Intramural 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), April 28, 2016
- **Invitation to Submit an Application:** June 16, 2016
- **Application Submission Deadline:** 11:59 p.m. ET, August 4, 2016
- **Peer Review:** September 2016
- **Programmatic Review:** October 2016

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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 2016 (FY16) JOINT PROGRAMMATIC REVIEW COMMITTEE 6 (JPC-6)/COMBAT CASUALTY CARE RESEARCH PROGRAM (CCCRP) PROLONGED FIELD CARE RESEARCH AWARD (PFCRA) 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 FY16 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 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 regulatory requirements in Appendix 3 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. 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 the regulatory requirements in Appendix 3 for additional information.

Military Relevance: Although the research outcomes are expected to benefit the 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.shtml

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://wrair-www.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 Component 2 to provide this documentation (see Section II.B., Full Application Submission Content, Component 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 Appendix 2, Administrative Information.

C. Eligibility Information

- ***This Program Announcement/Funding Opportunity is intended for intramural investigators only.*** Extramural investigators are required to apply to the FY16 JPC-6/ CCCRP PFCRA Announcement/Funding Opportunity through CDMRP eBRAP at https://ebrap.org/eBRAP/public/index.htm.
- Independent intramural investigators at all academic levels (or equivalent) are eligible to submit applications.
- 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 facilities. Regardless of 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 Material Transfer Agreements. The Government reserves the right to administratively withdraw any application that does not meet these eligibility criteria. ***Applications that require research to be performed completely by a non-DoD organization under a new service contract will not be considered for funding.***

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 the 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 intramural investigators only. Extramural investigators are required to apply to the FY16 JPC-6/CCCRP PFCRA Extramural Announcement/Funding Opportunity through CDMRP eBRAP at https://ebrap.org/eBRAP/public/index.htm.

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 $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 Research Award applications, depending on the received applications' quality, number, and Focus Areas addressed. 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.

FUNDS FOR THIS PROGRAM ARE PROGRAM ELEMENT 6.2, 6.3 AND 6.4 DOLLARS.

FUNDS ARE TO BE DISTRIBUTED AS FY16 AND FY17 FUNDS.

FY16 FUNDS MUST BE OBLIGATED BY SEPTEMBER 30, 2017.

FY17 FUNDS MUST BE OBLIGATED BY SEPTEMBER 30, 2018.

NOTE: Applications received under this mechanism will compete with applications received under the FY16 JPC-6/CCCRP Prolonged Field Care Research Award Extramural Announcement found at https://ebrap.org/eBRAP/public/index.htm.

II. SUBMISSION INFORMATION

Submission is a two-step process requiring both (1) pre-application submission and (2) application submission through the CDMRP eReceipt System (https://cdmrp.org/).

Start the submission process early. The CDMRP eReceipt System 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.

A. Pre-Application Submission Content

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

All pre-application components must be submitted by the indicated deadline by the PI through the CDMRP eReceipt System (https://cdmrp.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@cdmrp.org or 301-682-5507

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

- **Tab 1 – Application Information**
  - Enter the application information as described in the CDMRP eReceipt System before continuing the pre-application.

- **Tab 2 – Application Contacts**
  - Enter contact information for the PI responsible for the overall scientific and technical direction of this application and the organization's Resource Manager/Comptroller or equivalent personnel responsible for sponsored program administration. This contact information is ***required*** in the CDMRP eReceipt System. The pre-application will not be accepted without it. However, the CDMRP does not require approval of the pre-application by the Coordinating PI's organization.

- **Tab 3 – Collaborators and Conflicts of Interest (COIs)**
  - To avoid COIs during application screening and review processes, list the names of all scientific participants in the proposed research project, including co-investigators, mentors, collaborators, consultants, and subrecipients/subawardees. Add all individuals outside of the application who may have a COI in the review of the application (including those with whom the PI has a personal or professional relationship) and choose "COI" from the drop-down list. All Project PIs should be included.
  - 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.shtml. 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@cdmrp.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. 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.shtml). 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.

