Program Announcement

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

Prolonged Field Care Research Award

Funding Opportunity Number: W81XWH-16-DMRDP-CCCRP-PFCRA

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

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-Application Deadline:** 5:00 p.m. Eastern time (ET), May 12, 2016
- **Invitation to Submit an Application:** June 28, 2016
- **Application Submission Deadline:** 11:59 p.m. ET, August 18, 2016
- **End of Application Verification Period:** 5:00 p.m. ET, August 23, 2016
- **Peer Review:** October 2016
- **Programmatic Review:** November 2016

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I. FUNDING OPPORTUNITY DESCRIPTION

BEFORE APPLYING, NOTE: THIS PROGRAM ANNOUNCEMENT/FUNDING OPPORTUNITY IS INTENDED FOR EXTRAMURAL INVESTIGATORS ONLY. INTRAMURAL INVESTIGATORS ARE REQUIRED TO APPLY TO THE FY16 JPC-6/CCCRP PROLONGED FIELD CARE RESEARCH AWARD (PFCRA) INTRAMURAL ANNOUNCEMENT/FUNDING OPPORTUNITY THROUGH CDMRP eReceipt at https://cdmrp.org/Program_Announcements_and_Forms/.

- 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.

It is permissible, however, for an intramural investigator to be named as a collaborator in an application submitted by an extramural investigator. In such cases, the application from the extramural organization must include a letter from the collaborator's Commander or Commanding Officer at the intramural organization that authorizes the collaborator's involvement.

A. Program Description

Applications to the Fiscal Year 2016 (FY16) Joint Program Committee-6/Combat Casualty Care Research Program (JPC-6/CCCRP) are being solicited for the Defense Health Agency, Research, Development, and Acquisition (DHA RDA) Directorate, by the U.S. Army Medical Research Acquisition Activity (USAMRAA). As directed by the Office of the Assistant Secretary of Defense for Health Affairs [OASD (HA)], the DHA RDA Directorate manages and executes the Defense Health Program (DHP) Research, Development, Test, and Evaluation (RDT&E) appropriation. The U.S. Army Medical Research and Materiel Command (USAMRMC) Congressionally Directed Medical Research Programs (CDMRP) 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 DHP core research program areas within the DHP DHA RDA Directorate and is administered with oversight from the JPC-6. JPC-6 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 solutions 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

The intent of the PFCRA is to target the emerging need to provide extended trauma care prior to reaching a location that can provide definitive hemorrhage and contamination control. Trauma care during this period is often called "Prolonged Field Care" (PFC). Traditionally, improvements to the trauma care system have focused on shortening evacuation times from the point of injury to the first surgical site. However, in future conflicts or mass trauma events, it is anticipated that the initial evacuation time, and thus initial surgical hemorrhage and contamination control, may be delayed for hours or days.

This challenge also requires research to develop new solutions to provide for prolonged Damage Control Resuscitation (pDCR) including: support for medical providers in the out-of-hospital setting (point of injury, austere environment, or en route care) with limited resources; understanding the physiologic impact of pDCR; and techniques to mitigate the negative effects of delayed surgical intervention. The research and solutions must be focused on patient-level interventions and outcomes, rather than the broader trauma system. However, proposed research and solutions should consider the entire continuum of trauma care.

The JPC-6/CCCRP has identified three overarching Focus Areas for funding under this Program Announcement/Funding Opportunity. To meet the intent of the award mechanism, applications ***MUST*** specifically address at least one of the three PFCRA Focus Areas. Research not aligned to at least one of these Focus Areas will not be considered for funding. The FY16 JPC-6/ CCCRP PFCRA Focus Areas are:

Focus Area 1: Understand the clinical implications of PFC and pDCR, including:

- Improving the understanding of physiological parameters requiring monitoring and intervention in order to reduce morbidity and mortality during the acute treatment phase (up to 72 hours) of a traumatic brain injury (TBI).
- Characterization and mitigation of the pathophysiology of prolonged hypotension or hypotensive resuscitation (up to 72 hours).
- Characterization of the consequences of prolonged (over 2-4 hours) use of current prehospital hemostatic devices and methods, and/or identifying the limits of use and areas where alternative methods will be required.
- Identify and characterize prolonged field care challenges to providing organ support and critical care interventions.
- Evaluation of the physiologic impact of transportation following PFC and the effect on clinically relevant outcomes.

