

Program Announcement

for the

Defense Health Program

Defense Medical Research and Development Program

Department of Defense

Congressionally Directed Medical Research Programs

Peer Reviewed Orthopaedic Research Program

Clinical Trial Development Award

Funding Opportunity Number: W81XWH-14-PRORP-CTDA

Catalog of Federal Domestic Assistance Number: 12.420

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-Application Deadline:** 5:00 p.m. Eastern time (ET), June 27, 2014
- **Invitation to Submit an Application:** August 2014
- **Application Submission Deadline:** 11:59 p.m. ET, October 24, 2014
- **End of Application Verification Period:** 5:00 p.m. ET, October 29, 2014
- **Peer Review:** December 2014
- **Programmatic Review:** February 2015

Change for Fiscal Year 2014: The CDMRP eReceipt System has been replaced with the electronic Biomedical Research Application Portal (eBRAP). Principal Investigators and organizational representatives should register in eBRAP as soon as possible. All pre-applications must be submitted through eBRAP. In addition, applications submitted through Grants.gov will now be available for viewing, modification, and verification in eBRAP prior to at the end of the verification period.

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 2014 (FY14) Peer Reviewed Orthopaedic Research Program (PRORP) are being solicited for the Assistant Secretary of Defense for Health Affairs, Defense Health Program (DHP), by the U.S. Army Medical Research Acquisitions Activity (USAMRAA). The PRORP was initiated in 2009 to support research focused on optimizing recovery and restoration of function for military personnel with orthopaedic injuries sustained in combat or combat-related activities. Appropriations for the PRORP from FY09 through FY13 totaled \$218.5 million (M). The FY14 appropriation is \$30M.

The FY14 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 musculoskeletal 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 Government agencies are highly encouraged.

B. FY14 PRORP Focus Areas

All applications must propose planning and development activities for a clinical trial that addresses at least one of the following FY14 PRORP Clinical Trial Development Award (CTDA) Focus Areas:

- Identify and reduce the secondary health effects (e.g., joint contracture, obesity, metabolic syndrome, poor bone health) that follow reduced mobility from traumatic neuromusculoskeletal injury, excluding spinal cord injuries. The focus should be on injuries sustained prior to the age of 45 and secondary health effects that develop within 5 years of injury.
- Physical or occupational therapy (PT/OT) interventions to establish optimal rehabilitation and examine the comparative effectiveness of different PT/OT regimes, such as studies that establish optimal strategies for weight bearing progression, gait training, strengthening, and that prevent or treat post-traumatic joint stiffness and contracture in the ankle, knee, and/or elbow.
- Strategies to inhibit neuromas at surgical/amputation sites.
- The application of ***novel and/or innovative*** technologies and materials in prosthetic and orthotic device development toward the improvement or enhancement of:
 - Long-term socket performance, to include afferent and efferent user interface.
 - The fit of prosthetics, including the design and development of flexible socket suspension systems and incorporated interoperability of components to improve stability and usability.

- Socket performance (comfort, fit, moisture management, residual limb skin integrity, and durability). Novel upper extremity prosthetic sockets, including the design and development of flexible socket suspension systems, are highly encouraged.
- Myoelectric prosthetic durability (e.g., water resistance, waterproof components) to enhance the use of myoelectric prostheses in all military environments.

Studies that propose nominal or iterative advancements are not encouraged.

- Research toward osseointegration of upper extremity prostheses, including optimization of the skin-implant interface, prevention of infection, control strategies, and sensory feedback.
- Clinical trials to restore function after volumetric muscle loss, including physical therapy approaches.
- Research on treatment of non-battle orthopaedic injuries that impact unit readiness and reflect historical return to work rates less than 50% or longer than 6 months. Non-penetrating/non-ballistic injuries involving knee, shoulder, elbow, hip, or ankle will be considered, but funding will favor studies focusing on a single joint complex. Includes strategies for timing and effectiveness of treatment for multi-ligamentous knee injuries.

