Program Announcement

for the

Department of Defense

Defense Health Program

Congressionally Directed Medical Research Programs

Peer Reviewed Orthopaedic Research Program

Integrated Clinical Trial Award

Funding Opportunity Number: W81XWH-16-PRORP-ICTA

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

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-Application Submission Deadline:** 5:00 p.m. Eastern time (ET), September 7, 2016
- **Invitation to Submit an Application:** October 20, 2016
- **Application Submission Deadline:** 11:59 p.m. ET, December 7, 2016
- **End of Application Verification Period:** 5:00 p.m. ET, December 12, 2016
- **Peer Review:** February 2017
- **Programmatic Review:** April 2017

This Program Announcement/Funding Opportunity is one of two documents with instructions to prepare and submit an application for this funding opportunity. The second document, the General Application Instructions, is available for downloading from Grants.gov.

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I. FUNDING OPPORTUNITY DESCRIPTION

A. Program Description

Applications to the Fiscal Year 2016 (FY16) Peer Reviewed Orthopaedic Research Program (PRORP) 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 the Defense Health Program (DHP) Research, Development, Test, and Evaluation (RDT&E) appropriation. The managing agent for this Program Announcement/Funding Opportunity is the Congressionally Directed Medical Research Programs (CDMRP). The PRORP was initiated in 2009 to provide support for research of exceptional scientific merit focused on optimizing recovery and restoration of function for military personnel with orthopaedic injuries sustained in combat or combat-related duties. Appropriations for the PRORP from FY09 through FY15 totaled $278.5 million (M). The FY16 appropriation is $30M.

The FY16 PRORP challenges the scientific community to address the most significant gaps in care for the leading burden of injury and loss of fitness for military duty by funding innovative, high-impact, clinically relevant research to advance optimal treatment and rehabilitation from neuromusculoskeletal injuries (excluding spinal cord injuries) sustained during combat or combat-related activities. It is expected that any research findings would also provide benefit to the general population. Applications involving multidisciplinary collaborations among academia, industry, the military Services, the Department of Veterans Affairs (VA), and other Federal agencies are highly encouraged.

B. FY16 PRORP Focus Areas

All applications must integrate at least two (minimum of one from the Surgical Care category and one from the Rehabilitation category) and a maximum of four of the following FY16 PRORP Focus Areas into a cohesive project. Selection of the appropriate Focus Areas is the responsibility of the applicant. Studies that combine Focus Areas synergistically and propose significant advancements are particularly encouraged.

Surgical Care Focus Areas:

- Peripheral Nerve Injuries: Treatment strategies to improve outcomes from segmental peripheral nerve defects of motor and mixed (motor and sensory) peripheral nerve damage from crush or complete injury.
- Prevention of Heterotopic Ossification: Techniques to retard or prevent the development of human post-traumatic heterotopic ossification in the upper extremity.
- Volumetric Muscle Loss: Techniques to regenerate functional, innervated muscle units in treatment of volumetric muscle loss.
- Extremity Fractures: Strategies to optimize patient outcomes after extremity fracture, (i.e., time to begin rehabilitation, weight bearing strategy).

- Pelvic Ring Injuries: Treatment strategies to improve outcomes of complex pelvic ring injuries.
- Compartment Syndrome: Improvement of current diagnosis for compartment syndrome.
- Gaps in Clinical Practice Guidelines: Address gaps in current orthopaedic clinical practice guidelines (CPGs) and recommendations (http://www.usaisr.amedd.army.mil/cpgs.html). Applications under this Focus Area **must** specify which orthopaedically relevant CPG their application is intended to support. Applicants should also highlight the expected impact of their research on orthopaedic clinical practice.
- Surgical Techniques to Optimize Gait: Validation of surgical techniques to optimize gait efficiency and outcomes for patients with amputation or limb salvage.
- Soft Tissue Trauma: Strategies to develop and/or identify musculoskeletal extremity soft tissue trauma treatments affecting return to duty, work, or reintegration.

Rehabilitation Focus Areas:

- Post-Operative Pain Management: Develop and/or validate strategies for post-operative pain management following orthopaedic trauma that minimize or eliminate opioid use. The primary outcome measures should relate to rehabilitation endpoints and not focus solely on pain scores.
- Prosthetic and/or Orthotic Device Function: Development, validation and/or optimization of novel, innovative technologies to improve prosthetic and/or orthotic device function and durability, including intuitive efferent (motor) and afferent (sensory) user interfaces and considerations for interoperability.
- Secondary Physical Health Effects: Techniques or technologies that improve prediction, identification, and reduction of secondary physical health effects (e.g., obesity, arthrosis, osteoporosis, cardiovascular disease) following severe/high-energy traumatic neuromusculoskeletal non-spinal cord injury. The focus should be on injuries sustained between the ages of 18-50 and secondary physical health effects that develop within 5 years of injury.
- Physical or Occupational Therapy: Development and/or validation of optimal physical or occupational therapy treatment strategies and sequence of progression throughout the rehabilitation continuum to maximize functional outcomes following severe neuromusculoskeletal injury, excluding central nervous system. Examples include optimal timing, frequency, duration, and intensity of rehabilitation interventions.
- Barriers to Successful Therapy Outcomes: Identify, quantify, and stratify confounding treatable factors (e.g., pain, sleep, nutrition, compliance, etc.) that inhibit or delay optimal orthopaedic rehabilitation outcomes.
- Rehabilitation Outcomes: Development and/or validation of standardized measures to objectively assess and improve rehabilitation outcomes, including multi-limb trauma and/or psychosocial resiliency and reintegration, following neuromusculoskeletal injury.

C. Award Information

The PRORP is offering the Integrated Clinical Trial Award (ICTA) for the first time in FY16. The PRORP ICTA supports the rapid implementation of an interdisciplinary clinical trial that integrates both surgical and rehabilitation strategies and has the potential to have a major impact on both the treatment of combat-related orthopaedic injuries, as well as the treatment of nonbattle injuries that significantly impact unit readiness and return-to-duty/work rates.

Projects that follow patients across the continuum of care are highly encouraged. The projects should include both surgical and rehabilitation strategies that create a cohesive project. Surgical strategies are reconstruction and repair and/or application of biologics, pharmaceuticals, and devices for the purpose of restoration of native architecture, composition, and function of traumatically injured tissues. Rehabilitative strategies are those that restore function following injury or illness, with the goal of optimal health and independence. Projects should integrate principles and approaches from surgical and rehabilitative strategies, beyond what each approach would result in alone, with the goal of optimizing form, function, and independence for those who have sustained traumatic orthopaedic injuries. Care should be taken to avoid or account for confounding factors in the analyses.

All applications are required to articulate the relevance of the proposed interdisciplinary project to military and/or Veteran populations affected by orthopaedic injury. ***Collaboration with military and VA researchers and /or clinicians is encouraged. Studies that include active duty military or Veteran participants as all or a portion of the study population are encouraged.***

All funding amounts requested should be well-justified and appropriate to the scope of work proposed. ***Funding from this award mechanism must support one cohesive clinical trial and may not be used for preclinical research studies. Animal research is not allowed under the FY16 PRORP ICTA.*** 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, and/or efficacy. This outcome represents a direct effect on the human subject of that intervention or interaction. Principal Investigators (PIs) seeking funding for a preclinical research project should consider one of the other award mechanisms/funding opportunities being offered. The term "human subjects" is used in this Program Announcement/ Funding Opportunity to refer to individuals who will be recruited for or who will participate in the proposed clinical trial. For more information, a Human Subject Resource Document is provided at https://ebrap.org/eBRAP/public/Program

If the clinical trial involves the use of a drug that has not been approved by the U.S. Food and Drug Administration (FDA) for the proposed investigational use, then an Investigational New Drug (IND) application to the FDA that meets all requirements under the Code of Federal Regulations, Title 21, Part 312 (21 CFR 312) may be required and must be submitted to the FDA ***within 6 months of the award date***. 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 submitted to the FDA ***within 6 months of the award date***, or that the device is exempt from an IDE or qualifies for an abbreviated IDE, is required. The Government reserves the right to withdraw funding if an IND or IDE is necessary but has not been submitted to the

FDA within 6 months of the award date, or if documented status of the IND or IDE has not been obtained within 12 months of the award date.

