, demonstrates access to these populations, and has a viable plan for recruitment, consent, screening, and retention of appropriate subjects.
 - If applicable, whether there is evidence demonstrating availability of the device/intervention from its source for the duration of the proposed study.
 - Whether a member of the study team holds the IND/IDE and whether the timeline proposed for IND/IDE application is appropriate (if applicable).

- **Ethical Considerations (if applicable)**
 - How the level of risk to human subjects is minimized, and how the safety monitoring and reporting plan is appropriate for the level of risk.
 - How well the evidence shows that the procedures are consistent with sound research design and, when appropriate, that these procedures are already in use for diagnostic or treatment purposes.
 - To what degree privacy issues are appropriately considered.
 - To what degree the process for seeking informed consent is appropriate and whether safeguards are in place for vulnerable populations.
- **Statistical Plan**
 - To what degree the statistical plan, including sample size projections and power analysis, and data analysis plan are adequate for the study and all proposed correlative studies.
 - If applicable, whether the statistical plan compensates for the use of a subpopulation of a recruited sample population to ensure appropriate power can be achieved within the subpopulation study.
- **Impact**
 - To what extent the anticipated research outcomes or long-term vision of the proposed research may impact the development of precision medicine approaches for trauma care.
 - To what extent the proposed research has the potential to optimize survival and recovery from combat-related or trauma-induced injury.
 - To what extent the proposed research can benefit the general public.
 - If applicable, to what degree the proposed materiel or knowledge product represents an improvement to currently available pharmacologic agents, devices, or clinical guidance.
- **Transition Plan**
 - Whether the funding strategy described to bring the anticipated research outcome(s) to the next level of development and/or delivery to the military or civilian market is appropriate.
 - Whether appropriate collaborations and other resources for providing continuity of development are established and/or well described.
 - How the schedule and milestones for bringing the outcome(s) to the next level of development are appropriate.
 - If applicable, how well the potential risk analysis for cost, schedule, manufacturability, and sustainability is developed.
 - How well the application identifies intellectual property ownership, describes any appropriate intellectual and material property plan among participating organizations (if applicable), and addresses any impact of intellectual property

issues on product development and subsequent Government access to products supported by this Program Announcement/Funding Opportunity.

- **Personnel**

- Whether the composition of the research or study team (e.g., study coordinator, statistician) is appropriate.
- How the levels of effort by the PI and other key personnel are appropriate to ensure success of this project.
- Whether the levels of effort by the PI and other key personnel are appropriate to ensure success of this project.
- Whether the investigator(s) record(s) of accomplishment demonstrates his/her ability to accomplish the proposed work.

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

- **Budget**

- Whether the budget is appropriate for the proposed research.
- Whether the total maximum costs are equal to or less than the allowable total maximum costs as published in the Program Announcement/Funding Opportunity.

- **Application Presentation**

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

- **Environment**

- To what degree the scientific environment and the accessibility of institutional/organizational resources support the proposed research requirements (including collaborative arrangements).
- How the quality and extent of institutional/organizational support are appropriate for the proposed project.

2. 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:

- a. Ratings and evaluations of the peer reviewers**

- b. Relevance to the mission of the DHP and JPC-6/CCCRP, as evidenced by the following:**

- Adherence to the intent of the award mechanism
- Programmatic relevance
- Program portfolio composition
- Relative impact and military benefit

C. Application Review Dates

All application review dates and times are indicated on the [title page](#) of this Program Announcement/Funding Opportunity.

D. Notification of Application Review Results

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

IV. ADMINISTRATIVE ACTIONS

After receipt of pre-applications and applications from CDMRP eBRAP, the following administrative actions may occur:

A. Rejection

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

- Pre-Application Narrative exceeds page limit.
- Pre-Application Narrative is missing.
- The Pre-Application was submitted by an extramural investigator.

The following will result in administrative rejection of the application:

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

For applications including animal studies:

- Attachment 8, Animal Research Plan, is missing.

For applications recruiting human subjects:

- Attachment 10, Human Subject Recruitment and Safety Procedures, is missing.
- Attachment 11, Data Management, is missing.

For clinical trial applications:

- Attachment 9, IND/IDE Documentation, is missing.

B. Modification

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

C. Withdrawal

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

- An FY18 JPC-6/CCCRP PTCRA Programmatic Panel member is named as being involved in the research proposed or is found to have assisted in the pre-application or application processes including, but not limited to, concept design, application development, budget preparation, and the development of any supporting documentation. *A list of the FY18 JPC-6/CCCRP PTCRA Programmatic Panel members can be found at http://cdmrp.army.mil/dmr dp/panels/18jpc_6.*
- The application fails to conform to this Program Announcement/Funding Opportunity 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).
- 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. 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 Government. Refer to Appendix 2 for additional 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.
- Proposed research includes a Phase II or Phase III clinical trial.

D. Withhold

Applications that appear to involve research misconduct will be administratively withheld from further consideration pending institutional investigation. The institution will be required to provide the findings of the investigation to CDMRP for a determination of the final disposition of the application.

V. AWARD ADMINISTRATION INFORMATION

A. Award Notice

Awards will be made no later than September 30, 2019. Refer to [Appendix 2](#) for additional award administration information.

B. Administrative Requirements

Refer to [Appendix 2](#) for general information regarding administrative requirements.

C. Reporting and Deliverables

Refer to [Appendix 2](#), Administrative Information, for Reporting and Deliverable requirements for this award.

Quarterly technical progress reports, quad charts, and in-person presentations will be required.