C. Award Information

The PRORP CTDA is intended to support the planning and development activities necessary to support preparation for clinical trials with the potential to have a significant impact on Warfighters and Veterans recovering from traumatic orthopaedic injuries. The clinical trials proposed may be focused on any aspect of treatment of orthopaedic injuries that addresses at least one of the FY14 PRORP CTDA Focus Areas, including the evaluation of promising new products, pharmacologic agents (drugs or biologics), devices, clinical guidance, and/or emerging approaches and technologies. All applications are required to justify the relevance of the proposed project to military and/or Veteran populations affected by combat-related orthopaedic injury. Applicants addressing non-battle orthopaedic injuries must articulate how the trial has the potential to impact unit readiness and return-to-duty/work rates. ***Collaboration with military or VA researchers and clinicians, and inclusion of active duty military or Veteran participants as all or a portion of the future study population, is highly encouraged.***

The PRORP CTDA is a planning award designed to permit early peer review of the rationale and design of a proposed clinical trial and to provide support for the development of the elements essential for initiation of a clinical trial. This Program Announcement/Funding Opportunity is not designed for the collection of data to establish the proof of principle for a clinical trial. All applications must demonstrate that the rationale for the proposed clinical trial has already been clearly established, with appropriate supportive preliminary data. 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 exploratory information, safety, effectiveness, and/or efficacy. This outcome represents a direct effect on the human subject of that intervention or interaction. For more information on how to distinguish clinical research from clinical trials, see the Human Subject Resource Document at [https://cdmrp.org/Program Announcements and Forms/](https://cdmrp.org/Program%20Announcements%20and%20Forms/).

Activities allowed under the CTDA may include, but are not limited to:

- Developing the clinical protocol
- Composing the research team and initiating collaborations necessary for the future clinical trial
- Establishing access to an appropriate patient population
- Developing training procedures
- Resolving potential intellectual or material property issues
- Developing a transition plan with associated resources and collaborations to continue to the next phase of research or commercialization
- Establishing quality control/assurance procedures
- Developing data collection/data management procedures
- Developing a data analysis/statistical plan
- Addressing potential issues regarding test article purity and formulation
- Developing a safety monitoring plan
- Planning for and preparing a U.S. Food and Drug Administration (FDA) Investigational New Drug (IND)/Investigational Device Exemption (IDE) application
- Conducting other preparatory activities needed to support the future clinical trial

Each CTDA application can request support for preparations for a single clinical trial only. However, investigators may submit more than one CTDA application supporting preparations for different clinical trials.

As noted above, these activities do not involve the collection of data to support the rationale for a given approach, nor do they support the actual conduct of a clinical trial. Investigators interested in generating proof-of-principle data should consider the PRORP Idea Development Award (W81XWH-14-PRORP-IDA), which supports untested, innovative ideas, or the PRORP Translational Research Award (W81XWH-14-PRORP-TRA), aimed at supporting the translation of laboratory research into clinical application. Investigators seeking support to conduct a clinical trial should apply to the PRORP Clinical Trial Award (W81XWH-14-PRORP-CTA) mechanism.

Investigators awarded a PRORP CTDA are expected to apply to the PRORP Clinical Trial Award in the program year following completion of their CTDA (i.e., FY14 PRORP CTDA awardees would apply for an FY16 or FY17 PRORP Clinical Trial Award, if that award is offered). The FY16 or FY17 PRORP Clinical Trial Award application would include the results of the completed CTDA. Award of an FY14 PRORP CTDA is in no way an assurance of funding for a future PRORP Clinical Trial Award. The funding of FY16 or FY17 PRORP Clinical Trial Awards will be contingent upon the availability of federal funds for the program, and competitive selection. ***Note that if an IND or IDE is required for the conduct of the proposed clinical trial, submission of the IND or IDE application to the FDA should occur prior to submitting an application to a PRORP Clinical Trial Award.***

The PRORP Clinical Trial Award application requires extensive descriptions of clinical trial components. CTDA applicants are encouraged to reference the FY14 PRORP Clinical Trial Award Program Announcement to become familiar with these requirements and to help direct activities during the CTDA period. The FY14 PRORP Clinical Trial Award Program Announcement (W81XWH-14-PRORP-CTA) can be accessed at <http://cdmrp.army.mil/funding>.