Focus Area 2: Develop next-generation resuscitation and stabilization methods for PFC and pDCR, including:

- Novel or improved methods for resuscitation and stabilization of casualties with combined hemorrhagic shock and acute TBI, with or without other concomitant injuries.
- Point-of-injury/point-of-need/prehospital capabilities to monitor and/or stabilize acute TBI casualties. The goal is to enable earlier detection of life-threatening conditions, improve decision-making timelines, and/or mitigate progression of brain injury in pDCR and/or remote operating environment scenarios.
- Approaches to metabolic and tissue stabilization to enable prolonged out of hospital (prehospital and en route) survivability, and provide organ support and critical care in the prolonged field care environment.
- Novel approaches for improving oxygen delivery to tissues (not via ventilator) under conditions of prolonged hypotension and polytrauma.

Focus Area 3: Develop enhanced treatment of injuries during PFC and pDCR, including:

- TBI treatments (including cellular therapies, drugs, or devices) to decrease morbidity and mortality and improve immediate and long-term outcomes.
- Forward surgical techniques, knowledge products, and augmentative technology for surgical stabilization of life- and limb-threatening injuries. The goal is to decrease morbidity and mortality in the out-of-hospital (prehospital and en route) environment scenarios, to include intravascular techniques (such as resuscitative endovascular balloon occlusion of the aorta [REBOA]) and other advanced hemostatic approaches.
- Critical care knowledge, interventions, and simplified portable organ support technology to reduce, reverse, or treat organ failure and perfusion/reperfusion injury due to treatment effects of pDCR and/or remote operating environment scenarios.
- Knowledge and techniques to acutely stabilize and treat tissue injury, to include, but not limited to, burn injury, facial injury, chest wall crush/fractures, pelvic fractures, bony spine injury, extremity fractures, and large soft tissue defects. The goal is to prevent infection, minimize further tissue loss, protect underlying tissues/organs, reduce ischemia and secondary injury, reduce pain and suffering, and provide safe transport in support of pDCR and/or remote operating environment scenarios.

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, and 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 & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm). ***Phase II and Phase III clinical trials for 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 U.S. Food and Drug Administration (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 6, 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.

Reporting Guidelines: All projects should adhere to a core set of standards for rigorous study design and reporting to maximize the reproducibility and translational potential of preclinical research. The standards are described in Landis, S.C., et al. A call for transparent reporting to optimize the predictive value of preclinical research, *Nature* 2012, 490:187-191 (http://www.nature.com/nature/journal/v490/n7419/full/nature11556.html). While these standards are written for preclinical/animal studies, the basic principles of randomization, blinding, sample-size estimation, and data handling derive from well-established best practices in clinical studies and should be applied to those projects as well.

Research Involving Animals: All DoD-funded research involving new and ongoing research with animals must be reviewed and approved by the USAMRMC ORP Animal Care and Use Review Office (ACURO), in addition to the local Institutional Animal Care and Use Committee (IACUC) of record. IACUC approval at the time of submission is not required. Specific documents relating to the use of animals in the proposed research will be requested **if the application is selected for funding**. The ACURO must review and approve all animal use prior to the start of working with animals, including amendments to ongoing projects. PIs must submit the institutional animal use protocol, IACUC approval of that protocol, and a version of the animal use appendix titled "Research Involving Animals." ***Allow at least 2 to 3 months for ACURO regulatory review and approval processes for animal studies.*** Refer to General Application Instructions, Appendix 6, for additional information.

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 military relevance:

- 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

The following websites may be useful in identifying information about ongoing DoD and Department of Veterans Affairs (VA) areas of research interest:

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

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

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

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

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

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

Defense Advanced Research Projects Agency
http://www.darpa.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/nmcphc

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/

U.S. Army Medical Research Acquisition Activity
https://www.usamraa.army.mil/

U.S. Army Medical Research and Materiel Command
https://mrmc.amedd.army.mil

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

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

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

U.S. 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: If the proposed research involves access to military and/or VA population(s) and/or resource(s), the PI is responsible for establishing access. If possible, 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 doing 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 proposal

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/jsp/define/index.jsp). 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 intend 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 the General Application Instructions, Appendix 4, Section K.

C. Eligibility Information

- ***This Program Announcement/Funding Opportunity is intended for extramural investigators only.*** Intramural investigators are required to apply to the FY16 JPC-6/ CCCRP Prolonged Field Care Research Award (PFCRA) Intramural Announcement/ Funding Opportunity through CDMRP eReceipt at https://cdmrp.org/Program_Announcements_and_Forms/.
- Independent investigators at all academic levels (or equivalent) are eligible to submit applications.
- Cost sharing/matching is not an eligibility requirement.
- Eligible investigators must apply through an organization. Organizations eligible to apply include Federal agencies, national, international, for-profit, nonprofit, public, and private organizations.
- Refer to the General Application Instructions, Appendix 1, for general eligibility information.