The following are important aspects of submission for the Integrated Clinical Trial Award:

- The proposed clinical trial is expected to begin no later than 12 months after the award date, or 18 months for FDA-regulated studies.
- The proposed intervention to be tested should offer significant potential impact for military personnel and Veterans with combat-related orthopaedic injuries or non-battle orthopaedic injuries that impact unit readiness and return-to-duty/work.
- Inclusion of preliminary data relevant to the proposed clinical trial is required.
- The proposed clinical trial must be based on sound scientific rationale that is established through logical reasoning and critical review and analysis of the literature.
- The application should describe the planned indication for the product label, if appropriate. Likewise, it should include an outline of the development plan and regulatory strategy required to support that indication.
- The application should demonstrate availability of, and access to, a suitable patient population that will support a meaningful outcome for the study. The applicant should discuss how accrual goals will be achieved and how standards of care may impact the study enrollment.
- The application should demonstrate documented availability of and access to the drug/ compound, device, and/or other materials needed, as appropriate. The quality of the product should be commensurate with FDA manufacturing standards applicable to the type and phase of product being developed (i.e., Quality System Regulation, Good Manufacturing Practices).
- The application should demonstrate the study team has experience interacting with the FDA, to include previous FDA submissions, if applicable.
- The proposed clinical trial design should include clearly defined and appropriate endpoints, and follow Good Clinical Practice (GCP) guidelines.
- The application should include a clearly articulated statistical analysis plan, appropriate statistical expertise on the research team, and a power analysis reflecting sample size projections that will clearly answer the objectives of the study.
- The application should include a clearly articulated data management plan and use of an appropriate database to safeguard and maintain the integrity of the data. For FDA-regulated studies, compliance with 21 CFR 11 is required.
- The application should include a clearly articulated safety management plan outlining how safety and pharmacovigilance will be conducted, as applicable.
- The application should include a clearly articulated clinical monitoring plan outlining how the study will be monitored for GCP compliance.
- The application should include a study coordinator(s) who will guide the clinical protocol through the local Institutional Review Board (IRB) of record and other federal

agency regulatory approval processes, coordinate activities from all sites participating in the trial, and coordinate participant accrual.

- For studies determined to be greater than minimal risk to human subjects by the local IRB of record, the Department of Defense (DoD) requires an independent research monitor with expertise consistent with the nature of risk(s) identified within the research project. If applicable, refer to the General Application Instructions, Appendix 6, for more information on study reporting authorities and responsibilities of the research monitor.
- The application should include a Transition Plan (including potential funding and resources) showing how the product will progress to the next clinical trial phase and/or delivery to the market after the successful completion of the FY16 PRORP ICTA.
- The application should clearly demonstrate strong institutional support (refer to Section II.C., Full Application Submission Content, Supporting Documentation).
- Funded studies are required to file the study in the National Institutes of Health clinical trials registry, www.clinicaltrials.gov. Refer to the General Application Instructions, Appendix 6, Section C, for further details.

Multi-Institutional Clinical Trials: If the proposed clinical trial is multi-institutional, plans for communication and data transfer among the collaborating institutions, as well as how specimens and/or imaging products obtained during the study will be handled, should be included in the appropriate sections of the application. A separate intellectual and material property plan agreed upon by all participating institutions is also required for multi-institutional clinical trials.

Required Qualified Collaborator(s): The ICTA supports collaborative interdisciplinary research between/among physical therapists, occupational therapists, prosthetists, surgeons, and other orthopaedic care providers. To encourage meaningful and productive multidisciplinary collaborations, the project must include at least one investigator with orthopaedic rehabilitation expertise and at least one clinician who specializes in orthopaedic or trauma care. A clinician is defined as an individual who is credentialed (possesses the necessary degrees, licenses, and other certifications) and practicing as a care provider in a relevant capacity. Biographical sketches should include appropriate documentation of credentials. It is the responsibility of the PI and the collaborating investigators to describe how their combined expertise will better address the research question, why the work should be performed through collaboration rather than through separate efforts, and how the research design will create a reciprocal flow of ideas and information between the multiple disciplines represented. The proposed collaboration should involve substantial contributions from each of the key collaborators identified, with evidence of significant intellectual input from each key collaborator into the design of the project. The PI must submit a Qualified Collaborator Statement that clearly describes the proposed collaborator(s), the collaboration, and addresses how each of the criteria below are met. Use Attachment 9 (Study Personnel & Organization) to provide this statement (see Section II.C., Full Application Submission Content). In addition, each collaborator must provide a letter of collaboration describing his/her involvement in the proposed work. Use Attachment 2 to provide this documentation (see Section II.C., Full Application Submission Content, Supporting Documentation, Letters of Collaboration).

The following criteria must be met for the required Qualified Collaborator(s):

- A Qualified Collaborator must be an investigator with orthopaedic rehabilitation expertise or a clinician who specializes in orthopaedic or trauma care.
- The Qualified Collaborator(s) must significantly contribute to the project such that the proposed work could not be accomplished without his/her involvement. This is expected to include both intellectual input and research resources (e.g., supplies, reagents, equipment, personnel, services, tissue samples, or access to patients or populations).
- The Qualified Collaborator(s) and PI must each contribute a minimum of a 5% level of effort to the project. Contribution of the Qualified Collaborator(s) and PI should be reflected in the application budget.

Encouraged DoD and VA Collaboration and Alignment: Military relevance is a key feature of this award. Therefore, PIs are strongly encouraged to collaborate, integrate, and/or align their projects with military and/or VA research laboratories and programs. Although not a comprehensive list, the following websites may be useful in identifying information about DoD and VA areas of research interest, ongoing research, or potential opportunities for collaboration:

Air Force Office of Scientific Research
http://www.wpafb.af.mil/afrl/afosr/

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

Armed Forces Radiobiology Research Institute
http://www.usuhs.edu/afrri/

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 Technical Information Center
http://www.dtic.mil

Defense Threat Reduction Agency
http://www.dtra.mil/

Military Health System Research Symposium
https://mhsrs.amedd.army.mil/SitePages/Home.aspx

Military Infectious Diseases Research Program
https://midrp.amedd.army.mil

Military Operational Medicine Research Program
https://momrp.amedd.army.mil

Naval Health Research Center
http://www.med.navy.mil/sites/nhrc

Navy and Marine Corps Public Health Center
http://www.nmcphc.med.navy.mil/

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/

Telemedicine and Advanced Technology Research Center
http://www.tatrc.org/

Uniformed Services University of the Health Sciences
http://www.usuhs.edu/research

U.S. Army Institute of Surgical Research
http://www.usaisr.amedd.army.mil/

U.S. Army Research Institute of Environmental Medicine
http://www.usariem.army.mil/

U.S. Army Medical Research Institute of Infectious Diseases
http://www.usamriid.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. Department of Veterans Affairs, Office of Research and Development
http://www.research.va.gov

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

Walter Reed Army Institute of Research
http://wrair-www.army.mil

Use of Military and VA Populations or Resources: If the proposed research plan involves access to active duty military and/or VA patient populations or resources, the PI is responsible for establishing such access. If possible, access to target active duty military and/or VA patient populations/resources should be confirmed at the time of application submission by inclusion of a letter of support, signed by the lowest ranking person with approval authority, for studies involving active duty military Service members, Veterans, military- and/or VA-controlled study materials, and military and/or VA databases. If access cannot be confirmed at the time of application submission, the Government reserves the right to 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 either collaboration with a VA investigator, where the VA investigator has a substantial role in the research, or by advertising to the general public. Use Attachment 2 to provide this documentation (see Section II.C., Full Application Submission Content, Supporting Documentation).