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 ongoing DoD and VA areas of research interest:

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

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

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

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

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

Defense Medical Research and
Development Program
<http://dmrdp.fhpr.osd.mil/home.aspx>

Defense Technical Information Center
<http://www.dtic.mil>

Military Infectious Disease 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/>

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

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

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

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

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

U.S. Department of Veterans Affairs, Office
of Research and Development
<http://www.research.va.gov>

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

The Congressionally Directed Medical Research Programs (CDMRP) intends that 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 L.

D. Eligibility Information

- PIs must be at or above the level of Assistant Professor (or equivalent).
- Cost sharing/matching is not an eligibility requirement.
- Eligible investigators must apply through an organization. Organizations eligible to apply include national, international, for-profit, non-profit, public, and private organizations.
- Refer to the General Application Instructions, Appendix 1, for general eligibility information.

E. Funding

- The maximum period of performance is **18 months**.
- The maximum allowable total costs for the entire period of performance are **\$300,000**.
- 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 **18 months**.
- Regardless of the period of performance proposed, the applicant may not exceed the maximum allowable total costs. Indirect costs shall be proposed in accordance with the organization's negotiated rate agreement.

Refer to the General Application Instructions, Section II.C.4., for budget regulations and instructions for the Research & Related Budget. *For all federal agencies or organizations collaborating with federal agencies, budget restrictions apply as are noted in Section II.C.4. of the General Application Instructions.*

For this award mechanism, direct costs:

May be requested for (not all-inclusive):

- Salary
- Administrative costs
- Support for establishing collaborations
- Database generation
- Software development
- Costs associated with Institutional Review Board (IRB) and/or FDA applications and reviews
- Travel between collaborating organizations
- Travel costs of up to \$1,800 per year to attend scientific/technical meetings

Shall not be requested for:

- Clinical research costs
- Research or clinical equipment

Intramural (DoD), other federal agency, and extramural investigators are encouraged to apply to this Program Announcement/Funding Opportunity. 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. Intramural applicants and collaborators are reminded to coordinate receipt and commitment of funds through their respective resource managers. It is permissible for an intramural investigator to be named as a collaborator on an application submitted by an extramural investigator. In such cases, the extramural investigator must include a letter from the intramural collaborator's Commander or Commanding Officer that authorizes the involvement of the intramural collaborator.

As required of all applicants to this Program Announcement/Funding Opportunity, if PIs from federal agencies submit applications, they must submit through Grants.gov. Therefore, 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.

Awards to extramural organizations will consist solely of assistance agreements (Cooperative Agreements and Grants). Awards to intramural agencies and other federal agencies will be executed through the Military Interdepartmental Purchase Request (MIPR) or Funding Authorization Document (FAD) process. Direct transfer of funds from the recipient to a federal agency is not allowed except under very limited circumstances. Refer to the General Application Instructions, Section II.C.4. Research & Related Budget, for additional information on budget considerations for applications involving federal agencies.

The CDMRP expects to allot approximately \$1.2M of the \$30M FY14 PRORP appropriation to fund approximately four Clinical Trial Development Award applications, depending on the quality and number of applications received. Funding of applications received in response to this Program Announcement/Funding Opportunity is contingent upon the availability of federal funds for this program.

II. SUBMISSION INFORMATION

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

New for FY14: *The CDMRP has replaced its eReceipt System with eBRAP.* Submission remains a two-step process requiring both pre-application and application submission.

PIs must be registered in eBRAP in order to submit a pre-application and receive notification of the status of a pre-application or application. A key feature of eBRAP is that an organization's representatives and PIs are able to view and modify the Grants.gov application submissions associated with them, but only if the organization, Business Officials, and PIs are registered and affiliated to the organization in eBRAP (see *eBRAP User Guide* at <https://ebrap.org/eBRAP/public/UserGuide.pdf>). Upon completion of an organization's registration in eBRAP and approval by the CDMRP Help Desk, the organization name will be displayed in eBRAP to assist the organization's business officials and PIs as they register.