- **Tab 4 – Pre-Application Files**

  Note: At this time, the CDMRP eReceipt System is unable to read files made with Adobe Acrobat PDFMaker version 9.0 and higher. The documents should conform to the formatting guidelines outlined in Appendix 1.

  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 5 – Submit Pre-Application**
  - This tab must be completed for the pre-application to be accepted and processed.

- **Other Documents Tab**
  - This tab is not applicable during the pre-application submission process.

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.

B. Full Application Submission Content

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

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

The application consists of the following components, which are organized in the CDMRP eReceipt System by separate tabs. To access these tabs, go to "My Applications" and click on "View/Edit Application Information' for the log number for which an application has been invited for submission.

- **Tab 1 – Application Information**
  - This tab will be populated by the CDMRP eReceipt System. Do not change.
- **Tab 2 – Application Contacts**
  - This tab will be populated by the CDMRP eReceipt System. Do not change.
- **Tab 3 – Collaborators and Conflicts of Interest**
  - This tab will be populated by the CDMRP eReceipt System. To avoid COIs during application screening and review processes, review and update (if needed) the names of all scientific participants in the proposed research project, including co-

investigators, mentors, collaborators, consultants, and subrecipients/subawardees. In addition, add all individuals outside of the application who may have a COI in the review of the application (including those with whom the PI has a personal or professional relationship) and choose "COI" from the drop-down list.

- 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.shtml. 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@cdmrp.org or 301-682-5507.

- **Tab 4 – Required Files**
  - Submit each component as an individual PDF file. Refer to Appendix 1, for detailed formatting guidelines. Note: At this time, the CDMRP eReceipt System is unable to read files made with Adobe Acrobat PDFMaker version *9.0 and higher*.
    - **Component 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.

- **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 Administrative Information, Appendix 2, for more information about the CDMRP expectations for making data and research resources publicly available.

- **Component 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 Component 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.

- **Component 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.

- **Component 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?

- **Component 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.

- **Component 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.

- **Component 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.

- **Component 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 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 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 Regulatory Requirements, Appendix 3, 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 Regulatory Requirements, Appendix 3, for more information on study reporting authorities and responsibilities of the research monitor.

- **Potential benefits:** Describe known and potential benefits of the study to the human subject, a specific community, or society.

- **Component 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.

- **Component 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

- **Component 11: Budget and Budget Justification:** Use the Detailed Budget and Justification form available on the "Program Announcement and Forms" page in the CDMRP eReceipt System (https://cdmrp.org/Program_Announcements_and_Forms/). Upload as "Budget.pdf."

  Submit a detailed budget and justification that covers the entire period of performance (not just the first year). All costs must be entered in U.S. dollars. The budget and budget justification must be sufficiently detailed so that the Government can determine the proposed costs to be allowable, allocable, and reasonable for the proposed research. ***The Government reserves the right to request a revised budget and budget justification and/or additional information.*** **The budget should cover all costs for the Center and for the submitted projects but NOT for the alternate(s).**

  Budget Instructions: Complete the Detailed Budget and Justification form. Begin by entering the PI name, CDMRP Log number, and period of performance fields at the top of page F-1 of the Detailed Budget and Justification form. Following the guidelines below, enter the required information under "Detailed Budget for Year One" on pages F-1 (Senior/Key Person and Other Personnel) and F-2 (Other Direct Costs). On page F-3, fill in the appropriate total amounts for each budget category for each additional year (or partial year) of support requested under "Budget for Entire Proposed Period of Performance." Itemize all budget categories for the additional years and clearly justify each budget item for the entire period of performance in the Justification section on page F-4.

  - **Senior/Key Person and Other 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 previously provided. 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, and support staff.
- **Role on Project:** Identify the role of each participant listed. Describe his/her specific functions 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.

- **Other Direct Costs:** Itemize and clearly justify all additional direct costs as components of the budget categories listed below. Enter the itemized budget information for the first year on page F-2.
- **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.
- **Travel Costs:** Travel costs may include:
  - Required attendance at one 1-day In Progress Review meeting per year.