D. Funding

It is the responsibility of the PI to select the funding level that is most appropriate for the proposed research project. The requested budget level should be appropriate for the scope of research proposed.

Funding Level 1:

- The maximum period of performance is **3** years.
- The anticipated total costs (direct and indirect) budgeted for the entire period of performance will not exceed **$1.5 million (M).** Indirect costs are to be budgeted in accordance with the organization's negotiated rate. No budget will be approved by the Government exceeding **$1.5M** total costs or using an indirect rate exceeding the organization's negotiated rate.

Funding Level 2:

- The maximum period of performance is 3 years.
- The allowable range of total costs (direct and indirect) budgeted for the entire period of performance is between **$1.5M** and **$3.0M.** Indirect costs are to be budgeted in accordance with the organization's negotiated rate. No budget will be approved by the Government exceeding **$3.0M** total costs or using an indirect rate exceeding the organization's negotiated rate.

For both funding levels:

- The maximum period of performance is **3** years.
- All direct and indirect costs of any subaward (subgrant or subcontract) must be included in the total direct costs of the primary award.
- The applicant may request the entire maximum funding amount for a project that may have a period of performance less than the maximum **3** years.

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 Year 2 of 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

This Program Announcement/Funding Opportunity is intended for extramural investigators only. Intramural investigators are required to apply to the FY16 JPC-6/CCCRP Prolonged Field Care Research Award (PFCRA) Intramural Announcement/Funding Opportunity through CDMRP eReceipt at https://cdmrp.org/Program_Announcements_and_Forms/.

An intramural investigator is defined as a DoD military or civilian employee working within a DoD laboratory or medical treatment facility, or working in a DoD activity embedded within a civilian medical center. It is permissible for an intramural investigator to be named as a collaborator on an application submitted by an extramural investigator under this Program Announcement/Funding Opportunity. ***In such cases, the extramural investigator must include a letter from the intramural collaborator's Commander or Commanding Officer that authorizes the involvement of the intramural collaborator.***

Awards to extramural organizations will consist solely of assistance agreements (Cooperative Agreements and Grants). Subawards to intramural agencies and other Federal agencies may be executed through a direct fund transfer (e.g., the Military Interdepartmental Purchase Request [MIPR] or Funding Authorization Document [FAD] process). Direct transfer of funds from the recipient to a Federal agency is not allowed except under very limited circumstances. Refer to the General Application Instructions, Section II.C.4. Research & Related Budget, for additional information on budget considerations for applications involving Federal agencies. ***For Federal agencies or organizations collaborating with Federal agencies, budget restrictions apply as are noted in Section II.C.4. of the General Application Instructions***.

The JPC-6/CCCRP expects to allot approximately $27.6M of the FY16 and $20.2M of the FY17 DHP RDT&E appropriations to fund approximately 15 to 31 intramural and extramural FY16 Prolonged Field Care Award applications, depending on the received applications' quality, number, and Focus Areas addressed. 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 FY17 Defense Appropriations Bill has not been passed and there is no guarantee that any additional funds will be made available to support this program. The funding estimated for this Program Announcement/Funding Opportunity is approximate and subject to realignment. Funding of applications received in response to this Program Announcement/Funding Opportunity is contingent upon the availability of Federal funds for this program.

NOTE: Applications received under this mechanism will compete with applications received under the FY16 JPC-6/CCCRP Prolonged Field Care Research Award (PFCRA) Intramural Announcement found at https://cdmrp.org/Program_Announcements_and_Forms/.

II. SUBMISSION INFORMATION

Submission is a two-step process requiring both (1) pre-application submission through the electronic Biomedical Research Application Portal (eBRAP) (https://eBRAP.org/) and (2) application submission through Grants.gov (http://www.grants.gov/). Refer to the General Application Instructions, Section II.A. for registration and submission requirements for eBRAP and Grants.gov.

The pre-application and application submission process should be started early to avoid missing deadlines. There are no grace periods. Federal applicants must be familiar with Grants.gov requirements, including the need for an active System for Award Management (SAM) registration and a Data Universal Numbering System (DUNS) number. Refer to Appendix 3 of the General Application Instructions for further information regarding Grants.gov requirements.

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. A key feature of eBRAP is the ability of an organization's representatives and PIs to view and modify the Grants.gov application submissions associated with them. eBRAP will validate Grants.gov application files against the specific Program Announcement/Funding Opportunity requirements and discrepancies will be noted in an email to the PI and in the Full Application Files tab in eBRAP. 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.