Research Involving Human Anatomical Substances, Human Subjects, or Human Cadavers: All DoD-funded research involving new and ongoing research with human anatomical substances, human subjects, or human cadavers must be reviewed and approved by the U.S. Army Medical Research and Materiel Command (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 IRB or Ethics Committee (EC) review. Local IRB/EC approval at the time of submission is ***not*** required. The HRPO is mandated to comply with specific laws and requirements governing all research involving human anatomical substances, human subjects, or human cadavers that is supported by the DoD. These laws and requirements will necessitate information in addition to that supplied to the IRB/EC. ***Allow a minimum of 2 to 3 months for HRPO regulatory review and approval processes***. Refer to the General Application Instructions, Appendix 6, and the Human Subject Resource Document available on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) for additional information.

If the IRB determines that a trial presents greater than minimal risk to human subjects, the DoD requires an independent research monitor with expertise consistent with the nature of risk(s) identified within the research protocol. If applicable, please refer to the General Application Instructions, Appendix 6, for more information on study reporting authorities and responsibilities of the research monitor.

The CDMRP intends that information, data, and research resources generated under awards funded by this Program Announcement/Funding Opportunity be made available to the research community (which includes both scientific and consumer advocacy communities) and to the public at large. For additional guidance, refer to the General Application Instructions, Appendix 4, Section K.

D. Eligibility Information

- The PI must be an independent investigator at or above the level of Assistant Professor (or equivalent).
- A required Qualified Collaborator must be an independent investigator at or above the level of Assistant Professor (or equivalent) with expertise in orthopaedic rehabilitation or expertise in orthopaedic or trauma care.
- Cost sharing/matching is not an eligibility requirement.
- Eligible investigators must apply through an organization. Organizations eligible to apply include Federal agencies, national, international, for-profit, nonprofit, public, and private organizations.
- An intramural investigator is defined as a DoD military or civilian employee working within a DoD laboratory or medical treatment facility, or working in a DoD activity embedded within a civilian medical center. Submissions from intramural (DoD) organizations are allowed and encouraged for this Program Announcement/Funding Opportunity. Applicants submitting through their intramural organizations are reminded to coordinate receipt and commitment of funds through their respective resource managers. ***If an investigator at an intramural organization is named as a collaborator on an application submitted through an extramural organization, the application must include a letter from the collaborator's Commander or Commanding Officer at the intramural organization that authorizes the collaborator's involvement.***
- Refer to the General Application Instructions, Appendix 1, for general eligibility information.

E. Funding

- The maximum period of performance is **4** years.
- The anticipated total costs budgeted for the entire period of performance will not exceed **$4.5M**. Indirect costs are to be budgeted in accordance with the organization's negotiated rate. No budget will be approved by the Government exceeding **$4.5M** total costs or using an indirect rate exceeding the organization's negotiated rate.
- 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 **4** years.

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

- Travel costs for the PI and required Qualified Collaborator(s) to disseminate project results at one DoD PRORP In-Progress Review meeting in Year 3. For planning purposes, it should be assumed that the meeting will be held in the National Capital Area. These travel costs are in addition to those allowed for annual scientific/technical meetings.

May be requested for (not all-inclusive):

- Salary
- Clinical trial costs
- Research supplies and equipment
- Research-related subject costs
- Support for multidisciplinary collaborations, including travel
- Travel costs for up to three investigators to travel to two scientific/technical meetings per year in addition to the required IPR meeting described above.

Shall not be requested for:

- Preclinical research costs

Awards to extramural organizations will consist solely of assistance agreements (Cooperative Agreements and Grants). Awards to intramural (DoD) agencies and other Federal agencies may be managed through a direct fund transfer (e.g., the Military Interdepartmental Purchase Request [MIPR]; Funding Authorization Document [FAD] process; or DD Form 1144 Support Agreement). Direct transfer of funds from the recipient to a DoD agency is not allowed except under very limited circumstances. Refer to the General Application Instructions, Section II.C.4., for budget regulations and instructions for the Research & Related Budget. ***For Federal agencies or organizations collaborating with Federal agencies, budget restrictions apply as are noted in Section II.C.4. of the General Application Instructions***.

The CDMRP expects to allot approximately $4.5M of the $30M FY16 PRORP appropriation to fund approximately one Integrated Clinical Trial Award application, depending on the quality and number of applications received. Funding of applications received in response to this Program Announcement/Funding Opportunity is contingent upon the availability of Federal funds for this program.

II. SUBMISSION INFORMATION

Submission of applications that are essentially identical or propose essentially the same research project to different funding opportunities within the same program and fiscal year is prohibited and will result in administrative withdrawal of the duplicative application(s).

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

(2) application submission through Grants.gov (http://www.grants.gov/). Refer to the General Application Instructions, Section II.A., for registration and submission requirements for eBRAP and Grants.gov.

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

eBRAP is a multifunctional web-based system that allows PIs to submit their pre-applications electronically through a secure connection, to view and edit the content of their pre-applications and full applications, to receive communications from the CDMRP, and to submit documentation during award negotiations and period of performance. A key feature of eBRAP is the ability of an organization's representatives and PIs to view and modify the Grants.gov application submissions associated with them. eBRAP will validate Grants.gov application files against the specific Program Announcement/Funding Opportunity requirements and discrepancies will be noted in an email to the PI and in the Full Application Files tab in eBRAP. It is the applicant's responsibility to review all application components for accuracy as well as ensure proper ordering as specified in this Program Announcement/Funding Opportunity.

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

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

A. Where to Obtain the Grants.gov Application Package

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

B. Pre-Application Submission Content

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

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

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

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

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

- **Tab 1 – Application Information**
- **Tab 2 – Application Contacts**
    - Enter contact information for the PI. Enter the organization's Business Official responsible for sponsored program administration (the "person to be contacted on matters involving this application" in Block 5 of the Grants.gov SF424 (R&R) Form). The Business Official must either be selected from the eBRAP list or invited in order for the pre-application to be submitted.
    - Select the performing organization (site at which the PI will perform the proposed work) and the contracting organization (organization submitting on behalf of the PI, which corresponds to Block 5 on the Grants.gov SF424 (R&R) Form), and click on "*Add Organizations to this Pre-application.*" The organization(s) must either be selected from the eBRAP drop-down list or invited in order for the pre-application to be submitted.
    - It is recommended that PIs identify an Alternate Submitter in the event that assistance with pre-application submission is needed.
- **Tab 3 – Collaborators and Key Personnel**
    - Enter the name, organization, and role of all collaborators and key personnel associated with the application.
    - FY16 PRORP Programmatic Panel members should not be involved in any pre-application or application. For questions related to Programmatic Panel members and pre-applications or applications, refer to Section IV.C., Withdrawal, or contact the CDMRP Help Desk at help@eBRAP.org or 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). Applications that include names of personnel from either of these companies will be administratively withdrawn unless plans to manage conflicts of interest (COIs) are provided and deemed appropriate by the Government. Refer to the General Application Instructions, Appendix 1, for detailed information.

- **Tab 4 – Conflicts of Interest**
  - List all individuals other than collaborators and key personnel who may have a COI in the review of the application (including those with whom the PI has a personal or professional relationship). Refer to Appendix 1, Section C, of the General Application Instructions for further information regarding COIs.

- **Tab 5 – Pre-Application Files**

  Note: Upload documents as individual PDF files unless otherwise noted. eBRAP will not allow a file to be uploaded if the number of pages exceeds the limit specified below.

  Preproposal Narrative (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:

  - **Alignment with Focus Areas:** Explain how the proposed work addresses two of the FY16 PRORP Focus Areas (minimum of one from the Surgical Care category and one from the Rehabilitation category, maximum of four total). Describe how the proposed work is cohesive and integrates both surgical and rehabilitation strategies.
  - **Research Idea:** Identify the intervention to be tested and describe the projected outcomes for the cohesive project that includes both surgical and rehabilitation strategies. Describe the ideas and reasoning on which the proposed clinical trial is based; include relevant literature citations. Briefly describe the preliminary scientific evidence that supports the progression of this research into the phase of clinical trial proposed. Clearly specify which type (e.g., drug, device, surgical) of clinical trial is being proposed and indicate the phase of trial and/or class of device and regulatory status, as appropriate.
  - **Research Strategy:** Concisely state the project's hypothesis and/or objectives, specific aims, and endpoint measurements. Briefly describe the patient population(s) to be recruited for the clinical trial, access to the population(s), patient population availability, and the experimental approach. Outline the measures that will be attempted, if necessary, to increase subject throughput and subsequent enrollment.