- Attendance at one DoD-sponsored scientific/technical meeting. Include the meeting name, purpose, location, and date, if known, in the budget justification.
- Travel associated with the execution of the proposed work (if applicable). Reasonable costs for travel between collaborating organizations should be included and are not subject to the yearly cost limitation on travel to scientific/technical meetings. International travel may be requested but must be well justified, requested no less than 180 days before travel, and is subject to approval by the CCCRP.

- **Materials, Supplies, and Consumables:** The budget justification for supporting material and supply (consumable) costs should include a general description of expendable material and supplies. If animals are to be purchased, state the species, strain (if applicable), number to be used, cost per animal, and proposed vendor. If human cell lines are to be purchased, state the source, cost, and description.
- **Consultant Costs:** Regardless of whether funds are requested, include in the budget justification the names and organizational affiliations of all consultants, and include the daily consultant fee, travel expenses, nature of the consulting effort, and why consultants are required for the proposed research project.
- **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 their 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.
- **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 Expenses:** 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.
- **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:** This award is not intended to provide funds for indirect costs to the applicant organization. All direct and indirect costs of any proposed collaborator must be included in the total direct costs of the

primary award. 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.

- **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 (page F-4) of the Detailed Budget and Justification 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 Detailed Budget and Justification form. Applications must provide a plan delineating how all the FY16 funds will be obligated by 30 September 2017 and FY17 funds will be obligated by 30 September 2018. The plan must include the funding mechanism(s) that will be used to carry over funds between fiscal years, if applicable.
- PIs must plan to have 90% of FY16 funds disbursed and/or obligated by September 30, 2017. Any funding not obligated by September 30, 2017 may be withdrawn by the issuing Comptroller.
- PIs must plan to have 90% of FY17 funds disbursed and/or obligated by September 30, 2018. Any funding not obligated by September 30, 2018 may be withdrawn by the issuing Comptroller.

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 application rejection.

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.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 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 (their) 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. 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 posting of the funding recommendation in eReceipt. 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 applications from eReceipt, 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.
- Submission of the same research project to different Funding Opportunities within the same program (CDMRP DMRDP, http://cdmrp.army.mil/funding/dmrdp.shtml) and fiscal year.

For applications recruiting human subjects:

- Component 8, Human Subject Recruitment and Safety Procedures, is missing.
- Component 9, Data Management, is missing.

For clinical trial applications:

- Component 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.shtml.
- 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.shtml). 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.
- 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.

B. Reporting

Refer to the Administrative Information, Appendix 1, 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.

C. 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 JPC-6/CCCRP.

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 eReceipt 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@cdmrp.org

VII. APPLICATION SUBMISSION CHECKLIST

Application Components	Action	Completed
Component 1 – Project Narrative	Upload as "ProjectNarrative.pdf."	
Component 2 – Supporting Documentation	Upload as "Support.pdf."	
Component 3 – Technical Abstract	Upload as "TechAbs.pdf."	
Component 4 – Lay Abstract	Upload as "LayAbs.pdf."	
Component 5 – Statement of Work	Upload as "SOW.pdf."	
Component 6 – Impact and Military Benefit	Upload as "Impact.pdf."	
Component 7 – Transition Plan	Upload as "Transition.pdf."	
Component 8 – Human Subject Recruitment and Safety Procedures (required for all studies recruiting human subjects)	Upload as "HumSubProc.pdf."	
Component 9 – Data Management (required for all studies recruiting human subjects)	Upload as "Data_Manage.pdf."	
Component 10 – IND/IDE Documentation (required for clinical trials)	Upload as "IND_IDE.pdf."	
Component 11 – Budget and Budget Justification	Upload as "Budget.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 among 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. All contributors 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.
  - **Font Size:** 12 point, not condensed.
  - **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 and TIFF formats are not allowed. Please note that these types of objects are not allowed in the technical and public abstracts.
  - **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 Attachment Size:** Individual attachments should be no larger than 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. Eligibility Information

General eligibility for investigators, organizations, and agencies:

- Eligible Investigators: Includes all individuals, regardless of ethnicity, nationality, or citizenship status, who are employed by, or affiliated with, an eligible organization. ***Note: Awards are made to organizations only, not to individuals.*** Investigators must meet the specific Program Announcement/Funding Opportunity requirements.

