Program Announcement

Defense Health Program

Department of Defense

Congressionally Directed Medical Research Programs

Peer Reviewed Orthopaedic Research Program

Translational Research Partnership Award

Funding Opportunity Number: W81XWH-12-PRORP-TRPA

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), June 27, 2012
- **Invitation to Submit an Application:** August 2012
- **Application Submission Deadline:** 11:59 p.m. ET, September 25, 2012
- **Peer Review:** November 2012
- **Programmatic Review:** January 2013

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I. FUNDING OPPORTUNITY DESCRIPTION

A. Program Description

Applications for the Peer Reviewed Orthopaedic Research Program (PRORP) are being solicited by the Assistant Secretary of Defense for Health Affairs, Defense Health Program. The PRORP was established in fiscal year 2009 (FY09) 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 FY11 totaled $158.5 million (M). The FY12 appropriation is $30M.

The FY11 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.

B. Award Information

The PRORP Translational Research Partnership Award mechanism was first offered in FY09. Since then, 57 research projects have been proposed, and 13 (representing 36 individual awards) have been recommended for funding.

The Translational Research Partnership Award supports translational research that will accelerate the movement of promising ideas in orthopaedic research into clinical applications to benefit Warfighters with combat-relevant traumatic orthopaedic injuries. The award is designed to encourage multi-institutional, multidisciplinary research partnerships among ***two or three*** investigators (designated as partners) to accelerate the movement of promising research hypotheses into clinical application in a manner that would be less readily achievable through separate efforts. ***There must be at least one laboratory scientist and at least one clinician participating in the partnership.*** A clinician is defined as an individual who is credentialed (possesses the necessary degrees, licenses, and other certifications) as a care provider in any relevant capacity at the institution of record. In addition, ***at least one partner must have significant experience either in orthopaedic research or musculoskeletal medicine.*** Biographical sketches should include appropriate documentation of credentials. Partnerships between academic institutions and Government agencies and/or military investigators/clinicians are highly encouraged. ***All applications are required to justify the relevance of the proposed project to military and/or Veteran populations affected by combat or combat-related orthopaedic injury.***

Observations that drive a research hypothesis may be derived from a laboratory discovery, population-based studies, or a clinician's firsthand knowledge from providing care to patients. While the ultimate goal of translational research is to move an observation forward into clinical application, members of the partnership should view translational research as a two-way continuum between bench and bedside. The research plan must involve a reciprocal flow of ideas and information within the partnership. ***It should be clear that all partners have had***

substantial intellectual input into the design of the research project. A proposed project in which a clinical partner merely supplies tissue samples or access to patients will not meet the intent of this mechanism. Developmental pathways for translational research that may be useful for designing translational research studies for support under this mechanism may be found at (http://www.cancer.gov/aboutnci/trwg/Pathways-to-Clinical-Goals). These pathways, while created for cancer research initiatives, have broad applicability to other areas of research, are comprehensive, and span the entire translational research continuum from discovery of a target to clinical trials.

The Translational Research Partnership Award is not intended to support definitive clinical trials, but may support correlative studies that are associated with an existing clinical trial and projects that optimize the design of future definitive clinical trials. Some limited clinical testing of a novel intervention or device is permissible if the clinical testing is necessary to inform the next step in the continuum of translational research. Such clinical pilot studies should be small, represent only a portion of the proposed Statement of Work, and be utilized to establish feasibility of a potential approach or to aid in device or intervention refinement. Research projects may also include preclinical studies in animal models, human subjects, and human anatomical substances.

Investigators seeking support for a definitive clinical trial should utilize the FY12 PRORP Clinical Trial Award mechanism. A clinical trial is defined as a prospective accrual of patients for a study 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 distinguishing clinical trials from clinical research, a Human Subject Resource Document is provided at https://cdmrp.org/Program_Announcements_and_Forms/.