- **Impact:** Describe how the proposed cohesive project will have an impact on accelerating the movement of a promising treatment into clinical application. Address the project's relevance to patients who have sustained traumatic orthopaedic injuries.
- **Military Benefit:** Explain how the project will benefit military Service members and/or Veterans who have sustained combat-related orthopaedic injuries or non-battle orthopaedic injuries that impact unit readiness and return-to-duty/work. State explicitly how the proposed work may ultimately have an immediate and long-term impact on patient care and/or restoration of function for those who have sustained combat-related orthopaedic injuries.
- **Personnel:** Briefly state the qualifications of the PI, the required Qualified Collaborator(s), and other key personnel to perform the clinical trial (*detailed key personnel biographical sketches [six pages per individual] are allowed as part of pre-application supporting documentation, as described below*). Describe how the success of the project depends on the unique skills and contributions of the PI, the Qualified Collaborator(s), and other key personnel. Note any DoD or VA collaborations.

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

- **References Cited (one-page limit)**: List the references cited (including URLs if available) in the Preproposal Narrative using a standard reference format that includes the full citation (i.e., author[s], year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate
- **List of Abbreviations, Acronyms, and Symbols**: Provide a list of abbreviations, acronyms, and symbols used in the Preproposal Narrative.
- **Key Personnel Biographical Sketches (six-page limit per individual):** ***All biographical sketches should be uploaded as a single combined file.*** Biographical sketches should be used to demonstrate background and expertise through education, positions, publications, and previous work accomplished.
- **Quad Chart: Upload as "QuadChart.ppt."**: The Quad Chart template is a one-page PowerPoint file that must be downloaded from eBRAP at https://ebrap.org/eBRAP/public/Program.htm in the "Generic Forms for Application Submission" section, then completed and saved as a PPT or PPTX file.

- **Tab 6 – Submit Pre-Application**
  - This tab must be completed for the pre-application to be accepted and processed.

Pre-Application Screening

- **Pre-Application Screening Criteria**

  To determine the technical merits of the pre-application and the relevance to the mission of the DHP and the PRORP, pre-applications will be screened based on the following criteria:

  - **Research Idea:** How well the rationale is supported, and how well the background provided indicates the research is ready to move into a clinical trial. The degree to which the proposed clinical trial addresses the intent of the award mechanism and aligns with at least two of the FY16 PRORP Focus Areas (a minimum of one from the Surgical Care category and one from the Rehabilitation category).
  - **Research Strategy:** How well the specific aims, patient population, patient access, patient availability, and proposed methodology will address the hypothesis and achieve the desired outcomes. The degree to which the clinical volume or measures to increase volume and enrollment are likely to provide an adequately powered study.
  - **Impact:** The extent to which the study will make important contributions to patient care and/or restoration of function for those who have sustained traumatic orthopaedic injuries.
  - **Military Benefit:** The degree to which the proposed clinical trial, if successful, will improve clinical care for military Service members and Veterans who have sustained combat-related orthopaedic injuries or non-battle orthopaedic injuries that impact unit readiness and return-to-duty/work.
  - **Personnel:** How the background and experience of the PI, the required Qualified Collaborator(s), and other key personnel are appropriate to successfully complete the clinical trial. To what extent the unique skills and contributions of all key personnel contribute to the achievement of the desired outcomes.

- **Notification of Pre-Application Screening Results**

  Following the pre-application screening, PIs will be notified as to whether or not they are invited to submit applications; however, they will not receive feedback (e.g., a critique of strengths and weaknesses) on their pre-application. The estimated timeframe for notification of invitation to submit an application is indicated on the title page of this Program Announcement/Funding Opportunity. Invitations to submit a full application are based on the Pre-Application Screening Criteria as published above.

C. Full Application Submission Content

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

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

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

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

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

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

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

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

Grants.gov application package components: For the Integrated Clinical Trial Award, the Grants.gov application package includes the following components (refer to the General Application Instructions, Section II.C., for additional information on application submission):

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

2. **Attachments Form**

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

   The Project Narrative is NOT the formal clinical trial protocol. Instead, all essential elements of the proposed clinical trial necessary for scientific review must be included as directed in Attachment 1 (the Project Narrative) and Attachments 6-9 described below. Failure to submit these attachments as part of the application package will result in rejection of the entire application.

- **Attachment 1: Project Narrative (25-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, noting potential challenges and alternative solutions where appropriate.

  - **Background:** Describe in detail the rationale for the cohesive study that includes both surgical and rehabilitation strategies. Provide a literature review and describe the preliminary studies and/or preclinical data that led to the development of the proposed clinical trial. Provide a summary of other relevant ongoing, planned, or completed clinical trials and describe how the proposed study differs. Include a discussion of any current clinical use of the intervention under investigation, and/or details of its study in clinical trials for other indications (as applicable). The background section should clearly support the choice of study variables and should explain the basis for the study questions and/or study hypotheses. This section should establish the relevance of the study and explain the applicability of the proposed findings to the relevant FY16 PRORP Focus Areas.

    If the proposed clinical trial was initiated using other funding prior to this application, explain the history and background of the clinical trial and declare the source of prior funding. Specifically identify the portions of the study that would be supported with funds from this award.

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

  - **Study Design:** Describe the scope (pilot, Phase 0, Phase 1, etc.) and type of study to be performed (e.g., prospective, randomized, controlled) and outline the proposed methodology in sufficient detail to show a clear course of action. Describe potential challenges and alternative strategies where appropriate.

    - State the intervention to be tested and describe the projected outcomes.
    - Define the study variables (e.g., active drug, dose-response, etc.), outline why they were chosen, and describe how they will be measured. Include a description of appropriate controls and the endpoints to be tested.
    - Describe the study population and inclusion and exclusion criteria that will be used.
    - 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 how patient follow-up, as well as subject withdrawal, will be addressed.
- 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).
- If using psychometric measures, describe their reliability and validity.

- **Statistical Plan and Data Analysis:** Describe the statistical model and data analysis plan with respect to the study objectives. Specify the approximate number of human subjects to be enrolled. If multiple study sites are involved, state the approximate number to be enrolled at each site. Include a complete power analysis to demonstrate that the sample size is appropriate to meet the objectives of the study. Describe analytical techniques for managing multiple sites and care providers contributing patients to 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. All interim analyses (formal or informal, pre-planned or ad hoc) should be addressed in full.
- **Access to Target Population/Enrollment Strategy:** Describe access to the target population for the proposed study. Based on clinical volume reported in pre-application and updated for this submission (number of patients per month for last 12 months), state the projected quarterly enrollment for each study site (as appropriate), and provide a contingency plan, including a threshold at which the plan will be implemented, to be executed if enrollment fails to meet expectations.

- **Attachment 2: Supporting Documentation.** Start each document on a new page. Combine and upload as a single file named "Support.pdf." If documents are scanned to pdf, the lowest resolution (100 to 150 dpi) should be used. ***There are no page limits for any of these components unless otherwise noted. Include only those components described below; inclusion of items not requested will result in the removal of those items or may result in administrative withdrawal of the application.***
  - References Cited: List the references cited (including URLs, if available) in the Project Narrative using a standard reference format that includes the full citation (i.e., author[s], year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).
  - List of Abbreviations, Acronyms, and Symbols: Provide a list of abbreviations, acronyms, and symbols.
  - Facilities, Existing Equipment, and Other Resources: Describe the facilities and equipment available for performance of the proposed project and any additional facilities or equipment proposed for acquisition at no cost to the award. Indicate whether or not Government-furnished facilities or equipment are proposed for

use. If so, reference should be made to the original or present Government award under which the facilities or equipment items are now accountable. There is no form for this information.