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 will be 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. Marking of Proprietary Information

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

E. 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 the CDMRP eReceipt System at https://cdmrp.org/Program_Announcements_and_Forms/.

- **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 the CDMRP eReceipt System at https://cdmrp.org/Program_Announcements_and_Forms/.

F. 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 Office of the Assistant Secretary of Defense for Health Affairs and the Defense Health Agency, Research, Development, and Acquisition Directorate. 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 U.S. Department of Agriculture." Include required assurances, approvals, documents and information specified on the 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).

G. Sharing of Application Information

- The CDMRP shares application information with other Federal funding agencies (e.g., NIH, National Science Foundation, Department of Veterans Affairs) to inform funding priorities and decisions, and to increase transparency. In addition, award data are made available to the public through the CDMRP website and to other organizations such as the International Cancer Research Partnership. By sharing and leveraging this information, duplication of very expensive and time-consuming efforts can be avoided, allowing for the support of more investigators with Federal funds. The CDMRP believes that such sharing allows for a more expeditious translation of research results into knowledge, products, and procedures to improve human health. Updates on

CDMRP-funded awards including awardee information and published results are shared on the Defense Technical Information Center (DTIC).

H. 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** 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. (Adapted from http://grants.nih.gov/grants/policy/data_sharing/data_sharing_guidance.htm#unique)
    - **Final Research Data** are defined as recorded factual material commonly accepted in the scientific community as necessary to document and support research findings. These are not the summary statistics or tables; rather, final research data are the data on which summary statistics and tables are based. Final research data do not include laboratory notes or notebooks, partial datasets, preliminary analyses, drafts of scientific papers, plans for future research, peer review reports, communications with colleagues, or physical objects, such as gels or laboratory specimens. (Adapted from http://grants.nih.gov/grants/policy/data_sharing/data_sharing_guidance.htm#unique)
    - **Research Resources** 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, animal models, growth factors, combinatorial chemistry, DNA libraries, clones and cloning tools, methods, laboratory equipment and machines. (Adapted from https://grants.nih.gov/grants/intell-property_64FR72090.pdf.)

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. The USAMRMC believes that such sharing allows for a more expeditious translation of research results into knowledge, products, and procedures to improve human health. Depending on the Program Announcement/Funding Opportunity, 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 ClinicalTrials.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 the CDMRP eReceipt System under Reference Material at https://cdmrp.org/Program_Announcements_and_Forms/.

APPENDIX 3
REGULATORY REQUIREMENTS

A. Safety and Environmental Requirements

Based on recent changes to DoD compliance requirements (DA PAM 385-69, DA PAM 385-10, 32 CFR 651 6 Sep 2012), provisions previously required 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, Biological Select Agents or Toxins, specific chemical agent(s), or pesticides outside of an established laboratory. The USAMRMC Office of Surety and Environment will identify any need for compliance review and documents must be submitted upon request.

Additional information is available at: https://mrmc.amedd.army.mil/index.cfm?pageid=researcher_resources.environmental

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

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

PIs and applicant organizations **may not commence performance** of research involving the above, **or expend funding** on such efforts, until 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 September 13, 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 November 8, 2011, and available at http://www.dtic.mil/whs/directives/corres/pdf/321602p.pdf.

The ORP 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 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 subject 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 a determination from the ORP HRPO at USAMRMC.*** A timeframe for submission of the appropriate protocols and required approvals will be established during negotiations.

C. 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. All amendments or modifications must also be reviewed prior to initiation for the life of the award. PIs must submit the institutional animal use protocol, IACUC approval of that protocol, and a version of the animal use appendix titled "Research Involving Animals." For guidance on which version of the appendix to use, as well as links to both, visit the ACURO website at: https://mrmc.amedd.army.mil/index.cfm?pageid=Research_Protections.acuro_Animalappendix. ***Allow at least 2 to 3 months for regulatory review and approval processes for animal studies.***

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

D. 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 or human anatomical substances obtained from cadavers shall not begin until approval is granted in accordance with the Army Policy for Use of Human Cadavers for RDT&E, Education, or Training, 20 April 2012 (https://mrmc.amedd.army.mil/index.cfm?pageid=research_protections.overview). The USAMRMC ORP is the Action Office (usarmy.detrick.medcom-usamrmc.other.hrpo@mail.mil) for this policy. **HRPO must review the use of post-mortem specimens for compliance with the Army Cadaver Use 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 human cadaver research for USAMRMC ORP review and approval should be directed to the ORP at usarmy.detrick.medcom-usamrmc.other.hrpo@mail.mil.