All applications must propose a translational study addressing at least one of the following Focus Areas:

- Improvement of moisture management and residual limb skin care at the prosthetic socket interface.
- Improvement of the rate of nerve regeneration.
- Strategies to inhibit neuromas at surgical/amputation sites.
- The treatment of segmental bone injury in weight-bearing locations, including utilization of the Masquelet technique for bioactive membrane formation and identification of the best bone graft options. ***Only mature translational studies (e.g., those utilizing large animal models of long bone critical defects) are of interest; the development of novel bone void filler products is not of interest.***
- The treatment and prevention of heterotopic ossification. ***Only mature translational studies are of interest; the development and/or validation of new animal models of heterotopic ossification are/is not of interest.***
- Mitigation of the musculoskeletal and physiologic effects of reduced mobility for polytrauma patients, excluding spinal cord injury and behavioral/psychological effects.

- Short-term and long-term outcomes in limb salvage populations. May include retrospective or prospective observational clinical studies.
- Prevention or treatment of post-traumatic joint stiffness and contracture in the ankle, knee, and/or elbow, including physical therapy approaches.

In determining the Focus Areas for FY12, the PRORP Integration Panel (IP) strongly considered the research priorities set forth during the Extremity War Injuries VII Symposium held January 18-20, 2012, in Washington, DC.[1]

Applications must include preliminary and/or published data relevant to the Focus Area(s) and the proposed project; however, these data may come from fields other than orthopaedic research.

NESTED CAREER DEVELOPMENT OPTION

A nested Career Development opportunity is being offered as an optional addition to the Translational Research Partnership Award. The intent of the nested Career Development Option is to support research training opportunities for military investigators pursuing careers in orthopaedic research. This option supports individuals in the early stages of their careers by providing the experience necessary to pursue career opportunities at the forefront of orthopaedic trauma research and make significant contributions to combat-relevant orthopaedic research and clinical care.

- Career Development Principal Investigator (PI): Career Development PIs must be active-duty research- or physician-scientists at either the postdoctoral or early-career level as described in the Eligibility Information section (Section I.C). The Career Development PI may be the Initiating PI, a Partnering PI, or a co-investigator of the application. Only one Career Development PI may be included within a given Translational Research Partnership Award application. "To be named" Career Development PIs are not allowed.
- Orthopaedic Research Mentorship: A designated mentor is required. The mentor may be the PI of the application, a member of the research team, or outside of the research team. This mentor must be an established orthopaedic researcher, have a history of orthopaedic research funding, and have a record of orthopaedic research publications in peer-reviewed journals. In addition, the mentor must demonstrate a commitment to developing and sustaining the Career Development PI's research career in orthopaedic research. The mentor may request salary support, as appropriate to his/her level of effort. ***To promote collaboration between military and non-military organizations, it is encouraged, but not required, that the mentor be from an academic, VA, or other non-military organization.***
- Applications that contain a nested Career Development PI will qualify for a higher level of funding as described under the Funding section (Section I.D).

[1] Ficke JR, Obremsky WT, Gaines RJ, Pasquina PF, Bosse MJ, Mamczak CN, O'Toole RV, Archer KR, Born CT, Fleming ME, Watson JT, Gordon WT, Stannard JP, Rispoli DM, MacKenzie EJ, Wenke JC, Hsu JR, Pollak AN, and Anderson R. Extremity War Injuries VII – A Decade of War: Reprioritization of Research for Combat Casualty Care. *J Am Acad Orthop Surg* (in press).

- Supporting documentation should include a biographical sketch for the Career Development PI, a Career Development Statement, and a letter of support from the Career Development PI's primary mentor. A biographical sketch must also be provided for the mentor if not already included as a key personnel biographical sketch in the Translational Research Partnership Award application.
- ***To qualify for the nested Career Development option, all requirements described above must be included in the application. If these requirements are not met, the Government reserves the right to review the application for a traditional Translational Research Partnership Award.***

Use of Human Subjects and Human Biological Substances: All Department of Defense (DoD)-funded research involving new and ongoing research with human subjects and human biological substances must be reviewed and approved by the U.S. Army Medical Research and Materiel Command (USAMRMC) Office of Research Protections (ORP), Human Research Protection Office (HRPO), in addition to the Institutional Review Board (IRB) of record. IRB approval at the time of submission is NOT required. The HRPO is mandated to comply with specific laws and directives governing all research involving human subjects that is supported by the DoD. These laws and directives will require information in addition to that supplied to the IRB of record. Funded applications that include clinical pilot studies may be required to obtain an independent, external scientific review of the clinical protocol prior to HRPO review. Allow a minimum of 4 months for regulatory review and approval processes. Refer to the General Application Instructions, Appendix 5, for more information.