- Publications and/or Patents: Include a list of relevant publication URLs and/or patent abstracts. If publications are not publicly available, then copies of up to five published manuscripts may be included in Attachment 2. Extra items will not be reviewed.
- Letters of Organizational Support (one-page limit per letter): 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 Confirming Access to Military or VA Patient 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 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.
- Letters of Collaboration (one-page limit per letter): 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. Include a letter from the Required Qualified Collaborator(s) describing his/her involvement in the proposed work.
- Letters of Commitment (if applicable) (one-page limit per letter): If the proposed study involves use of a commercially produced investigational drug, device, or biologic, provide a letter of commitment from the commercial entity indicating availability of the product for the duration of the study, support for the proposed phase of research, and support for the indication to be tested.
- Intellectual Property
  - Intangible property acquired, created, or developed under this award will be subject to all rights and responsibilities established at 2 CFR 200.315. Should the applicant intend to use, in the performance of this program, pre-existing, legally protected and perfected intangible property and for which no Federal funds had been used in the development of said property, the applicant must:
    - Clearly identify all such property;
    - Identify the cost to the Federal government for use or license of such property, if applicable; or
    - Provide a statement that no property meeting this definition will be used on this project.

        - Intellectual and Material Property Plan (if applicable): Provide a plan for resolving intellectual and material property issues among participating organizations.
    - Data and Research Resources Sharing Plan: Describe how data and resources generated during the performance of the project will be shared with the research community. Refer to the General Application Instructions, Appendix 4, Section K for more information about the CDMRP expectations for making data and research resources publicly available.

- **Attachment 3: Technical Abstract (one-page limit): Upload as "TechAbs.pdf."** The technical abstract is used by all reviewers. Abstracts of all funded research projects will be posted publicly. ***Do not include proprietary or confidential information.*** Use only characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed.
    - Background: State the FY16 PRORP Focus Areas (minimum of one from the Surgical Care category and one from the Rehabilitation category, maximum of four total) that will be addressed by the proposed research and briefly describe how the collaborative effort cohesively addresses these Focus Areas. Present the ideas and rationale behind the proposed clinical trial.
    - Objective/Hypothesis: State the objective to be reached/hypothesis to be tested.
    - Specific Aims: State the specific aims of the study.
    - Study Design: Briefly describe the study design including appropriate controls.
    - Military Benefit and Clinical Impact: State briefly how the proposed project, if successful, will have an immediate and/or long-term impact on optimizing recovery and restoration of function for Service members and/or Veterans with orthopaedic injuries sustained in combat or combat-related activities, as well as their family members, caregivers, and the general public. Briefly describe how the proposed project will have an impact on patient care for those who have sustained traumatic orthopaedic injuries.

- **Attachment 4: Lay Abstract (one-page limit): Upload as "LayAbs.pdf."** The lay abstract is used by all reviewers. Abstracts of all funded research projects will be posted publicly. ***Do not include proprietary or confidential information and do not duplicate the technical abstract.*** Use only characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed.
    - Clearly describe the objectives and rationale for the proposed study in a manner readily understood by readers without a background in science or medicine.
    - Describe the ultimate applicability and impact of the research.
        - Which FY16 PRORP Focus Areas (a minimum of one from the Surgical Care category and one from the Rehabilitation category, maximum of four total) will be addressed?

- What types of patients will it help, and how will it help them?
- What are the potential clinical applications, benefits, and risks?
- What is the projected timeline it may take to achieve the expected patient-related outcome?

- Describe how the proposed project will benefit Service members and/or Veterans who sustained combat-related orthopaedic injuries, as well as their families, caregivers, and the general public.

- **Attachment 5: Statement of Work (SOW) (three-page limit): Upload as "SOW.pdf."** The suggested SOW format and examples specific to different types of research projects are available on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm). For the Integrated Clinical Trial Award mechanism, use the SOW format example titled "SOW for Clinical Research (Including Trials, Special Populations)." The SOW must be in PDF format prior to attaching. Refer to the General Application Instructions, Section II.C.2., for detailed guidance on creating the SOW.

- **Attachment 6: Human Subject Recruitment and Safety Procedures (no page limit): Upload as "HumSubProc.pdf."** The Human Subject Recruitment and Safety Procedures attachment should include the components listed below.

  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 trials (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 trials proposing to include military personnel as volunteers, refer to the General Application Instructions, Appendix 6, for more information.***

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

  Inclusion of Women and Minorities in Study. Consistent with the Belmont Report, "Ethical Principles and Guidelines for the Protection of Human Subjects," and Congressional legislation, special attention is given to inclusion of women and/or minorities in studies funded or supported by the 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 trial.

c. Description of the Recruitment Process: Explain methods for identification of potential human subjects (e.g., medical record review, obtaining sampling lists, health care provider identification). ***Include a description of any considerations unique to recruitment from military treatment facilities or VA medical centers, if applicable.***

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

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 trial.
- Include information regarding the timing and location of the consent process.
- Address issues relevant to the mental capacity of the potential human subject (e.g., altered capacity due to administration of any mind-altering substances such as tranquilizers, conscious sedation or anesthesia, brain injury, stress/life situations, or human subject age), if applicable.
- Address how privacy and time for decision making will be provided and whether or not the potential human subject will be allowed to discuss the study with anyone before making a decision.
- Consider the need for obtaining ongoing consent or for re-assessing capacity over the course of a long-term study and describe any relevant procedures to assure continued consent.
- Describe the plan for the consent of the individual's Legally Authorized Representative (LAR) to be obtained prior to the human subject's participation in the study. State law defines who may act as the LAR. The local IRB of record should be consulted for guidance regarding who can serve as LAR for research at the study site. Note: The PI must describe a clear intent to benefit for human subjects who cannot give their own consent to participate in the proposed clinical trial to be in compliance with Title 10 United States Code Section 980 (10 USC 980) (http://www.gpo.gov/fdsys/pkg/USCODE-2011-title10/pdf/USCODE-2011-title10-subtitleA-

partII-chap49-sec980.pdf). If applicable, refer to the General Application Instructions, Appendix 6, for more information.

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

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. Please 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 trial. Consider psychological, legal, social, and economic risks as well as physical risks. If the risks are unknown, this should be stated. If applicable, any potential risk to the study personnel should be identified.
- **Risk management and emergency response:**
  - Describe how safety surveillance and reporting to the IRB and FDA (if applicable) will be managed and conducted.
  - Describe all safety measures to minimize and/or eliminate risks to human subjects and study personnel or to manage unpreventable risks. 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.
  - If the IRB determines that a trial presents greater than minimal risk to human subjects, the DoD requires an independent research monitor with expertise consistent with the nature of risk(s) identified within the research protocol. If applicable, refer to the General Application

Instructions, Appendix 6, for more information on study reporting authorities and responsibilities of the research monitor.

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

- **Attachment 7: Intervention (no page limit): Upload as "Intervention.pdf."** The Intervention attachment should include the components listed below.

  a. Description of the Intervention: State the intervention to be tested and describe the particular outcomes. As applicable, the description of the intervention should include the following components: complete name and composition, storage and handling information, source, dose, schedule, administration route, washout period, duration of the intervention, and concomitant medications allowed. Description of devices should include general concept of design, detailed operational instructions, any potential risks to users, and intended benefits. Other types of interventions should be fully described.

  Summarize key preclinical pharmacological findings, dosage studies, and other clinical studies (if applicable) that examine the safety of the intervention.

  b. Study Procedures: 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 (GLPs), Good Manufacturing Practices (GMPs), and other regulatory considerations will be established, monitored, and maintained, as applicable.

  c. Clinical Monitoring Plan: Describe how the study will be conducted by and monitored for ICH E6 (International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use) GCP compliance, by an independent clinical trial monitor (or clinical research associate). The monitoring plan should describe the types of monitoring visits to be conducted, the intervals (based on level of risk), how corrective actions will be reported to the Sponsor and PI, and how they will be corrected and prevented by the clinical trial site/PI.