E. Research Involving the Secondary Use of Data/Specimens

All USAMRMC supported research involving the secondary use of human data, records, human tissue, or human specimens (hereafter referred as data/specimens) must be reviewed for compliance with Federal and DoD human subjects protection requirements and approved by the ORP prior to implementation. USAMRMC ORP HRPO review includes assessing the source of the data/specimens and whether the initial manner and consent for the data/specimen collection permits use in the DoD-funded research protocol. HRPO review, approvals, and determinations for specimen research are based upon the nature of the research, the source of the data/specimens, use and/or disclosure of identifiable health information, privacy and confidentiality protections, and whether the individual providing the data/specimens allowed the use of their data/specimens for research. For additional guidance and instructions on HRPO review of any DoD-funded research activities involving access, use, and analysis of data/specimens, investigators should submit the HRPO Submission Form for Secondary research found on the ORP HRPO website. https://mrmc.amedd.army.mil/index.cfm?pageid=Research_Protections.hrpo

F. Research Involving Human Subjects

In addition to local IRB review, investigators must submit all USAMRMC-funded research protocols involving human subjects for review and approval by the USAMRMC ORP HRPO prior to implementation of the research. The focus of this review is to validate the 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 should only be used as a guide; it is not intended to be a source for human subjects protection regulations. Questions regarding applicable human subjects protection regulations, policies, and guidance should be directed to the local IRB, the ORP HRPO (usarmy.detrick.medcom-usamrmc.other.hrpo@mail.mil), and/or the U.S. Food and Drug Administration 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 that 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 HRPO submission and review of research involving human subjects can be found at https://mrmc.amedd.army.mil/index.cfm?pageid=research_protections.hrpo.

1. **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) Federalwide Assurance (FWA) or DoD Assurance.
2. **Training:** Personnel involved in human subjects research must have completed appropriate training in the protection of human subjects. Documentation confirming

completion of appropriate training may be required during the regulatory review process.

3. **Informed Consent Form:** The following must appear in the consent form:
   - A statement that the U.S. DoD 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.
4. **Intent to Benefit:** The requirements of 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 for 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 is a much narrower definition of ***human subject***. Research with experimental subjects must involve an intervention or interaction where the primary purpose of the research is to collect data regarding the effects of the intervention or interaction.

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

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

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

- Observing recruitment and enrollment procedures and the consent process for individuals, groups or units;
- Overseeing study interventions and interactions;

- Reviewing monitoring plans and Unanticipated Problems Involving Risk to Subjects or Others (UPIRTSO) reports; and/or
- Overseeing data matching, data collection, and analysis.

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

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

A curriculum vitae or biographical sketch and documentation of human subjects protection training for the research monitor must be provided. There should be no apparent COI, 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.

C. Clinical Trial Registry

PIs are required to register clinical trials individually on http://clinicaltrials.gov/ using a Secondary Protocol ID number designation of "CDMRP-Log Number" (e.g., CDMRP-PC16####). If several protocols exist under the same application, the Secondary Protocol ID number must be designated "CDMRP-Log Number-A, B, C, etc." (e.g., CDMRP-PC16####-A). Clinical trials must be registered prior to enrollment of the first patient. All trials that meet the definition on the NIH database (see http://prsinfo.clinicaltrials.gov/, click on "Support Materials (including data element definitions") are required to register. Failure to do so may result in a civil monetary penalty and/or the withholding or recovery of grant funds as per U.S. Public Law 110-85.

D. Research Involving Recombinant DNA Molecules

The recipient assures that all work involving the use of recombinant DNA will be in compliance with guidance provided at http://www4.od.nih.gov/oba.