Note: Submission of either the pre-application to eBRAP or application to Grants.gov does not require registering an organization and affiliating its Business Officials and PIs in eBRAP; however, the ability to view and modify the Grants.gov application in eBRAP is contingent upon the registration and affiliation. *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. Any other application component cannot be changed after the end of the application verification period.* If verification is not completed by the end of the application verification period, the application will be reviewed as submitted through Grants.gov, provided there is no cause for administrative rejection of the application (see [Section IV.A., Rejection](#)).

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.

A. Where to Obtain the Application Package

To obtain the complete application package, including all required forms, perform a Grants.gov (<http://www.grants.gov/>) basic search using the Funding Opportunity Number: W81XWH-14-PRORP-CTDA.

B. Pre-Application Submission and Content Form

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

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

A change in PI or organization after submission of the pre-application will be allowed only at the discretion of the US Army Medical Research Acquisition Activity (USAMRAA) Contracting/Grants Officer.

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):

- **Application Information – Tab 1**
- **Application Contacts – Tab 2**
 - It is recommended that PIs identify an Alternate Submitter in the event that assistance with pre-application submission is needed.

- **Collaborators and Conflicts of Interest (COI) – Tab 3**

FY14 PRORP Steering Committee (SC) members should not be involved in any pre-application or application. For questions related to SC 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.

- **Required Files – Tab 4**

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

Preproposal Narrative (two-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:

- **Focus Area:** Explain how the proposed trial will address at least one of the FY14 PRORP CTDA Focus Areas.
- **Research Idea:** Describe the reasoning on which the proposed clinical trial is based; include relevant literature citations. Briefly describe the level of scientific evidence that supports the progression of this research to a clinical trial. State the hypothesis to be tested and/or the objectives to be attained. 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. Briefly describe the intended patient population(s) to be recruited for the clinical trial.
- **Development Plan:** Describe the planning activities to be undertaken with regard to clinical protocol development and clinical trial preparations, and the timeline for execution. Include relevant information regarding the status of FDA review and/or approval, as applicable.
- **Personnel:** Briefly state the PI's background and expertise in conducting clinical trials.
- **Military Benefit:** Describe how the proposed clinical trial will have an impact on accelerating the movement of a promising treatment for combat-related orthopaedic injury into a military clinical application, and/or how the research has the potential to impact unit readiness and return-to-work/duty rates.

- **Pre-Application Supporting Documentation:** The items to be included as supporting documentation for the pre-application *must be uploaded as individual documents* and are limited to:
 - References Cited (one-page limit): List the references cited (including URLs if available) in the Preproposal Narrative using a standard reference format that includes the full citation (i.e., author[s], year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).
 - List of Abbreviations, Acronyms, and Symbols: Provide a list of abbreviations, acronyms, and symbols used in the Preproposal Narrative.
 - Key Personnel Biographical Sketches (four-page limit per individual).
- **Submit Pre-Application – Tab 5**
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:** The degree to which the proposed research addresses the intent of the award mechanism and aligns with at least one of the FY14 PRORP CTDA Focus Areas. How well the rationale is supported, and how well the background provided indicates the research is ready to move into a clinical trial.
 - **Development Plan:** How well the proposed clinical trial preparations are designed. The degree to which the proposed activities will successfully prepare the study for application to a PRORP Clinical Trial Award Program Announcement/Funding Opportunity and subsequent clinical trial initiation.
 - **Personnel:** How the PI's background and expertise are appropriate to initiating and conducting the proposed clinical trial.
 - **Military Benefit:** How the proposed work, if successful, would provide a significant benefit to military service members and Veterans who have sustained combat-related orthopaedic injuries or traumatic orthopaedic injuries that impact unit readiness and return-to-duty/work.
- **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.

C. Application Submission Content and Forms

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

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

New for FY14: *Applications submitted through and validated by Grants.gov will be retrieved and processed by eBRAP to allow for review, modification, and verification.* The PI and organizational representatives will receive an email request from eBRAP to review, modify, and verify the application submitted to Grants.gov. During this verification period, the PI may upload missing files (excluding those listed in [Section IV.A., Rejection](#)), replace files, and re-categorize files. These modifications must be completed by the end of the verification period.