- **Attachment 8: Data Management (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.
- **Data reporting:** Describe how data will be reported and how it will be assured that the documentation will support a regulatory filing with the FDA, if applicable.
- **Sharing study results:** In cases where the human subject could possibly benefit medically or otherwise from the information, explain whether or not the results of screening and/or study participation will be shared with human subjects or their primary care provider, to include results from any screening or diagnostic tests performed as part of the study.

b. Laboratory Evaluations:

- **Specimens to be collected, schedule, and amount:** All specimens that will be collected for study purposes must be clearly stated. The collection schedule and amount of material collected must also be clearly described.
- **Evaluations to be made:** Describe all evaluations that will be made for study purposes. Explain how the results of laboratory evaluations will be used to meet the objectives of the study (or to monitor safety of human subjects).
- **Storage:** Describe specimen storage, to include location of storage, how long specimens will be stored, any special conditions required, labeling, and specimen disposition. Outline the plan to store specimens for future use to include considerations for informed consent and providing human subjects with an opportunity to decline participation in the study.
- **Labs performing evaluations and special precautions:** Identify the laboratory performing each evaluation, as well as any special precautions that should be taken in handling the samples. Special precautions that

should be taken by the human subject before, during, or after the laboratory procedure should be clearly defined. If transport of samples is required, describe provisions for ensuring proper storage during transport.

- **Attachment 9: Study Personnel and Organization (no page limit): Start each document on a new page. Combine into one document and upload as "Personnel.pdf."** The Study Personnel and Organization attachment should include the components listed below.

  a. Organizational Chart: Provide an organizational chart identifying key members of the study team including institution/center/department and name each person's role on the project. If the study is determined to be greater than minimal risk by the local IRB of record, a medical monitor (external to the study and not reimbursed by the study) and study coordinator(s) should be included. If applicable, include any external consultants or other experts who will assist with FDA applications. While there is no specified format for this information, a table(s) or diagram is recommended. Note: This item may be made available for programmatic review.

  b. Study Personnel Description: Briefly describe the roles of the individuals listed in the organizational chart on the project. Describe relevant experience and qualifications that demonstrate appropriate expertise for the given role. An external research monitor (if applicable) and study coordinator(s) should be included.

  c. Study Management Plan: Provide a plan for ensuring the standardization of procedures among staff and across sites (if applicable). If the proposed clinical trial is multi-institutional, plans for communication and data transfer between the collaborating institutions, as well as how data, specimens, and/or imaging products obtained during the study will be handled, should be included. Provide a plan for real-time communication among collaborating institutions (if applicable).

  d. Qualified Collaborator Statement: Provide a statement that identifies the Qualified Collaborator(s) and addresses all criteria, as described in Section I.C., Award Information. It should be clear that the success of the project depends on the unique skills and contributions of both the PI and the Qualified Collaborator(s).

- **Attachment 10: Military Benefit and Clinical Impact Statement (two-page limit). Upload as "MilBenClinImpact.pdf."**

  State explicitly how the proposed clinical trial, if successful, will accelerate the movement of the product, pharmacologic agent, device, procedure, clinical guidance, and/or emerging technology into clinical practice for those Service members and/or Veterans who have sustained combat-related orthopaedic injuries. Further, describe the impact of this study on the lives of individuals recovering from combat-related or non-battle orthopaedic injuries, including but not limited to how the expected results of the proposed work will contribute to the goal of decreasing the clinical impact of these injuries. When applicable, also describe the

impact of the study on unit readiness and return-to-duty/work capabilities. The following are examples of ways in which proposed studies, if successful, may demonstrate military benefit. ***Although not all-inclusive***, these examples are intended to help PIs frame the military relevance of the proposed research:

- Has the potential to change the standard of care for military orthopaedic injuries
- Proposes new paradigms or challenges existing paradigms in patient care of military orthopaedic injuries
- Contributes to development or validation of evidence-based policy or guidelines for patient evaluation and care of military orthopaedic injuries

Demonstrate how the proposed study is responsive to the healthcare needs of the military Service members and/or the Veteran population. If active duty military or Veteran population(s) will be used in the proposed research project, describe the population(s), the appropriateness of the population(s) for the proposed study, and the feasibility of using the population(s). If a non-military population will be used for the proposed research project, explain how the population simulates the targeted population (i.e., military Services and/or the Veteran population). Show how the proposed study complements ongoing DoD or VA areas of orthopaedic research interest, if applicable. Describe how the study design will replicate field conditions, if applicable.

- Describe the potential impact of the proposed clinical trial the outcomes of individuals with regard to the FY16 PRORP Focus Areas addressed in the application.
- ***Describe the short-term impact:*** Detail the anticipated outcomes that will be directly attributed to the results of the proposed clinical trial.
- ***Describe the long-term impact:*** Explain the long-range vision for implementation of the intervention in the clinic or field, and describe the anticipated long-term benefits for the targeted population.
- Describe any relevant controversies or treatment issues that will be addressed by the proposed clinical trial.
- Describe any potential issues that might limit the impact of the proposed clinical trial.
- Describe how the intervention represents an improvement over currently available interventions and/or standards of care, if applicable.

- **Attachment 11: Transition Plan (one-page limit). Upload as "Transition.pdf."** Describe/discuss the methods and strategies proposed to move the intervention to the next phase of development (clinical trials, commercialization, and/or delivery to the civilian or military market) after successful completion of the award. Outline the regulatory strategy. Applicants are encouraged to work with their organization's Technology Transfer Office (or equivalent) to develop the transition plan. PIs are encouraged to explore developing relationships with industry and/or other funding agencies to facilitate moving the product into the next phase of

development. The post-award transition plan should include the components listed below.

- The planned indication for the product label, if appropriate, and an outline of the development plan required to support that indication.
- Describe in detail the FDA regulatory strategy, to include considerations for compliance with GMP, GLP, and Good Clinical Practice (GCP) (if appropriate).
- Details of the funding strategy to transition to the next level of development and/or commercialization (e.g., partners, internal/external funding opportunities to be applied for).
- For Knowledge Products, a description of collaborations and other resources that will be used to provide continuity of development including proposed development or modification of CPGs and recommendations, provider training materials, patient brochures, and other clinical support tools, scientific journal publications, models, simulations, and applications. A "Knowledge Product" is a non-materiel product that addresses an identified need, topic area, or capability gap, is based on current evidence and research, aims to transition into medical practice, training, tools, or to support materiel solutions (systems to develop, acquire, provide, and sustain medical solutions and capabilities), and educates or impacts behavior throughout the continuum of care, including primary prevention of negative outcomes.
- A brief schedule and milestones for transitioning the intervention to the next phase of development (next-phase clinical trials, commercialization, delivery to the military or civilian market, incorporation into clinical practice, and/or approval by the FDA). Include identification of the FDA regulatory strategy (if appropriate).
- Ownership rights/access to the intellectual property necessary for the development and/or commercialization of products or technologies supported with this award and the Government's ability to access such products or technologies in the future.
- A description of collaborations and other resources that will be used to provide continuity of development.
- A risk analysis for cost, schedule, manufacturability, and sustainability.

- **Attachment 12: IND/IDE Documentation (no page limit):** If submitting multiple documents, start each document on a new page. **Combine and upload as a single file named "IND-IDE.pdf."**
  - Complete the IND/IDE Documentation Form, which is available for download on the Full Announcement page for this Program Announcement/Funding Opportunity on Grants.gov.
  - State whether the trial requires regulation by the FDA. If FDA regulation is required, describe the planned indication for the proposed product and whether

an IND/IDE is necessary. If an IND or IDE is required, it must be submitted to the FDA ***within 6 months of the award date.***

- If an IND or IDE has already been obtained for the investigational drug or device pertaining to the indication to be studied, provide evidence in the form of formal communication (e.g., letterhead correspondence) from the FDA.
- If an IND or IDE application has been submitted and is still pending, indicate when it was submitted and provide an explanation of the status of the IND or IDE application (e.g., past the critical 30-day period, pending response to questions raised by the FDA, on clinical hold).
- Identify any consultants or experts who will assist in the regulatory application, if applicable, and include a copy of any curricula vitae or biographical sketches in the Key Personnel Biographical Sketches section of the application. Provide a summary of previous meetings with the FDA on development of this product, if appropriate. A copy of the Agency meeting minutes should be included if available. Provide copies of communications from the FDA relevant to the most recent status of the IND or IDE application.
- If the IND or IDE application is not yet submitted, provide evidence that an IND or IDE will be submitted ***within 6 months of award date***. Examples include results and minutes of a pre-IND or pre-IDE meeting with the FDA, a pre-IND/pre-IDE meeting request to the FDA, or other communication with the FDA. Provide the anticipated date of IND/IDE submission.
- If an IND or IDE is not required for the proposed study, or if it qualifies for an abbreviated IDE, provide evidence in the form of formal communication (e.g., letterhead correspondence) from the FDA or the IRB of record to that effect. Devices qualifying for an abbreviated IDE must comply with the abbreviated IDE requirements but do not require the submission of an IDE application to the FDA.