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

Application viewing, modification, and verification in eBRAP is strongly recommended, but not required. ***The Project Narrative and Budget cannot be changed after the application submission deadline.*** Prior to the full application deadline, a corrected or modified full application package may be submitted. Other application components may be changed until the end of the application verification period. After the end of the application verification period, the full application cannot be modified.

A. Where to Obtain the Grants.gov Application Package

To obtain the Grants.gov application package, including all required forms, perform a basic search using the Funding Opportunity Number W81XWH-16-DMRDP-CCCRP-PFCRA in Grants.gov (http://www.grants.gov/).

B. 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. This unique eBRAP log number will be needed during the application process on Grants.gov.**

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

PIs 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 preapplication, the PI must contact the CDMRP Help Desk at help@eBRAP.org or 301-682-5507.

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

- **Tab 1 – Application Information**
- **Tab 2 – Application Contacts**
  - Enter contact information for the PI. Enter the organization's Business Official responsible for sponsored program administration (the "person to be contacted on matters involving this application" in Block 5 of the Grants.gov SF424 (R&R) Form). 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, which corresponds to Block 5 on the Grants.gov SF424 (R&R) Form), 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.
  - It is recommended that PIs identify an Alternate Submitter in the event that assistance with pre-application submission is needed.
- **Tab 3 – Collaborators and Key Personnel**
  - Enter the name, organization, and role of all collaborators and key personnel associated with the application.
  - FY16 JPC-6/CCCRP Prolonged Field 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 FY16 JPC-6/CCCRP Prolonged Field Care Research Award Programmatic Panel members can be found at http://cdmrp.army.mil/dmrdp/panels/17jpc_6. For questions related to Programmatic Panel members and pre-applications or applications, refer to Section IV.C., Withdrawal, or contact the CDMRP Help Desk at help@eBRAP.org or
  - 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. For FY16, 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 conflicts of interest (COIs) are provided and

deemed appropriate by the Government. Refer to the General Application Instructions, Appendix 1, for detailed information.

- **Tab 4 – Conflicts of Interest (COIs)**
  - 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). Refer to Appendix 1, Section C of the General Application Instructions for further information regarding COIs.

- **Tab 5 – Pre-Application Files**

  Note: Upload document(s) 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 (three-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, specific aims, and briefly describe the experimental approach. State the developmental stage of the proposed research (e.g., preclinical human/animal or clinical trial).
  - **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 may impact trauma care during a PFC and/or pDCR scenario. 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 addresses at least one of the three FY16 PRCRA Focus Areas.

  Pre-Application Supporting Documentation: The items to be included as supporting documentation for the pre-application ***must be uploaded as individual documents*** 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 (five-page limit per individual).

- 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, and experimental design 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 research and improve patient care. How well the proposed study will directly or indirectly benefit military Service members in a PFC and/or pDCR scenario.
  - **Alignment with Focus Areas:** How well the project addresses at least one FY16 PRCRA 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.

C. Full Application Submission Content

The application process should be started early on Grants.gov to avoid missing deadlines. There are no grace periods. Verify the status of your organization's Entity registration in the SAM well in advance of the application submission deadline. Allow 3 to 4 weeks to complete the entire SAM registration process. Refer to the General Application Instructions, Section II, for additional information.

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

All contributors and administrators to the application must use matching compatible versions of Adobe software when editing and preparing application components. The use of different software versions will result in corruption of the submitted file. See Section II.C. of the General Application Instructions for details on compatible Adobe software.

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

Each application submission must include the completed Grants.gov application package provided in Grants.gov for this Program Announcement/Funding Opportunity. The Grants.gov application package is submitted by the Authorized Organizational Representative through the Grants.gov portal (http://www.grants.gov/).

Note: The Project Narrative and Budget Form cannot be changed after the application submission deadline.

If either the Project Narrative or the budget fails eBRAP validation or if the Project Narrative or Budget Form needs to be modified, an updated Grants.gov application package must be submitted via Grants.gov as a "Changed/Corrected Application" with the previous Grants.gov Tracking ID ***prior to the application submission deadline***.

Grants.gov application package components: For the FY16 JPC-6/CCCRP Prolonged Field Care Research Award, the Grants.gov application package includes the following components (refer to the General Application Instructions, Section II.C., for additional information on application submission):

1. **SF424 (R&R) Application for Federal Assistance Form:** Refer to the General Application Instructions, Section II.C., for detailed information.