Note: *Changes to either the Project Narrative or Budget are not allowed in eBRAP; if such changes are required, the entire application package must be submitted through Grants.gov as a “Changed/Corrected Application” with the Previous Grants.gov Tracking ID **prior to the application submission deadline (which occurs earlier than the end of the application verification period).***

Grants.gov application package components: For the Clinical Trial Development 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. SF 424 (R&R) Application for Federal Assistance Form:** Refer to the General Application Instructions, Section II.C., for detailed information.
- 2. Attachments Form**
 - **Attachment 1: Project Narrative (10-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 will 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.

- Describe in detail the rationale for the future clinical trial and include a literature review, preliminary studies, and preclinical data that led to its development.
- Describe the hypothesis and/or objectives of the future clinical trial.
- State the anticipated outcomes to be measured by the future clinical trial.
- Specify the target population for the trial, and how access is available to such a population.

- Explain the intervention to be tested, including relevant information about its source, FDA approval/review status (if applicable), availability, efficacy, dosing (if applicable), and mechanism of action (if known). Describe the indication planned for the product label, if appropriate.
- State the overarching goals of the work to be conducted during the CTDA funding period.
- Describe plans to finalize the experimental design and develop the clinical protocol and related documents (e.g., consent form, questionnaires).
- Describe the PI's background and expertise in orthopaedic research and in conducting large-scale clinical trials. Describe the experience and contributions of other key study team members.
- Describe plans for further developing the research team and any proposed research resource or professional collaborations, if applicable. Include plans for training team members, as appropriate.
- Describe plans to identify and resolve potential intellectual or material property issues, as applicable.
- Describe how a transition plan to move the clinical trial product/outcome(s) to the next phase of clinical trials and/or delivery to the market after successful completion of the proposed clinical trial will be developed.
- Describe how a management plan and related Standard Operating Procedures, if applicable, will be developed.
- Describe how sample size estimates will be obtained, how a plan for statistical analyses will be developed, and how a human subject recruitment plan will be formulated. Include plans to engage a statistician and other experts as appropriate.
- Describe plans to develop data collection/monitoring procedures, a data analysis plan, and other data collection tools.
- Describe how clinical and safety monitoring plans will be developed, including how the study will be monitored for Good Clinical Practices (GCP) compliance.
- Address how plans to coordinate IRB submission and approval at each study site, as applicable, will be developed.
- If applicable, describe detailed plans for carrying out the IND/IDE application process, including milestones and planned interactions with the FDA. The path to FDA application and approval (IND/IDE or other) for the clinical trial should be outlined as clearly as possible.
- Describe how a plan to share and disseminate data and other resources created by the future clinical with the greater research community will be developed.
- Describe how other preparatory activities will be accomplished.
- **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 may result in the removal of those items or administrative withdrawal of the application.***

- References Cited: List the references cited (including URLs if available) in the Project Narrative using a standard reference format that includes the full citation (i.e., author[s], year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).
- List of Abbreviations, Acronyms, and Symbols: Provide a list of abbreviations, acronyms, and symbols.
- Facilities, Existing Equipment, and Other Resources: Describe the facilities and equipment available for performance of the proposed project and any additional facilities or equipment proposed for acquisition at no cost to the award. Indicate whether or not Government-furnished facilities or equipment are proposed for use. If so, reference should be made to the original or present Government award under which the facilities or equipment items are now accountable. There is no form for this information.
- Publications and/or Patent Abstracts (five-document limit): Include relevant publication URLs and/or patent abstracts. If publications are not publicly available, then a copy/copies of the published manuscript(s) must be included in Attachment 2. Extra items will not be reviewed.
- Letters of Organizational Support: Provide a letter (or letters, if applicable), signed by the Department Chair or appropriate organization official, confirming the laboratory space, equipment, and other resources available for the work to be conducted under the PRORP CTDA mechanism.
- Letters of Collaboration: Provide a signed letter from each collaborating individual or organization that will demonstrate that the PI has the support or resources necessary for the proposed work to be conducted under the PRORP CTDA mechanism.
- Intellectual Property
 - Background and Proprietary Information: All software and data first produced under the award are subject to a federal purpose license in accordance with applicable DoD Grant and Agreement Regulations (DoDGAR) requirements. Provide a list of all background intellectual property to be used in the project or provide a statement that none will be used. If applicable, state and identify the proprietary information that will be provided to the Government and indicate whether the applicant will require a waiver of the federal purpose license.
 - Intellectual and Material Property Plan (if applicable): Provide a plan for resolving intellectual and material property issues among participating organizations.