- **Attachment 13: Surveys, Questionnaires, and Other Data Collection Instruments, if applicable (no page limit): Upload as "Surveys.pdf."** The Surveys, Questionnaires, and Other Data Collection Instruments attachment should include a copy of the most recent version of surveys, questionnaires, data collection forms, rating scales, interview guides, or other instruments. For each instrument, describe how the information collected is related to the objectives of the study. Describe how and when the instrument(s) will be administered. Describe how the instrument(s) will be adapted to the subject population, if applicable.

- **Attachment 14: Collaborating DoD Military Facility Budget Form(s), if applicable: Upload as "MFBudget.pdf."** If a Military Facility (military health system facility, research laboratory, treatment facility, dental treatment facility, or a DoD activity embedded with a civilian medical center) will be a collaborator in performance of the project, complete the Collaborating DoD Military Facility Budget Form, available for download on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm), including a budget justification, for each Military Facility as instructed. The costs per year

should be included on the Grants.gov Research and Related Budget form under subaward costs. Refer to the General Application Instructions, Section II.C.7., for detailed information**.**

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

   - PI Biographical Sketch (six-page limit): Upload as "Biosketch_LastName.pdf." The suggested biographical sketch format is available on the "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) in eBRAP. The National Institutes of Health Biographical Sketch may also be used. All biographical sketches should be submitted in the portable document format (pdf) that is not editable.

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

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

4. **Research & Related Budget:** Refer to the General Application Instructions, Section II.C.4., for detailed information.

   - Budget Justification (no page limit): Upload as "BudgetJustification.pdf." The budget justification for the entire period of performance must be uploaded to the Research & Related Budget after completion of the budget for Period 1.

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

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

   Collaborating DoD Military Facilities Form: A Military Facility collaborating in the performance of the project should be treated as a subaward for budget purposes. However, do not complete the Grants.Gov R & R Subaward Budget Attachment Form; instead, complete the Collaborating DoD Military Facility Budget Form (use Attachment 14, Collaborating DoD Military Facility Budget Form) to show all direct and indirect costs. The costs per year should be included on the Grants.gov Research and Related Budget form under subaward costs. Refer to the General Application Instructions, Section II.C.7., for detailed information.

D. Applicant Verification of Grants.gov Submission in eBRAP

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

E. Submission Dates and Times

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

F. Other Submission Requirements

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

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

III. APPLICATION REVIEW INFORMATION

A. Application Review and Selection Process

All applications are evaluated by scientists, clinicians, and consumers in a two-tier review process. The first tier is peer review of applications against established criteria for determining technical merit. Each application is evaluated for its own merit, independent of other applications. The second tier is a programmatic review that makes recommendations for funding to the DHA RDA Directorate and the OASD(HA), based on technical merit, the relevance to the mission of the DHP and PRORP, the specific intent of the award mechanism, and to other specified evaluation criteria in the Program Announcement/Funding Opportunity. Programmatic review is a comparison-based process in which applications with scientific and technical merit compete in a common pool. ***The highest-scoring applications from the first tier of review are***

not automatically recommended for funding. Funding recommendations depend on various factors as described in Section III.B.2., Programmatic Review. Additional information about the two-tier process used by the CDMRP can be found at http://cdmrp.army.mil/about/fundingprocess.

All CDMRP review processes are conducted confidentially to maintain the integrity of the meritbased selection process. Panel members sign a statement that application and evaluation information will not be disclosed outside the panel. Violations of confidentiality can result in the dissolving of a panel(s) and other corrective actions. In addition, personnel at the applicant or collaborating organizations are prohibited from contacting persons involved in the review process to gain protected evaluation information or to influence the evaluation process. Violations of these prohibitions will result in the administrative withdrawal of the organization's application. Violations by panel members or applicants that compromise the confidentiality of the review process may also result in suspension or debarment from Federal awards. Furthermore, the unauthorized disclosure of confidential information of one party to another third party is a crime in accordance with Title 18 United States Code 1905.

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:

   - **Military Benefit and Clinical Impact**
     - How well the proposed clinical trial addresses a minimum of two (one from the Surgical Care category and one from the Rehabilitation category, maximum of four total) FY16 PRORP ICTA Focus Areas.
     - How relevant the anticipated outcomes of the proposed clinical trial are to individuals with orthopaedic injuries.
     - How well the project addresses a critical issue in treatment of non-battle orthopaedic injuries that impact unit readiness and the ability to return to work/ duty, if applicable.
     - To what extent the practical application of the proposed intervention will have a long-term benefit for individuals with combat-related orthopaedic injuries and impact patient care and/or quality of life.
     - How well the proposed study population represents the targeted patient population that might benefit from the proposed intervention.
     - How the potential outcomes of the proposed clinical trial will provide/improve short-term benefits for individuals with orthopaedic injuries.
     - To what degree the intervention represents an improvement over currently available interventions and/or standards of care.
   - **Research Strategy**
     - How well the scientific rationale for the proposed clinical trial is supported by the preliminary data, critical review and analysis of the literature, and/or laboratory/preclinical evidence.

- How well the study aims, hypotheses and/or objectives, experimental design, methods, data collection procedures, and analyses are designed to address the clinical objective.
- How well the inclusion and randomization criteria meet the needs of the proposed clinical trial.
- How well the exclusion criteria are justified.
- How well plans to collect specimens and conduct laboratory evaluations are addressed, if applicable.
- To what degree the data collection instruments (e.g., surveys, questionnaires), if applicable, are appropriate to the proposed study.

- **Statistical Plan**
  - To what degree the statistical model and data analysis plan are suitable for the planned study.
  - How the statistical plan, including sample size projections and power analysis, is adequate for the study and all proposed correlative studies.
  - If applicable, whether the statistical plan compensates for the use of a subpopulation of a recruited sample population to ensure appropriate power can be achieved within the subpopulation study.
- **Intervention**
  - Whether there is evidence of support, indicating availability of the intervention from its source, for the duration of the proposed clinical trial (if applicable).
  - To what degree the intervention addresses the clinical need(s) described.
  - To what degree the PI has provided preclinical and/or clinical evidence to support the safety of the intervention.
  - To what degree the regulatory strategy is well-described and feasible including:
    - Whether a member of the study team holds the IND/IDE for the indication proposed or whether the timeline proposed for obtaining the IND/IDE, abbreviated IDE, or exemption is appropriate (if applicable).
    - For investigator-sponsored INDs, whether there is evidence of appropriate institutional support, including capabilities to ensure monitoring as required by the FDA.
    - Whether plans to comply with GMP, GLP, and GCP guidelines are appropriate.
  - Whether measures are described to ensure the consistency of dosing of active ingredients for nutritional supplements (if applicable).
- **Recruitment, Accrual, and Feasibility**
  - How well the PI addresses the availability of human subjects for the clinical trial and the prospect of their participation.

- Whether the PI has demonstrated access to the proposed human subject population.
- The degree to which the recruitment, informed consent, screening, and retention processes for human subjects will meet the needs of the proposed clinical trial.
- How well the application identifies possible delays (e.g., slow accrual, attrition) and presents adequate contingency plans to resolve them.
- To what extent the current clinical volume and proposed measures to increase volume ensure adequate study enrollment, if applicable.
- To what extent the proposed clinical trial might affect the daily lives of the individual human subjects participating in the study (e.g., Will human subjects still be able to take their regular medications while participating in the clinical trial? Are human subjects required to stay overnight in a hospital?)