2. **Attachments Form**

   Each attachment to the Grants.gov application forms must be uploaded as an individual PDF file in accordance with the formatting guidelines listed in Appendix 2 of the General Application Instructions. For all attachments, ensure that the file names are consistent with the guidance. Grants.gov will reject attachments with file names longer than 50 characters or incorrect file names that contain characters other than the following: A-Z, a-z, 0-9, underscore, hyphen, space, and period. In addition, Grants.gov has file size limits that may apply in some circumstances. Individual attachments may not exceed 20 MB and the file size for the entire Grants.gov application package may not exceed 200 MB.

   - **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 least one of the FY16 PFCRA Focus Areas.

- **Objectives/Specific Aims/Hypothesis:** Provide a description of the purpose and objectives of the study with detailed specific aims and hypotheses.
- **Research Design and Methods:** Describe the experimental design, methods, and analyses including appropriate controls in sufficient detail for analysis. Describe the statistical model and data analysis plan with respect to the study objectives as appropriate for the type of study.

  For Animal Studies:

  - 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).

  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.
  - 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., flowchart or diagram) of study evaluations and follow-up procedures.
  - Discuss how compliance with Good Laboratory Practices (GLP), Good Manufacturing Practices (GMP), 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 during the duration of the proposed study.

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 analysis 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.

o **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.

o **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 the General Application Instructions, Appendix 4, Section K 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 Patent Abstracts: 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 collaborator, include a letter from the collaborator's Commander or Commanding Officer at the intramural organization that authorizes the collaborator's involvement.
- 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.
- Intangible Property: 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; or provide a statement that no property meeting this definition will be used on this project.

- 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 publically. ***Do not include proprietary or confidential information.*** Use only characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed.

  The technical abstract should be clear and concise and, at a minimum, provide the following information:

  - 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.
  - Study Design: Briefly describe the study design including appropriate controls. For studies enrolling human subjects, describe the population and enrollment targets.
  - Impact: Identify the FY16 PFCRA Focus Area(s) to be addressed and briefly describe how the proposed research will impact those area(s) in military and civilian PFC and/or pDCR scenarios.

- **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 publically. ***Do not include proprietary or confidential information.*** Use only characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed. ***Do not duplicate the technical abstract.***

  Lay abstracts should be written using the outline below:

  - Describe the objectives and rationale for the research in a manner that will be readily understood by readers without a science or medical background.
  - Describe the ultimate applicability of the research.
  - Which FY16 PFCRA Focus Area(s) will be addressed?
  - How can the proposed research impact the Focus Area(s) addressed?
  - What are the potential clinical applications, benefits, and risks?

- What types of military and/or civilian patients will it help, and how will it help them?

- **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 FY16 JPC-6/ CCCRP Prolonged Field Care Research Award mechanism, use the SOW format example titled "SOW (Statement of Work) Generic Format." The SOW must be in PDF format prior to attaching. Refer to the General Application Instructions, Section II.C.2., for detailed guidance on creating the SOW.

- **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.
  - Long-Term Impact: Describe the anticipated long-term vision for implementation of the proposed intervention or knowledge product during a PFC and/or pDCR scenario. Describe the anticipated long-term benefits for the targeted population.
  - Military Benefit: Clearly articulate how the proposed research can optimize survival and recovery from combat-related injury in current and future operational scenarios involving PFC and/or pDCR.
  - Public Purpose: Concisely describe how this research can benefit the general public.
  - Compare the proposed materiel or knowledge product to currently available pharmacologic agents, devices, or clinical guidance, if applicable.

- **Attachment 7: Transition Plan (one-page limit). Upload as "Transition.pdf."** Provide information on the methods and strategies proposed to move the product 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.

- **Attachment 8: Human Subject Recruitment and Safety Procedures (required for all studies recruiting human subjects; no page limit): Upload as "HumSubProc.pdf."** The Human Subject Recruitment and Safety Procedures attachment should include the components listed below.

  a. Study Population: Describe the target population (to whom the study findings will be generalized) and the nature, approximate number, and pertinent demographic characteristics of the accessible population at the study site(s) (population from whom the sample will be recruited/drawn). Demonstrate that the research team has access to the proposed study population. Furthermore, discuss past efforts in recruiting human subjects from the target population for previous clinical studies (if applicable). Address any potential barriers to accrual and plans for addressing unanticipated delays. Include justification of any age, race, ethnicity, or sex limitations provided. ***For clinical studies proposing to include military personnel, refer to the General Application Instructions, Appendix 6, for more information.***