- **Attachment 3: Technical Abstract (one-page limit):** Upload as “TechAbs.pdf.”

The technical abstract is used by all reviewers as a description of the project’s key aspects. Therefore, clarity and completeness within the space limits of the technical abstract are highly important.

- Background: State the FY14 PRORP CTDA Focus Area(s) addressed by the proposed future clinical trial. Present the ideas and reasoning behind the clinical trial.
- Objective/Hypothesis: State the objective/hypothesis to be tested by the future clinical trial. Describe the overall research goals for the study.
- Development Plan: Briefly describe the nature of the planning activities to be conducted under this award mechanism to develop the proposed clinical trial.
- Military Benefit: State briefly how the future clinical trial, if successful, will have an impact on combat-related orthopaedic injury research, unit readiness, return-to-duty/work, and/or patient care.

- **Attachment 4: Lay Abstract (one-page limit):** Upload as “LayAbs.pdf.”

Lay abstracts should be written using the following outline.

- Describe the objectives and rationale for the application in a manner that will be *readily understood by readers without a background in science or medicine*.
 - Do not duplicate the technical abstract.
- Describe the ultimate applicability of the proposed clinical trial.
 - 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?
- Briefly describe how the proposed project will benefit military populations and impact combat-related orthopaedic research and patient care.

- **Attachment 5: Statement of Work (SOW) (three-page limit):** Upload as “SOW.pdf.” Refer to the General Application Instructions, Section II.C.2., for detailed guidance on creating the SOW.

The suggested SOW format and examples specific to different types of research projects are available on the eBRAP “Program Announcement and Forms” web page (<https://ebrap.org/eBRAP/public/Program.htm>). For the Clinical Trial Development Award mechanism, use the SOW format example titled “SOW (Statement of Work) Generic Format.” The SOW must be in PDF format prior to attaching.

- **Attachment 6: Military Benefit Statement (one-page limit):** Upload as “MilBen.pdf.”

State explicitly how the proposed future clinical trial, if successful, will accelerate the movement of the product, pharmacologic agent, device, clinical guidance,

and/or emerging technology into clinical practice for combat-related orthopaedic injuries. Further, describe the impact of this study on the lives of individuals recovering from combat-related 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. For applicants addressing the Focus Area on non-battle orthopaedic injuries, 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 have an impact. ***Although not all-inclusive***, these examples are intended to help PIs frame the impact 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

Demonstrate how the proposed clinical trial is responsive to the health care needs of the military services and/or the Veteran population. If active duty military or Veteran population(s) will be used in the clinical trial, 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 clinical trial, explain how the population simulates the targeted population (i.e., military services and/or Veterans). Show how the proposed study complements ongoing DoD and/or VA areas of orthopaedic research interest. Describe how the study design will replicate field conditions, if applicable.

- 3. Research & Related Senior/Key Person Profile (Expanded):** Refer to the General Application Instructions, Section II.C.3., for detailed information.
 - PI Biographical Sketch (four-page limit): Upload as “Biosketch_LastName.pdf.”
 - PI Previous/Current/Pending Support (no page limit): Upload as “Support_LastName.pdf.”
 - Key Personnel Biographical Sketches (four-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.”
- 5. Project/Performance Site Location(s) Form:** Refer to the General Application Instructions, Section II.C.5., for detailed information.
- 6. R & R Subaward Budget Attachment(s) Form (if applicable):** Refer to the General Application Instructions, Section II.C.6., for detailed information.