Use of Military and VA Populations: If applicable, access to target military or VA patient population(s) should be confirmed at the time of application submission. A letter of support, signed by the lowest ranking person with approval authority, should be included for studies involving active duty military, Veterans, military and/or VA-controlled study materials, and military and/or VA databases.

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. While 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 Congressionally Directed Medical Research Programs (CDMRP) intends that data and research resources generated by CDMRP-funded research activities 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

- Independent investigators at all academic levels (or equivalent) are eligible to submit applications.
    - There must be at least one laboratory scientist and at least one clinician participating in the partnership.
    - At least one partner must have significant experience either in orthopaedic research or musculoskeletal medicine.
- Nested Career Development Option: Career Development PIs must be active-duty military and must have at the time of application submission:
    - Completed a doctoral-level degree,
    - A total of less than 8 years of postdoctoral clinical or research experience (excluding clinical residency or fellowship training) at the time of application submission, and
    - Been awarded less than $500,000 in direct costs in aggregate as a PI of Federal or private, non-mentored, peer reviewed grants.
- Cost sharing/matching is not an eligibility requirement.
- Refer to the General Application Instructions, Appendix 1, for general eligibility information.

D. Funding

- The maximum period of performance is **3** years.
- The maximum allowable direct costs for the entire period of performance are **$750,000** plus indirect costs.
    - If requesting the Nested Career Development Option, the maximum allowable direct costs for the entire period of performance are **$975,000**, 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 **3** years.
- 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.
- Each partner will be a PI, and a separate award will be made to each PI's organization.
- The PIs are expected to be equal partners in the research, and direct cost funding should be divided accordingly, unless otherwise warranted and clearly justified.

Refer to the General Application Instructions, Section II.C., for budget regulations and instructions for the Research & Related Budget. In addition, for this award mechanism, direct costs:

Must be requested for:

- Travel costs of up to $1,800 for the PI to attend one DoD research-related meeting to be specified by the CDMRP during the award performance period. These travel costs are in addition to those allowed for annual scientific/technical meetings.

May be requested for (not all-inclusive):

- Salary of non-government personnel
- Research supplies
- Equipment
- Training-related costs for Nested Career Development PI
- Clinical research costs
- Independent scientific review of clinical protocol
- Support for multidisciplinary collaborations
- Travel between collaborating organizations
- Travel costs of up to $1,800 per year to attend scientific/technical meetings

The PRORP expects to allot approximately $3.6M of the $30M FY12 PRORP appropriation to fund approximately three Translational Research Partnership 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 multi-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/).

The Translational Research Partnership Award is structured to accommodate at least two, and up to a maximum of three, PIs. ***One partner will be identified as the Initiating PI and will be responsible for the majority of the administrative tasks associated with application submission.*** The other PI(s) will be identified as the Partnering PI(s). Initiating and Partnering PIs each have different submission requirements; however, all PIs should contribute significantly to the development of the proposed research project, including the Project Narrative, Statement of Work, and other required components.. The Initiating PI must complete the pre-application submission process and submit the contact information for each Partnering PI. Each Partnering PI will then be notified separately by email. ***Please note that each Partnering PI must follow the link in this email and register with CDMRP eReceipt in order to associate his/her grant application package with that of the Initiating PI.*** If an application is invited, only the Initiating PI will receive a letter of invitation via email from CDMRP. The letter will provide the information necessary to begin the application submission through Grants.gov.

Submission of the same research project to different funding opportunities within the same program and fiscal year is prohibited. The Government will reject duplicative applications.

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-12-PRORP-TRPA.