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

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

  c. Description of the Recruitment Process: Explain methods for identification of potential human subjects (e.g., medical record review, obtaining sampling lists, 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 administration of any mind-altering substances such as tranquilizers, conscious sedation or anesthesia, brain injury, stress/life situations, or human subject age), if applicable.
- Address how privacy and time for decision making will be provided and whether or not the potential human subject will be allowed to discuss the study with anyone before making a decision.
- Consider the need for obtaining ongoing consent or for re-assessing capacity over the course of a long-term study and describe any relevant procedures to assure continued consent.
- Describe the plan for the consent of the individual's Legally Authorized Representative (LAR) to be obtained prior to the human subject's participation in the study. State law defines who may act as the LAR. The local IRB of record should be consulted for guidance regarding who can serve as LAR for research at the study site. Note: The PI must describe a clear intent to benefit for human subjects who cannot give their own consent to participate in the proposed clinical study to be in compliance with Title 10 United States Code Section 980 (10 USC 980) (http://www.gpo.gov/fdsys/pkg/USCODE-2011-title10/pdf/USCODE-2011-title10-subtitleA-partII-chap49-sec980.pdf). If applicable, refer to the General Application Instructions, Appendix 6, for more information.
- ***Assent.*** If minors or other populations that cannot provide informed consent are included in the proposed clinical study, a plan to obtain assent (agreement) from those with capacity to provide it, or a justification for a waiver of assent, should be provided. PIs should consult with their local IRB to identify the conditions necessary for obtaining assent.

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

f. Risks/Benefits Assessment:

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

- **Risk management and emergency response:**
    - Describe how safety surveillance and reporting to the IRB and FDA (if applicable) will be managed and conducted.
    - Describe all safety measures to minimize and/or eliminate risks to human subjects and study personnel or to manage unpreventable risks. Include safeguards and planned responses such as dose reduction or stopping criteria based on toxicity grading scales or other predetermined alert values.
    - Discuss the overall plan for provision of emergency care or treatment for an adverse event for study-related injuries, to include who will be responsible for the cost of such care.
    - Address any special precautions to be taken by the human subjects before, during, and after the study (e.g., medication washout periods, dietary restrictions, hydration, fasting, pregnancy prevention).
    - Describe any special care (e.g., wound dressing assistance, transportation due to side effects of study intervention impairing ability to drive) or equipment (e.g., thermometers, telemedicine equipment) needed for human subjects enrolled in the study.
    - For a study in which the IRB determines there is greater than minimal risk to human subjects, the DoD requires an independent research monitor with expertise consonant with the nature of risk(s) identified within the research protocol. If applicable, refer to the General Application Instructions, Appendix 6, for more information on study reporting authorities and responsibilities of the research monitor.
- **Potential benefits:** Describe known and potential benefits of the study to the human subject, a specific community, or society.

- **Attachment 9: 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.

- **Attachment 10: IND/IDE Documentation (required for clinical trials; no page limit): Upload as a single file named "IND-IDE.pdf."** If submitting multiple documents, start each document on a new page. Combine and upload as a single file.

a. Complete the IND/IDE Documentation Form, which is available on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm).

b. 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.

  Studies that require an FDA IND/IDE application (or international equivalent thereof) must submit documentation of regulatory approval to the DoD within 12 months of the DoD award date to demonstrate continued progress and ensure continuation of payment

- **Attachment 11: Collaborating DoD Military Facility Budget Form(s), if applicable: Upload as "MFBudget.pdf."** If a Military Facility (military health system facility, research laboratory, treatment facility, dental treatment facility, or a DoD activity embedded with a civilian medical center) will be a collaborator in performance of the project, complete the Collaborating DoD Military Facility Budget Form, available for download on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm), including a budget justification, for each Military Facility as instructed. Refer to the General Application Instructions, Section II.C.7., for detailed information.

3. **Research & Related Senior/Key Person Profile (Expanded):** Refer to the General Application Instructions, Section II.C.4., for detailed information.

   - PI Biographical Sketch (five-page limit): Upload as "Biosketch_LastName.pdf." The suggested biographical sketch format is available on the "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) in eBRAP. The five-page National Institutes of Health Biographical Sketch may also be used. All biographical sketches should be submitted in the portable document format (pdf) file 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."
   - Key Personnel Biographical Sketches (five-page limit each): Upload as "Biosketch_LastName.pdf."

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

4. **Research & Related Budget:** Refer to the General Application Instructions, Section II.C.4., for detailed information.
   - Budget Justification (no page limit): Upload as "BudgetJustification.pdf." The budget justification for the entire period of performance must be uploaded to the Research & Related Budget after completion of the budget for Period 1.

5. **Project/Performance Site Location(s) Form:** Refer to the General Application Instructions, Section II.C.5., for detailed information.

6. **R & R Subaward Budget Attachment(s) Form (if applicable):** Refer to the General Application Instructions, Section II.C.6., for detailed information.