D. Verification of Grants.gov Application in eBRAP

For FY14, a new process has been initiated whereby organizational representatives and PIs can view their applications as submitted through Grants.gov and prior to peer review of the application. This will enable applicants to make modifications prior to scientific and programmatic evaluation of applications, provided the modifications are made by either the end of the application verification period or, for changes to the Project Narrative or Budget, by the application submission deadline.

After application submission to Grants.gov, eBRAP will retrieve and validate the application submission. eBRAP will notify the organizational representatives and PI via email and instruct them to log into eBRAP to review, modify, and verify the application. Files that fail eBRAP validation will be noted in both the email and in the Full Application Files tab. eBRAP does not validate the accuracy or completeness of content in the files. PIs are strongly encouraged to review all application components. If either the Project Narrative or the Budget fail eBRAP validation, an updated Grants.gov application package must be submitted via Grants.gov prior to the application submission deadline, which occurs earlier than the end of the application verification period. *The Project Narrative and Budget cannot be changed after the application submission deadline. Any other application component cannot be changed after the end of the application verification period.*

E. Submission Dates and Times

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

F. Other Submission Requirements

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

All applications must be submitted through Grants.gov. Applicant organizations and all subrecipient organizations must have a Data Universal Numbering System (DUNS) number to submit applications to Grants.gov. The applicant organization must also be registered in the Entity Management functional area of the System for Award Management (SAM) with an “Active” status to submit applications through the Grants.gov portal. Refer to the General Application Instructions, Appendix 3, for information on Grants.gov requirements.

III. APPLICATION REVIEW INFORMATION

A. Application Review and Selection Process

All applicants are evaluated by scientists, clinicians, and consumer advocates using a two-tier review process. The first tier is peer review of applications against established criteria for determining technical merit. The second tier is a programmatic review that makes recommendations for funding to the Office of the Assistant Secretary of Defense for Health Affairs, based on (a) technical merit and (b) the relevance to the mission of the DHP and PRORP

and to the specific intent of the award mechanism. The highest-scoring applications from the first tier of review are not automatically recommended for funding. Additional information about the two-tier process used by the CDMRP can be found at <http://cdmrp.army.mil/about/fundingprocess>.

All CDMRP review processes are conducted confidentially to maintain the integrity of the merit-based selection process. Panel members sign a non-disclosure 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:

- **Potential Military Benefit and Clinical Impact**
 - How the anticipated outcomes of the future clinical trial, if successful, will be relevant to individuals with combat-related orthopaedic injuries, if applicable.
 - 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.
 - How the anticipated outcomes of the proposed clinical trial will provide/improve the short-term benefits for individuals with traumatic orthopaedic injuries.
 - How significantly the long-term benefits for implementation of the intervention may impact patient care and/or quality of life.
 - The degree to which the results of the proposed clinical trial are expected to affect clinical practice.
- **Scientific Rationale and Feasibility**
 - How well the rationale and proof of principle for the clinical trial are supported by the background and preliminary data presented.
 - Whether the intervention proposed is appropriate for testing the hypothesis/answering the objectives of the proposed clinical trial.
 - How well the intervention is described, and whether it will be available in sufficient quantities to the study team for conduct of the clinical trial.

- **Development Plan**

- How well the necessary steps for preparing to initiate a clinical trial are described and feasibly addressed by the work proposed.
- How well potential challenges are described and alternative solutions are proposed.
- The degree to which the plans to finalize the experimental design and develop the clinical protocol and associated documents are well constructed.
- How the plans to develop data collection and monitoring tools and data analyses are appropriate to the scope of the proposed clinical trial.
- How the plans for safety and clinical monitoring, including compliance with GCP if applicable, will be developed during the preparation period.
- How well considerations such as statistical support and planning, intellectual and material property agreements, and development of a transition plan are addressed.
- To what extent the plans for carrying out IRB and IND/IDE (or other FDA) application and review processes, if applicable, are feasible and likely to lead to success.
- How well the plans for other preparatory activities are described and whether they are appropriate for the future clinical trial proposed.