D. Award Transfers

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

VI. AGENCY CONTACTS

A. CDMRP Help Desk

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

Phone: 301-682-5507

Email: help@eBRAP.org

VII. APPLICATION SUBMISSION CHECKLIST

Application Components	Upload Order	Action	Completed
Attachments	1	Project Narrative: Upload as Attachment 1 with file name "ProjectNarrative.pdf."	
	2	Supporting Documentation: Upload as Attachment 2 with file name "Support.pdf."	
	3	Technical Abstract: Upload as Attachment 3 with file name "TechAbs.pdf."	
	4	Lay Abstract: Upload as Attachment 4 with file name "LayAbs.pdf."	
	5	Statement of Work: Upload as Attachment 5 with file name "SOW.pdf."	
	6	Impact and Military Benefit: Upload as Attachment 6 with file name "Impact.pdf."	
	7	Transition Plan: Upload as Attachment 7 with file name "Transition.pdf."	
	8	Animal Research Plan: Upload as Attachment 8 with file name "AnimRschPln.pdf."	
	9	IND/IDE Documentation: Upload as Attachment 9 with file name "IND_IDE.pdf" (required for clinical trials).	
	10	Human Subject Recruitment and Safety Procedures: Upload as Attachment 10 with file name "HumSubProc.pdf" (required for all studies recruiting human subjects).	
	11	Data Management: Upload as Attachment 11 with file name "Data_Manage.pdf" (required for all studies recruiting human subjects).	
Key Personnel		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.	
Budget		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		Upload Project/Performance Site Location(s) Form as "Performancesites.pdf."	

APPENDIX 1 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 Program Announcement/Funding Opportunity (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 2 ADMINISTRATIVE INFORMATION

A. Disclosure of Proprietary Information

Do not include proprietary information in a pre-application or abstract. Proprietary information should only be included in a full application if necessary for evaluation.

Proprietary information submitted in an application may be disclosed outside the Government for the sole purpose of technical evaluation. Evaluators must agree that proprietary information in the application will be used for evaluation purposes only and will not be further disclosed or used.

All applications may be subject to public release under the Freedom of Information Act (FOIA) to the extent that they are incorporated into an award document; applications that are not selected for funding will not be subject to public release.

B. Marketing of Proprietary Information

Conspicuously and legibly mark any proprietary information that is included in the application.

C. Conflict of Interest

All awards must be free of COIs, as defined at 32 CFR 32.42, that could bias the research results. Prior to award, applicants are required to disclose all potential or actual COIs along with a plan to manage them. An award may not be made if it is determined that a COI cannot be adequately managed.

D. Reporting Requirements

Reporting requirements and deliverables will be determined prior to award 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 award period and will detail the findings, their potential impact to the Military or Veteran 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>.

E. 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 Defense Health Program and Congress on the accomplishments of the program.

- **Acknowledgment:** The recipient agrees that in the release of information relating to this award 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 Defense Health Agency, Research, Development, and Acquisition Directorate through the Clinical Research Intramural Initiative Program. 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 (https://mrmc.detrick.army.mil/index.cfm?pageid=Research_Protections.acuro&rn=1).
 - “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>)

F. 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**⁴ 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**⁵ are defined as recorded factual material commonly accepted in the scientific community as necessary to document and support research findings.

⁴ Adapted from https://grants.nih.gov/grants/policy/data_sharing/data_sharing_guidance.htm#unique

⁵ Adapted from https://grants.nih.gov/grants/policy/data_sharing/data_sharing_guidance.htm#final

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**⁶ 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.
- ***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>).
 - **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 Clinical Trials.gov (<https://www.clinicaltrials.gov/>).
 - **Systems Biology:** If the project includes systems biology (SB)-related research, the PI may be required to make SB 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 Reference Material at <https://ebrap.org/eBRAP/public/Program.htm>.***

⁶ Adapted from <http://www.gpo.gov/fdsys/pkg/FR-1999-12-23/pdf/99-33292.pdf>

APPENDIX 3 REGULATORY REQUIREMENTS

A. Surety, Safety, and Environmental Requirements

Based on recent changes to Department of Defense (DoD) compliance requirements (DA PAM 385-69, **DA PAM 385-10**, 32 CFR 651.6 September 2012), provisions previously requested for Safety and Environmental Compliance have been removed. However, in certain instances, compliance review may require submission of additional documentation prior to the awarding of any assistance agreement. Such instances may include use of Army-provided infectious agents or toxins, select biological agents or toxins, select chemical agent(s), or pesticides outside of an established laboratory. The US Army Medical Research and Materiel Command (USAMRMC) Office of Surety, Safety, and Environment will identify any need for compliance review and documents must be submitted upon request.

B. 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 research involving human subjects, human anatomical substances or data, and use of human cadavers. ***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 3 to 4 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 (Available as PDF at 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 subject protection regulations. Questions regarding applicable human subject 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.hrpo. 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.usarmc.other.hrpo@mail.mil if further clarification regarding applicability of 10USC 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 monitors' 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.

APPENDIX 4 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 Program Announcement/Funding Opportunity. No budget will be approved by the Government exceeding the cost limit stated in the specific Program Announcement/Funding Opportunity. 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.

Begin by entering the PI name, eBRAP Log number, and period of performance fields 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 material 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 the required IPR meeting each year.

Travel costs may include:

- Travel costs for up to 1 investigator to travel to 1 scientific/technical meeting per year.
- 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 I.F., Funding.)
- **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 one.

- **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**, FY19 funding will be obligated by **September 30, 2020**, and FY20 funding will be obligated by **September 30, 2021**. 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 FY18-20 funding not obligated by above stated deadlines may be withdrawn by the issuing Comptroller.