B. Pre-Application Submission Content and Form

All pre-application components must be submitted by the Initiating 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 application should be the same as those identified in the pre-application. If any changes are necessary after submission of the pre-application, the PI must contact the CDMRP Help Desk at help@cdmrp.org or 1-301-682-5507. Requests for a change in PI or organization will be allowed only at the discretion of the U.S. Army Medical Research Acquisition Activity (USAMRAA) Contracting/Grants Officer.

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 (COI) – Tab 3**

  FY12 PRORP IP members should not be involved in any pre-application or application. For questions related to IP members and pre-applications or applications, refer to Section IV.C., Withdrawal, or contact the CDMRP Help Desk at help@cdmrp.org or 1-301-682-5507.

  The Initiating PI must enter the contact information for Partnering PI(s) in the Partnering PI section.

- **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 work addresses at least one of the FY12 PRORP Translational Research Partnership Award Focus Areas.
  - **Research Idea:** Describe the ideas and reasoning on which the proposed research is based; include relevant literature citations. Show how the perspective of each partner contributed to the development of the hypothesis.
  - **Research Strategy:** Concisely state the project's objective and specific aims. Briefly describe the experimental approach.
  - **Partnership:** Describe how the project depends on the unique skills of each partner. Describe how the proposed partnership involves a substantial contribution by each partner and the reciprocal flow of ideas and information. If applicable, describe the roles of the Career Development PI and mentor in the project.
  - **Translational Potential:** Describe how the proposed research will allow for a reciprocal flow of ideas between basic and clinical science. Explain how the project will accelerate promising scientific observations into clinical applications.
  - **Military Benefit:** Describe how the proposed research will provide a significant benefit in the near-term and/or long-term to individuals who have sustained combat or combat-related orthopaedic injuries.

  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.

- Key Personnel Biographical Sketches (four-page limit per individual): Include biographical sketches for the Initiating and Partnering PIs.

- **Submit Pre-Application – Tab 5**

  This tab must be completed for the pre-application to be accepted and processed by the 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 Department of Defense (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 FY12 PRORP Translational Research Partnership Award Focus Areas. How well the rationale supports the research idea.
  - **Research Strategy:** How well the specific aims and proposed methodology support the research idea and objectives.
  - **Translational Potential:** How the project will translate promising, well-founded research findings into clinical applications.
  - **Partnership:** How the partners' backgrounds and expertise are appropriate to accomplish the proposed research in a way that could not be accomplished by either a single investigator or through separate efforts. How the disciplines are appropriate for the proposed research.
  - **Military Benefit:** The degree to which the proposed partnership and research, if successful, will accelerate the movement of new diagnostic and therapeutic approaches in orthopaedic research into clinical application and ultimately benefit the health and lives of Warfighters who have experienced or may experience combat-relevant orthopaedic injury.

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

  Following the pre-application screening, Initiating 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. It is the responsibility of the Initiating PI to inform the Partnering PI(s) of the invitation to submit an application. Pre-application notification dates are indicated on the title page of this Program Announcement/Funding Opportunity.

C. Application Submission Content and Form

Applications will not be accepted unless the Initiating 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/). For the Translational Research Partnership Award, additional application components are also required and should be submitted as directed below.

The CDMRP requires separate Grants.gov application package submissions for the Initiating PI and each Partnering PI. Initiating and Partnering PIs will each be assigned unique log numbers by the CDMRP eReceipt System. Each Grants.gov application package must be submitted using the unique log number.

Application Components for the Initiating PI:

Grants.gov application package components: For the Translational Research Partnership 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 10-page limit of the Project Narrative is inclusive of any figures, tables, graphs, photographs, diagrams, chemical structures, pictures, pictorials, cartoons, and other relevant information needed to judge the application.

     Describe the proposed project in detail using the outline below. ***The Project Narrative must include preliminary data to support the feasibility of the proposed project; however, these data may come from fields other than orthopaedic research.***

     - **Background:** Present the ideas and reasoning behind the proposed research. Cite relevant literature. Describe previous experience most pertinent to this application.
     - **Hypothesis or Objective:** State the hypothesis to be tested or the objective to be reached.
     - **Specific Aims:** Concisely explain the project's specific aims. If the proposed research is part of a larger study, present only tasks that the PRORP award would fund.