- **Personnel and Communication**

- Whether the composition of the study team is appropriate for the proposed preparatory work.
- To what degree the PI and study team's background and expertise are appropriate to accomplishing both the proposed preparatory work and the future clinical trial (e.g., statistical expertise, expertise in orthopaedic injury, and clinical studies).
- How the plans to establish collaborations and/or research resources to strengthen the study team and research design are appropriate and feasible.
- How the levels of effort of the study team members are appropriate for the successful conduct of the proposed preparatory work.
- How well the proposed process for development of a management plan will address the relative complexity of the clinical trial

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

- **Environment**

- The degree to which the scientific environment is appropriate for the proposed research.

- How well the research requirements are supported by the availability of and accessibility to facilities and resources (including collaborative arrangements).
 - To what degree the quality and extent of institutional support are appropriate.
 - If applicable, to what degree the intellectual and material property plan is appropriate.
 - **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, 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 FY14 PRORP, as evidenced by the following:**
 - Adherence to the intent of the award mechanism
 - Program portfolio composition
 - Programmatic relevance
 - Relative military benefit

C. Recipient Qualification

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

D. Application Review Dates

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

E. Notification of Application Review Results

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

IV. ADMINISTRATIVE ACTIONS

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

A. Rejection

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

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

The following will result in administrative rejection of the application:

- Submission of an application for which a letter of invitation was not received.
- Project Narrative exceeds page limit.
- Project Narrative is missing.
- Budget is missing.
- Submission of the same research project to different funding opportunities within the same program and fiscal year.

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.
- Following application submission to Grants.gov, the PI will receive an email request from eBRAP to review, modify, and verify the application submitted to Grants.gov. During this verification period, the PI may upload missing documents (excluding those listed in [Section IV.A., Rejection](#)), replace files, and re-categorize files. These modifications must be completed by the end of the application verification period; otherwise, the application will be reviewed as submitted.

C. Withdrawal

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

- A FY14 PRORP SC 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 FY14 PRORP SC members can be found at <http://cdmrp.army.mil/prorp/panels/panel14>.
- The application fails to conform to this Program Announcement/Funding Opportunity description to the extent that appropriate review cannot be conducted.

- Total costs as shown on the Research & Related Budget exceed the maximum allowed by this Program Announcement/Funding Opportunity.
- 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).
- Inclusion of any employee of CDMRP review contractors in applications for funding without adequate plans to mitigate conflicts of interest. Refer to the General Application Instructions, Section II.B., 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 PI does not meet the eligibility criteria.
- The proposed project is not relevant to at least one of the FY14 PRORP CTDA Focus Areas.
- The proposed project includes the collection of data to establish proof of principle for the future clinical trial.
- The proposed project is, or requests funding for, a clinical trial.

D. Withhold

Applications that appear to involve research misconduct will be administratively withheld from further consideration pending institutional investigation. The institution will be required to provide the findings of the investigation to 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, 2015. Refer to the General Application Instructions, Appendix 4, for additional award administration information.

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 J, for general information on reporting requirements.

Quarterly technical progress reports with quad charts will be required.

E. Award Transfers

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

VI. AGENCY CONTACTS

A. CDMRP Help Desk

Questions related to Program Announcement/Funding Opportunity content or submission requirements as well as questions related to the submission of the pre-application through 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

B. 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

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 application package. If the 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	Action	Completed
SF-424 (R&R) Application for Federal Assistance	Complete form as instructed.	
Attachments Form	Project Narrative: Upload as Attachment 1 with file name "ProjectNarrative.pdf."	
	Supporting Documentation: Upload as Attachment 2 with file name "Support.pdf."	
	Technical Abstract: Upload as Attachment 3 with file name "TechAbs.pdf."	
	Lay Abstract: Upload as Attachment 4 with file name "LabAbs.pdf."	
	Statement of Work: Upload as Attachment 5 with file name "SOW.pdf."	
	Military Benefit Statement: Upload as Attachment 6 with file name "MilBen.pdf."	
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.	