D. Applicant Verification of Grants.gov Submission in eBRAP

Prior to the end of the application verification period, PIs and organizational representatives can review and modify in eBRAP certain components of an application submitted to Grants.gov. Following retrieval and processing of the Grants.gov application, eBRAP will notify the organizational representatives and PI by email to log into eBRAP to review, modify, and verify the Grants.gov application submission. eBRAP will validate retrieved files against the specific Program Announcement/Funding Opportunity requirements and discrepancies will be noted in both the email and in the Full Application Files tab in eBRAP. eBRAP does not confirm the accuracy of file content. It is the applicant's responsibility to review all application components and ensure proper ordering as specified in the Program Announcement/Funding Opportunity. ***If either the Project Narrative or the budget fails eBRAP validation or needs to be modified, an updated Grants.gov application package must be submitted via Grants.gov as a "Changed/Corrected Application" with the previous Grants.gov Tracking ID prior to the application submission deadline.*** The Project Narrative and Budget Form cannot be changed after the application submission deadline.

E. 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 application rejection.

F. Other Submission Requirements

Refer to the General Application Instructions, Appendix 2, for detailed formatting guidelines.

All extramural applications must be submitted through Grants.gov. Applicant organizations and all subrecipient organizations must have a DUNS number to submit applications to Grants.gov. The applicant organization must also be registered in the Entity Management functional area of the SAM with an "Active" status to submit applications through the Grants.gov portal. Refer to the General Application Instructions, Section II.A., for information on Grants.gov registration requirements.

III. APPLICATION REVIEW INFORMATION

A. Application Review and Selection Process

All applications are evaluated by scientists, clinicians, and consumer advocates using 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 RDA Directorate and the OASD (HA), based on (a) technical merit and (b) 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.

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 18 USC 1905.

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 critical review and analysis of the literature/preliminary studies/preclinical data and scientific rationale supports the research project.
     - How relevant and applicable the proposed research and findings are to at least one of the FY16 PFCRA 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 sound research design.
     - How well the PI acknowledges potential problems and addresses alternative approaches.
     - Whether the research can be completed within the proposed period of performance.

- To what degree the statistical model and data analysis plan are suitable for the planned study.
- How well the PI has outlined a plan for the sharing of data and research resources as appropriate for the type of study.

For applications involving animal research:

- How well the animal study is designed to achieve the objectives, including the choice of model and endpoints/outcome measures to be used.
- How well the study is designed to achieve reproducible and rigorous results, including controls, sample size estimation, blinding, randomization, and data handling.

For clinical trials:

- Whether there is evidence demonstrating availability of the intervention from its source for the duration of the proposed study.
- How the intervention or knowledge product compares with currently available interventions and/or standards of care.
- Whether a member of the study team holds the IND/IDE or whether the timeline and plan proposed for IND/IDE application is appropriate (if applicable).

For clinical trials and research involving human subjects:

- How well the PI describes the population(s) of interest, demonstrates access to these populations, has a viable plan for recruitment, consent, screening, and retention of appropriate subjects, and identifies sampling methods to gain a representative sample from the population(s) of interest.
- How well plans for addressing ethical and regulatory considerations have been developed, including mitigation of risk, consideration of privacy issues, and the process for obtaining informed consent.
- How the statistical plan, including sample size projections and power analysis, is adequate for the study and all proposed correlatives studies.
- Whether the statistical plan compensates for the use of a subpopulation of a recruited sample population to ensure appropriate power can be achieved within the subpopulation study, if applicable.

- **Impact and Military Benefit**
  - How significantly the potential research progress or long-term vision of the proposed research may impact PFC and/or pDCR scenarios.
  - To what extent the proposed research can optimize survival and recovery from combat-related injury in current and future operational scenarios involving PFC and/or pDCR.
  - 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 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.
  - 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.
- **Budget**
  - Whether the budget is appropriate for the proposed research and within the limitations of this Program Announcement/Funding Opportunity.
- **Personnel**
  - How well the background and expertise of the PI and other key personnel demonstrate their ability to perform the proposed research or clinical trial.
  - Whether the composition of the research or study team (e.g., study coordinator, statistician) is appropriate.
  - 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:

- **Environment**
  - To what degree the scientific environment and the accessibility of institutional/ organizational resources support the proposed research.
  - How the quality and extent of institutional/organizational support are appropriate for the proposed project.
- **Application Presentation**
  - To what extent the writing, clarity, and presentation of the application components influence the review.

2. **Programmatic Review:** To make funding recommendations and select the application(s) that, individually or collectively, will best achieve the program objectives, the following equally considered 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

C. Recipient Qualification

For general information on required qualifications for award recipients, refer to the General Application Instructions, Appendix 1.