- **Ethical Considerations**
  - How the level of risk to human subjects is minimized, and how the safety monitoring and reporting plan is appropriate for the level of risk.
  - How well the evidence shows that the procedures are consistent with sound research design and, when appropriate, that these procedures are already in use for diagnostic or treatment purposes.
  - Whether a research monitor with expertise consistent with the nature of the potential risk(s) is identified, if applicable.
  - To what degree privacy issues are appropriately considered.
  - To what degree the process for seeking informed consent is appropriate and whether safeguards are in place for vulnerable populations.
- **Transition Plan and Regulatory Strategy**
  - Whether the identified next level of development and/or commercialization is realistic.
  - Whether the funding strategy described to bring the intervention to the next level of development (e.g., higher phase clinical trial, transition to industry, delivery to the market, incorporation into standard practice, approval by the FDA) is reasonable and realistic.
  - How the regulatory strategy and development plan to support a product label change, if applicable, are appropriate and well described.
  - Whether the proposed collaborations and other resources for providing continuity of development, including proposed development or modification of clinical practice guidelines and recommendations, provider training materials, patient brochures, and other clinical support tools, scientific journal publications, models, simulations, and applications are established and/or achievable.
  - How the schedule and milestones for bringing the intervention to the next level of development (e.g., higher phase clinical trial, transition to industry, delivery

to the market, incorporation into standard practice, and/or approval by the FDA) are achievable.

- Whether the risk analysis for cost, schedule, manufacturability, and sustainability is realistic and reasonable.
- How well the application identifies intellectual property ownership, describes an appropriate intellectual and material property plan among participating organizations (if applicable), and addresses the impact of any intellectual property issues on product development and subsequent Government access to products supported by this Program Announcement/Funding Opportunity.

- **Personnel and Communication**
  - Whether the composition of the study team (e.g., study coordinator, statistician) is appropriate.
  - To what degree the study team's background and expertise are appropriate to accomplish the proposed work (e.g., statistical expertise, expertise in the disease, and clinical studies).
  - Whether the Required Qualified Collaborator's experience, expertise, and involvement in the study significantly contribute to the project such that the proposed work could not be accomplished without his/her involvement.
  - Whether the Required Qualified Collaborator is contributing both intellectual input and research resources to the project.
  - To what extent the levels of effort are appropriate for successful conduct of the proposed trial.
  - How well the logistical aspects of the proposed clinical trial (e.g., communication plan, data transfer and management, standardization of procedures) meet the needs of the proposed clinical trial.

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

- **Environment**
  - To what degree the scientific environment, clinical setting, and the accessibility of institutional resources support the clinical trial at each participating center or institution (including collaborative arrangements).
  - Whether there is evidence for appropriate institutional commitment from each participating institution.
- **Budget**
  - Whether the budget is appropriate for the proposed research and within the limitations of this Program Announcement/Funding Opportunity.
- **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 criteria are used by programmatic reviewers:

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

   b. **Relevance to the mission of the DHP and FY16 PRORP, as evidenced by the following:**

      - Adherence to the intent of the award mechanism
      - Program portfolio composition
      - Regulatory and developmental risk
      - Relative military benefit and clinical impact

C. Recipient Qualification

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

D. Application Review Dates

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

E. Notification of Application Review Results

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

IV. ADMINISTRATIVE ACTIONS

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

A. Rejection

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

- Preproposal Narrative 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.
- Human Subject Recruitment and Safety Procedures (Attachment 6) is missing.

- Intervention (Attachment 7) is missing.
- Data Management (Attachment 8) is missing.
- Study Personnel and Organization (Attachment 9) 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:

- An FY16 PRORP 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 PRORP Programmatic Panel members can be found at http://cdmrp.army.mil/prorp/panels/panels16***.
- The application fails to conform to this Program Announcement/Funding Opportunity description to the extent that appropriate review cannot be conducted.
- Inclusion of URLs, with the exception of links in References Cited and Publication and/or Patent Abstract sections.
- Page size is larger than 8.5 inches x 11.0 inches (approximately 21.59 cm x 27.94 cm).
- To preserve the integrity of its peer and programmatic review processes, the CDMRP discourages inclusion of any employee of its review contractors having any role in the preparation, research or other duties for submitted applications. For FY16, the identities of the peer review contractor and the programmatic review contractor may be found at the CDMRP website (http://cdmrp.army.mil/about/2tierRevProcess). Applications that include names of personnel from either of these companies will be administratively withdrawn unless plans to manage COIs are provided and deemed appropriate by the Government. Refer to the General Application Instructions, Appendix 1, for detailed information.
- Personnel from applicant or collaborating organizations are found to have contacted persons involved in the review process to gain protected evaluation information or to influence the evaluation process.
- The proposed research is not a clinical trial.
- The proposed project includes preclinical animal research.
- Submission of the same research project to different Funding Opportunities within the same program and fiscal year.

D. Withhold

Applications that appear to involve research misconduct will be administratively withheld from further consideration pending organizational investigation. The organization will be required to provide the findings of the investigation to the USAMRAA Grants Officer for a determination of the final disposition of the application.

V. AWARD ADMINISTRATION INFORMATION

A. Award Notice

Awards will be made no later than September 30, 2017. Refer to the General Application Instructions, Appendix 4, for additional award administration information.

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

B. Administrative Requirements

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

C. National Policy Requirements

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

D. Reporting

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

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

E. Award Transfers

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

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

VI. VERSION CODES AND AGENCY CONTACTS

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

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

B. CDMRP Help Desk

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

Phone: 301-682-5507

Email: help@eBRAP.org

C. Grants.gov Contact Center

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

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

Email: support@grants.gov

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

VII. APPLICATION SUBMISSION CHECKLIST

Grants.gov Application Components	Upload Order	Action	Completed
SF-424 (R&R) Application for Federal Assistance		Complete form as instructed.	
Attachments Form	1	Project Narrative: Upload as Attachment 1 with file name "ProjectNarrative.pdf."	
	2	Supporting Documentation: Upload as Attachment 2 with file name "Support.pdf."	
	3	Technical Abstract: Upload as Attachment 3 with file name "TechAbs.pdf."	
	4	Lay Abstract: Upload as Attachment 4 with file name "LayAbs.pdf."	
	5	Statement of Work: Upload as Attachment 5 with file name "SOW.pdf."	
	6	Human Subject Recruitment and Safety Procedures: Upload as Attachment 6 with file name "HumSubProc.pdf."	
	7	Intervention: Upload as Attachment 7 with file name "Intervention.pdf."	
	8	Data Management: Upload as Attachment 8 with file name "Data_Manage.pdf."	
	9	Study Personnel and Organization: Upload as Attachment 9 with file name "Personnel.pdf."	
	10	Military Benefit and Clinical Impact Statement: Upload as Attachment 10 with file name "MilBenClinImpact.pdf."	
	11	Transition Plan: Upload as Attachment 11 with file name "Transition.pdf."	
	12	IND/IDE Documentation: Upload as Attachment 12 with file name "IND-IDE.pdf."	
	13	Surveys, Questionnaires, and Other Data Collection Instruments: Upload as Attachment 13 with file name "Surveys.pdf," if applicable.	
	14	Collaborating DoD Military Facility Budget Form(s): Upload Attachment 14 with file name "MFBudget.pdf," if applicable.	
Research & Related Senior/Key Person Profile (Expanded)		Attach PI Biographical Sketch (Biosketch_LastName.pdf) to the appropriate field.	
		Attach PI Previous/Current/Pending Support (Support_LastName.pdf) to the appropriate field.	
		Attach Biographical Sketch (Biosketch_LastName.pdf) for each senior/key person to the appropriate field.	
		Attach Previous/Current/Pending (Support_LastName.pdf) for each senior/key person to the appropriate field.	
Research & Related Budget		Complete as instructed. Attach Budget Justification (BudgetJustification.pdf) to the appropriate field.	
Project/Performance Site Location(s) Form		Complete form as instructed.	
R & R Subaward Budget Attachment(s) Form		Complete form as instructed.	