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-13-PRORP-CTDA

Catalog of Federal Domestic Assistance Number: 12.420

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-Application Submission Deadline:** 5:00 p.m. Eastern time (ET), April 4, 2013
- **Invitation to Submit an Application:** mid-May 2013
- **Application Submission Deadline:** 11:59 p.m. ET, July 18, 2013
- **Peer Review:** To Be Determined
- **Programmatic Review:** To Be Determined

This Program Announcement 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 2013 (FY13) 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 duties. Appropriations for the PRORP from FY09 through FY12 total $188.5 million (M). The executing agent for the PRORP is the Congressionally Directed Medical Research Programs (CDMRP).

The FY13 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. Applications involving multidisciplinary collaborations among academia, industry, the military services, the Department of Veterans Affairs (VA), and other federal Government agencies are highly encouraged.

Funding of applications received in response to this Program Announcement/Funding Opportunity is contingent upon the availability of FY13 federal funds for this program. As of the release of this Program Announcement/Funding Opportunity, the FY13 Defense Appropriations Bill has not been passed and there is no guarantee that any funds will be made available to support this Program Announcement/Funding Opportunity. Funding allotted for this Program Announcement/Funding Opportunity is approximate and subject to change.

B. Award Information

The PRORP Clinical Trial Development Award (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 military combat-related orthopaedic injuries. The clinical trials proposed may be focused on any aspect of treatment of combat-related orthopaedic injuries that addresses the FY13 PRORP CTDA Focus Areas outlined below, 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. ***Collaboration with military researchers and clinicians is encouraged, and studies that plan to include active duty military or Veteran participants as all or a portion of the study population will be given higher priority for funding during programmatic review.***

All applications must propose planning activities for a clinical trial that addresses at least one of the following FY13 PRORP CTDA Focus Areas:

- Characteristics of and strategies for optimizing long-term (5 to 10 years) functional outcomes for traumatic military amputee and/or limb salvage patients.

- Strategies to prevent or mitigate post-traumatic osteoarthritis resulting from fracture and/or ligament injury, including novel surgical approaches and other interventions for treatment, the effect of weight bearing, and retrospective studies of the impact of prior surgical interventions on the occurrence of post-traumatic osteoarthritis.
- Surgical interventions for combat-related spine fractures and instability.
- Physical or occupational therapy (PT/OT) interventions, such as studies that establish optimal strategies for weight bearing progression or studies that examine the comparative effectiveness of different PT/OT regimens.
- Establishment of bone, joint, and soft tissue health guidelines based upon validated measures to aid clinicians in returning patients safely to high-impact activities, including but not limited to, validation of markers of bone quality that can predict susceptibility to injury, and comparative effectiveness studies of training and therapeutic interventions to improve bone quality and muscle function that maximize performance while minimizing injury.
- Interventions to improve secondary health effects (e.g., joint contracture, obesity, cardiovascular disease, poor bone health) that follow reduced mobility from primary neuromusculoskeletal injury, excluding spinal cord injuries.
- Maintenance or enhancement of long-term socket performance and fit of prosthetics, including the design and development of flexible socket suspension systems, the evaluation of socket performance (comfort, fit, and durability), and the application of new technologies to improve existing prosthetic sockets.
- Studies to improve moisture management and residual limb skin care at the prosthetic socket interface.
- Clinical studies on the effectiveness of local strategies to minimize surgical site infections, including but not limited to local application of antibiotics, debridement techniques, and/or subatmospheric wound dressing.

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 funding opportunity is not designed for the collection of preliminary 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.

Activities allowed under a 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.
- Investigating 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.
- Developing quality control/assurance procedures.
- Developing data collection/data management procedures.
- Developing a data analysis/statistical plan.
- Assessing 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. Investigators interested in generating proof-of-principle data should consider the PRORP Idea Development Award, which supports untested, innovative ideas, or the PRORP Translational Research Award, aimed at supporting the translation of laboratory research into clinical application.

Investigators awarded a CTDA are expected to apply to the PRORP Clinical Trial Award in the program year following completion of the CTDA (i.e., FY13 CTDA awardees would apply for an FY15 or FY16 Clinical Trial Award, if that award is offered). The FY15 (or FY16) Clinical Trial Award application would include the results of the completed CTDA. Award of an FY13 CTDA is in no way an assurance of funding for a future PRORP Clinical Trial Award. The funding of FY15 (or FY16) PRORP Clinical Trial Awards will be contingent upon the availability of federal funds for the program.