D. Application Review Dates

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

E. Notification of Application Review Results

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

IV. ADMINISTRATIVE ACTIONS

After receipt of pre-applications from eBRAP or applications from Grants.gov, the following administrative actions may occur:

A. Rejection

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

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

The following will result in administrative rejection of the application:

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

For applications recruiting human subjects:

- Attachment 8, Human Subject Recruitment and Safety Procedures, is missing.
- Attachment 9, Data Management, is missing. ***For clinical trial applications:***
- Attachment 10, IND/IDE Documentation, is missing.

B. Modification

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

C. Withdrawal

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

- A FY16 JPC-6/CCCRP Prolonged Field Care Research Award 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 FY16 JPC-6/CCCRP Prolonged Field Care Research Award Programmatic Panel members can be found at http://cdmrp.army.mil/dmrdp/panels/17jpc_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. For FY16, 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 the General Application Instructions, Appendix 1, for detailed information.
- Personnel from applicant or collaborating organizations are found to have contacted persons involved in the review process to gain protected evaluation information or to influence the evaluation process.
- The proposed research includes a Phase II or Phase III clinical trial for FDA licensure of drugs or definitive testing for device clearance by the FDA.

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 the USAMRAA Grants Officer 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, 2017. Refer to the General Application Instructions, Appendix 4, for additional award administration information.

Any assistance instrument awarded under this Program Announcement/Funding Opportunity will be governed by the award terms and conditions, which conform to DoD's implementation of the Office of Management and Budget (OMB) circulars applicable to financial assistance. Terms and conditions of new awards made after December 26, 2014 may include revisions to reflect DoD implementation of new OMB guidance in the Code of Federal Regulations, Title 2, Part 200, "Uniform Administrative Requirements, Cost Principles, and Audit Requirements for Federal Awards" (2 CFR part 200).

B. Administrative Requirements

Refer to the General Application Instructions, Appendix 4 for general information regarding administrative requirements.

C. National Policy Requirements

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

D. Reporting

Refer to the General Application Instructions, Appendix 4, Section H, for general information on reporting requirements.

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

E. Award Transfers

The organization transfer of an award supporting a clinical trial is strongly discouraged and in most cases will not be allowed. Approval of a transfer request will be on a case-by-case basis at the discretion of the Grants Officer. An organizational transfer of an award will not be allowed in the last year of the (original) period of performance or any extension thereof.

Refer to the General Application Instructions, Appendix 4, Section L, for general information on organization or PI changes.

VI. VERSION CODES AND AGENCY CONTACTS

A. Program Announcement/Funding Opportunity and General Application Instructions Version Codes

Questions related to this Program Announcement/Funding Opportunity should refer to the Program name, the Program Announcement/Funding Opportunity name, and the Program Announcement/Funding Opportunity version code [20160210d]. The Program Announcement/ Funding Opportunity numeric version code will match the General Applications Instructions version code [20160210].

B. 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 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

C. Grants.gov Contact Center

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

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

Email: support@grants.gov

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

VII. APPLICATION SUBMISSION CHECKLIST

Grants.gov Application Components	Upload Order	Action	Completed
SF424 (R&R) Application for Federal Assistance		Complete form as instructed.	
Attachments Form	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	Human Subject Recruitment and Safety Procedures: Upload as Attachment 8 with file name "HumSubProc.pdf" (required for all studies recruiting human subjects).	
	9	Data Management: Upload as Attachment 9 with file name "Data_Manage.pdf" (required for all studies recruiting human subjects).	
	10	IND/IDE Documentation: Upload as Attachment 10 with file name "IND_IDE.pdf" (required for clinical trials).	
	11	Collaborating DoD Military Facility Budget Form(s): Upload as Attachment 11 with file name "MFBudget.pdf," if applicable.	
Research & Related Senior/Key Person Profile (Expanded)		Attach PI Biographical Sketch (Biosketch_LastName.pdf) to the appropriate field.	
		Attach PI Previous/Current/Pending Support (Support_LastName.pdf) to the appropriate field.	
		Attach Biographical Sketch (Biosketch_LastName.pdf) for each senior/key person to the appropriate field.	
		Attach Previous/Current/Pending (Support_LastName.pdf) for each senior/key person to the appropriate field.	
Research & Related Budget		Complete as instructed. Attach Budget Justification (BudgetJustification.pdf) to the appropriate field.	
Project/Performance Site Location(s) Form		Complete form as instructed.	
R & R Subaward Budget Attachment(s) Form		Complete form as instructed.	