- **Research Strategy:** Describe the experimental design, methods, and analyses, including appropriate controls, in sufficient detail for analysis. Address potential problem areas and present alternative methods and approaches. Describe the statistical plan for the research proposed. If human subjects or human biological samples will be used, include a detailed plan for the recruitment of subjects or the acquisition of samples. ***This award may not be used to conduct definitive clinical trials,*** though limited feasibility testing in human subjects as a portion of the Statement of Work is permissible.
- **Partnership:** Describe how the research project depends on the unique skills of each member of the partnership. Provide the time commitment of each partner toward the proposed research project. Describe how the proposed partnership involves a substantial contribution by each partner, with a reciprocal flow of ideas and information. Demonstrate how the partnership will maximize the use of existing resources and minimize unnecessary duplication. Describe the communication plan and provide evidence of institutional support for resolving potential intellectual and material property issues and removing institutional barriers to achieve high levels of cooperation.

- **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 component unless otherwise noted. Include only those components described below; inclusion of items not requested may result in administrative rejection 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 USAMRMC. Indicate if Government-owned facilities or equipment are proposed for use. Reference should be made to the original or present contract 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 they must be included. 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, reflecting the laboratory space, equipment, and other resources available for the project. For PI(s) who are practicing clinicians, the institution must clearly demonstrate

a commitment to the clinician's research. ***If a Career Development PI is included in the application, letters from the Career Development PI's immediate supervisor and Commander must be provided that demonstrate a commitment to allow the Career Development PI to participate in the project.***

- Mentor Letter of Support for Optional Nested Career Development PI (if applicable): Provide a letter signed by the primary mentor in support of the nested Career Development PI. Describe the following:
  - How the Career Development PI's achievements indicate a potential for a successful career in orthopaedic research.
  - How the training environment will promote the development of the Career Development PI as an orthopaedic researcher.
  - The mentor's qualifications, including how the research being performed under the mentor's direction is relevant to combat-related orthopaedic injury.
  - The mentor's proposed interactions with the Career Development PI, and the degree to which the Career Development PI will participate in the execution of the application if funded.
- 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.
- Intellectual and Material Property Plan (if applicable): Provide a plan for resolving intellectual and material property issues among participating organizations.
- Data and Research Resources Sharing Plan: Describe how data and resources generated during the performance of the project will be shared with the research community. Refer to the General Application Instructions, Appendix 4, for more information about the CDMRP expectations for making data and research resources publicly available.

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

  The technical abstract is used by all reviewers; however, programmatic reviewers do not have access to the full application and rely on the technical abstract for appropriate description of the project's key aspects. Technical abstracts should be written using the following outline.

  - Background: State the FY12 PRORP focus area(s) addressed by the proposed research. Present the ideas and reasoning behind the proposed work.
  - Objective/Hypothesis: State the objective/hypothesis to be tested. Describe the overall research goals for the study.
  - Specific Aims: State the specific aims of the study.
  - Study Design: Briefly describe the study design including appropriate controls.

- Translational Partnership: Describe how the proposed partnership will accelerate promising, well-founded research findings into clinical application.
- Military Benefit: State briefly how the proposed project, if successful, will have an impact on combat-relevant 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 research.
    - What types of patients will it help, and how will it help them?
    - What are the potential research and clinical applications, benefits, and risks?
    - What is the projected time it may take to achieve a clinically relevant outcome?
  - Briefly describe how the proposed project will benefit military populations and impact combat-relevant orthopaedic research and/or 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.

  Each PI must submit an identical copy of a jointly created SOW. The contributions of the Initiating PI and Partnering PI(s) should be noted for each task.

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

  Describe the impact of this study on the lives of individuals recovering from combat-relevant orthopaedic injuries, including but not limited to how the expected results of the proposed work will contribute to the goals of decreasing the clinical impact of these injuries.