The PRORP Clinical Trial Award application requires extensive descriptions of clinical trial components. CTDA applicants are encouraged to reference the PRORP FY13 Clinical Trial Award Program Announcement to become familiar with these requirements and to help direct activities during the CTDA period. The PRORP FY13 Clinical Trial Award Program Announcement can be accessed at http:/cdmrp.army.mil/funding.

Encouraged DoD 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 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 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 K.

C. Eligibility Information

- PIs must be at or above the level of Assistant Professor (or equivalent).
- Cost sharing/matching is not an eligibility requirement.
- Organizations eligible to apply include national, international, for-profit, non-profit, public, and private organizations. Both intramural (i.e., DoD) and extramural investigators are encouraged to apply to this Program Announcement/Funding Opportunity.
- Refer to the General Application Instructions, Appendix 1, for general eligibility information.

D. Funding

- The maximum period of performance is **18 months**, though it is expected that 12 months will be sufficient for most applications.
- The maximum allowable direct costs for the entire period of performance are **$200,000** plus indirect costs.
- 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 direct 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.

In addition, for this award mechanism, direct costs:

May be requested for (not all-inclusive):

- Salary of non-Government personnel (includes contract research personnel at Government facilities)
- Administrative costs
- Support for establishing collaborations
- Teleconferences and other means of communication
- Database generation
- Software development
- Costs associated with 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) and extramural investigators are encouraged to apply to this Program Announcement/Funding Opportunity. ***For all federal agencies or organizations collaborating with federal agencies, budget restrictions apply and are so noted in Section II.C.4. of the General Application Instructions.*** As required of all applicants to this Program Announcement, if PIs from federal agencies submit full applications, they must submit through Grants.gov. Therefore, federal applicants must be familiar with Grants.gov requirements, including the need for System for Award Management (SAM) and a Data Universal Numbering System (DUNS)

number. Refer to Appendix 3 of the General Application Instructions for further information regarding Grants.gov requirements.

The PRORP expects to allot approximately $1.2M of the FY13 PRORP appropriation to fund approximately 4 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 CDMRP eReceipt System (https://cdmrp.org/) and (2) application submission through Grants.gov (http://www.grants.gov/).

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-13-PRORP-CTDA.

B. Pre-Application Submission Content and Form

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

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

- **Application Information – Tab 1**
- **Application Contacts – Tab 2**
- **Collaborators and Conflicts of Interest – Tab 3**

  FY13 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 (301-682-5507).

- **Required Files – Tab 4**

  Preproposal Narrative (two-page limit): The Preproposal Narrative page limit applies to text and any figures, tables, graphs, photographs, diagrams, chemical structures, pictures, pictorials, and cartoons.

  The Preproposal Narrative should include the following:

  - **Focus Area:** Explain how the proposed trial addresses at least one of the FY13 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, behavioral) of clinical trial is being proposed and indicate the phase of trial and/or class of device and regulatory status, as appropriate. If already established, briefly describe the 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**.**

  Pre-Application Supporting Documentation: The items to be included as supporting documentation for the pre-application are limited to:

  - References Cited (one-page limit): List relevant references 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). The inclusion of Internet URLs to references is encouraged.
  - 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 by CDMRP.

- **Other Documents Tab**

  No additional documents are required**.**

Pre-Application Screening

- **Pre-Application Screening Criteria**

  To determine the technical merits of the pre-application and the relevance to the mission of the DoD 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 FY13 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 thought out. The degree to which the proposed activities will successfully prepare the study for application to a Clinical Trial Award 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:** The degree to which the proposed clinical trial, if successful, will impact care for Warfighters who have sustained combat-related orthopaedic injuries.

- **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 Form

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/).

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 (8-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. Include potential problems and associated alternative strategies wherever possible:

- 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.
- 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).
- 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).
- 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 investigate 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.
- Describe plans to develop data collection/monitoring procedures, a data analysis plan, and other data collection tools.
- 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 tentative 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 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 project.
  - Letters of Collaboration (if applicable): Provide a signed letter from each collaborating individual or organization that will demonstrate that the PI has the support or resources necessary for the proposed work.
  - 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, 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."

  Technical abstracts should be written using the following outline:

  - Background: State the FY13 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 to develop the proposed clinical trial.
  - Military Benefit: State briefly how the proposed project, if successful, will have an impact on combat-related orthopaedic injury research 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 clinical research.
    - 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., for detailed information, including guidance on appropriate SOW formats.