  Demonstrate how the proposed study is responsive to the health care needs of the Armed Forces and/or the U.S. Veteran population. If active duty military or Veteran population(s) will be used in the proposed research project, describe the population(s), the appropriateness of the population(s) for the proposed study, and the feasibility of using the population. If a non-military population will be used for the proposed research project, explain how the population simulates the targeted population (i.e., Armed Forces 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.

- **Attachment 7: Translation Statement (one-page limit):** Upload as "Translation.pdf."

  State explicitly how the proposed research is translational in nature, allowing for the reciprocal transfer of ideas between basic and clinical science. Explain how the experience and expertise of the partners is complementary and will accelerate the movement of the results to clinical application. Provide information on the methods and strategies proposed to move the product to the next phase of development, clinical trials, and/or delivery to the military or civilian market after successful completion of the award.

- **Attachment 8: Letters Confirming Access to Target Military or VA Patient Population(s), if applicable:** Upload as "Access.pdf."

  If applicable, provide a letter(s) of support, signed by the lowest ranking person with approval authority, for studies involving active duty military and/or Veteran populations, military and/or VA-controlled study materials, and military and/or VA databases.

- **Attachment 9: Career Development Statement, if applicable (three-page limit):** Upload as "CareerDev.pdf."

  The required Career Development Statement from the proposed PI should:

  - Identify the primary mentor. Multiple mentors may be proposed, if appropriate, but one must be identified as primary.
  - Describe a Career Development Plan, which may include coursework, hands-on laboratory and clinical techniques, conferences, seminars, teaching responsibilities, and/or clinical responsibilities.
  - Describe the research that will be performed by the Career Development PI in the context of the proposed project.
  - Articulate career goals and how the proposed research training will promote a career in orthopaedic trauma research.

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."
     - Include biographical sketches for both the Initiating and Partnering PI(s).
     - If applying under the Nested Career Development Option, include biographical sketches for the Career Development PI and mentor.
   - Key Personnel Current/Pending Support (no page limit): Upload as "Support_LastName.pdf."

- Include current/pending support for both the Initiating and Partnering PI(s).
- If applying under the Nested Career Development Option, include the current/pending support of the Career Development PI and mentor.

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."

   Initiating and Partnering PIs must each submit a budget and justification specific to their own portion of the effort as part of their separate Grants.gov application packages. The Research & Related Budget for the Initiating PI should not include budget information for the Partnering PI(s), even if they are at the same organization. The combined total direct costs for the Initiating and Partnering PI(s)' budgets cannot exceed $975,000.

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.

Application Components for the Partnering PI(s):

Each Partnering PI must follow the link in the email from CDMRP eReceipt and complete the registration process prior to the application submission deadline in order to associate his/her grant application package with that of the Initiating PI.

The application submission process for the Partnering PI(s) uses an abbreviated application package of forms and attachments from Grants.gov that includes:

1. **SF 424 (R&R) Application for Federal Assistance Form**

2. **Attachments Form**

   - **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 on completing the SOW. ***Each PI must submit an identical copy of a jointly created SOW. The contributions of the Initiating PI and Partnering PI(s) should be noted for each task.***

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

   - Budget Justification (no page limit): Upload as "BudgetJustification.pdf."

   Initiating and Partnering PIs must each submit a budget and justification specific to their own portion of the effort as part of their separate Grants.gov application

packages. The Research & Related Budget for the Partnering PI(s) should not include budget information for the Initiating PI, even if they are at the same organization. The combined total direct costs for the Initiating and Partnering PI(s)' budgets cannot exceed $975,000.

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

5. **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. Organizations are required to provide a Data Universal Numbering System (DUNS) number and register with the Central Contractor Registry (CCR) 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 compares applications to each other and makes recommendations for funding to the Office of the Assistant Secretary of Defense for Health Affairs, based on technical merit, the relevance to the mission of the DoD and 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. Each level of review requires panelists to sign a non-disclosure statement attesting that application and evaluation information will not be disclosed outside the panel. Violations of the non-disclosure statement can result in the dissolving of a panel(s) and other corrective actions. Organizational personnel and PIs 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 panelists or PIs that compromise the confidentiality of the review process may also result in suspension or debarment of their employing organizations 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 criteria, which are of equal importance:

   - **Translational Potential**
     - The degree to which the project, if successful, will lead to the translation of promising, well-founded laboratory or clinical research findings into clinical applications for combat-relevant orthopaedic injuries.
   - **Research Strategy and Feasibility**
     - How well the scientific rationale supports the project and its feasibility, as demonstrated by a critical review and analysis of the literature and/or logical reasoning.
     - How well the hypotheses or objectives, aims, experimental design, methods, and analyses are developed and support completion of the aims.
     - How well the PI acknowledges potential problems and addresses alternative approaches.
     - The degree to which the plan to study military populations, if applicable, is appropriate and feasible.
   - **Military Benefit**
     - To what degree the proposed project could, if successful, make a significant impact the lives of those affected by combat-relevant orthopaedic injuries.
     - How well the project addresses a critical problem in combat-relevant orthopaedic research or medicine.
     - The degree to which the proposed project, if successful, will advance the research methods, understanding of, and/or treatment of combat-relevant orthopaedic injuries.
   - **Partnership and Personnel**
     - The degree to which the proposed partnership will advance orthopaedic research in a way that could not be accomplished by investigators working independently.
     - How well the application supports the requirement that all partners contribute substantially to the development and implementation of the research plan, and to the reciprocal flow of ideas.

- How well the multiple institutions (if applicable) and multiple disciplines within the partnership will support the proposed project.
- How well the partners' background, expertise, and levels of effort will support the proposed project.
- Whether there is sufficient evidence of a plan to resolve intellectual and material property issues.
- ***Nested Career Development applicants (if applicable):***
  - How the qualifications of the Career Development PI will add to the project.
  - How the Career Development PI will benefit from participation in this project.
  - How well the mentor, training environment, and career development plan are suited to providing the Career Development PI with a training experience that will further his/her career at the forefront of orthopaedic research.

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.
  - The degree to which 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.
- **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 influenced the review.

2. **Programmatic Review:** To determine the application's relevance to the mission of the DoD and 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 in relation to FY12 PRORP Focus Areas
- Programmatic relevance

- Ratings and evaluations of the peer reviewers
- Relative military benefit

C. Recipient Qualification

Refer to the General Application Instructions, Appendix 1, for additional information on organization and Government agency requirements.

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 scientific peer review summary statement on the strengths and weaknesses of the application.

IV. ADMINISTRATIVE ACTIONS

After receipt of pre-applications from CDMRP eReceipt 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.
- All associated (Initiating and Partnering PI) applications are not submitted by the deadline.

B. Modification

- Pages exceeding the specified limits will be removed prior to review for all documents other than the Project Narrative and 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 FY12 PRORP IP 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 FY12 PRORP IP members can be found at http://cdmrp.army.mil/prorp/default.
- 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.
- The proposed research is a definitive clinical trial.
- The partnership does not include at least one clinician and one laboratory scientist.
- The partnership does not include an investigator with significant experience in orthopaedic research or orthopaedic medicine.
- The PI(s) does not meet the eligibility criteria.
- The proposed project is not relevant to at least one of the FY12 PRORP Translational Research Partnership Award Focus Areas.

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 U.S. Army Medical Research Acquisition Activity (USAMRAA) Contracting/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, 2013. 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. In addition to written progress reports, oral presentations may be requested.

D. Award Transfers

Changes in PI are not allowed, except under extenuating circumstances that will be evaluated on a case-by-case basis and at the discretion of the Grants Officer.

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: 1-301-682-5507

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: 1-800-518-4726

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. 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	Initiating PI Completed	Partnering PI 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.		
	Upload Translation Statement (Translation.pdf) as Attachment 7.		
	Upload Letters Confirming Access to Target Military or VA Patient Population(s) (Access.pdf) as Attachment 8.		
	Upload Career Development Statement, if applicable, (CareerDev.pdf) as Attachment 9.		
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 form 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.		