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

  State explicitly how the proposed 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. 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 U.S. 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 the U.S. Veteran population). Show how the proposed study complements ongoing DoD 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., for detailed information.

   - PI Biographical Sketch (four-page limit): Upload as "Biosketch_LastName.pdf."
   - PI 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 Current/Pending Support (no page limit): Upload as "Support_LastName.pdf."

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

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

D. 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 any one of the deadlines will result in application rejection.

E. 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 applications are evaluated by scientists, clinicians, and consumer advocates using a two-tier review process. The first tier is a 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, Health Affairs), based on technical merit, the relevance to the mission of the DHP and the PRORP and 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 review 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 Criteria

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.
        - How the anticipated outcomes of the proposed clinical trial will provide/ improve the short-term benefits for individuals with combat or combat-related 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 will affect clinical practice for military combat-related orthopaedic injuries.

- **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 adequately 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 documents are well constructed.
  - How the plans to develop data collection and monitoring tools and data analyses are appropriate to the scope of the clinical trial.
  - How well considerations such as statistical support and planning, intellectual and material property agreements, and development of a transition plan are addressed.
  - How well the plans for carrying out IRB and IND/IDE (or other FDA) application and review process are outlined and feasible.
  - 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:

- **Budget**
  - Whether the budget is appropriate for the proposed work and within the limitations of this Program Announcement/Funding Opportunity.
- **Application Presentation**
  - To what extent the writing, clarity, and presentation of the application components influenced the review.

2. **Programmatic Review:** To determine the application's relevance to the mission of the DoD and the PRORP, as well as to make funding recommendations, the following criteria are used by programmatic reviewers:

- Adherence to the intent of the award mechanism
- Program portfolio composition
- Programmatic relevance
- Ratings and evaluations of the peer reviewers
- 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 notification of the funding recommendation. Each PI will receive a peer review summary statement on the strengths and weaknesses of the application.

IV. ADMINISTRATIVE ACTIONS

After receipt of pre-applications from the CDMRP eReceipt System 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 specified limits will be removed prior to review for all documents other than the Project Narrative and the Preproposal Narrative.
- Documents not requested will be removed.
- Following the application deadline, the PI may be contacted by CDMRP via email with a request to provide certain missing supporting documents (excluding those listed in Section IV.A., Rejection). The missing documents must be provided by 5:00 p.m. ET on the second full business day following the date the email was sent. Otherwise, the application will be reviewed as submitted.

C. Withdrawal

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

- A FY13 PRORP Steering Committee (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 document. A list of the FY13 PRORP SC members can be found at http://cdmrp.army.mil/prorp/panels/panel13.
- The application does not conform to this Program Announcement/Funding Opportunity description to an extent that precludes appropriate review.
- Direct 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 FY13 PRORP CTDA Focus Areas.
- The proposed project includes the collection of preliminary data to establish proof of principle for the future 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, 2014. Refer to the General Application Instructions, Appendix 4, for additional award administration information.

B. Administrative and National Policy Requirements

Refer to the General Application Instructions, Appendix 4, Section D, for general information regarding administrative and national policy requirements.

C. Reporting

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

Quarterly technical progress reports will be required.

D. Award Transfers

Refer to the General Application Instructions, Appendix 4, Section F, 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 the CDMRP eReceipt System should be directed to the CDMRP Help Desk, which is available Monday through Friday from 8:00 a.m. to 5:00 p.m. ET. Response times may vary depending upon the volume of inquiries.

Phone: 301-682-5507

Email: help@cdmrp.org

B. Grants.gov Contact Center

Questions related to application submission through the 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 Form	Complete form as instructed.	
Attachments Form	Upload Project Narrative (ProjectNarrative.pdf) as Attachment 1.	
	Upload Supporting Documentation (Support.pdf) as Attachment 2.	
	Upload Technical Abstract (TechAbs.pdf) as Attachment 3.	
	Upload Lay Abstract (LayAbs.pdf) as Attachment 4.	
	Upload Statement of Work (SOW.pdf) as Attachment 5.	
	Upload Military Benefit Statement (MilBen.pdf) as Attachment 6.	
Research & Related Senior/Key Person Profile (Expanded)	Attach PI Biographical Sketch (Biosketch_LastName.pdf) to the appropriate field.	
	Attach PI 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 Current & Pending Support (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.	