

# Program Announcement

Department of Defense Congressionally Directed Medical Research Programs

Peer Reviewed Orthopaedic Research Program

Orthopaedic Rehabilitation Clinical Consortium Award

Funding Opportunity Number: W81XWH-10-PRORP-ORCCA

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## **I. FUNDING OPPORTUNITY DESCRIPTION**

### **A. Program Description**

The Peer Reviewed Orthopaedic Research Program (PRORP) was established in fiscal year 2009 (FY09) to address 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. Appropriations for the PRORP in FY09 totaled \$112 million (M). The FY10 appropriation is \$22.5M.

The FY10 PRORP challenges the scientific community to design innovative research that will foster new directions for and address neglected issues in the field of combat-related orthopaedic injury research. Though the PRORP supports groundbreaking research, all projects must demonstrate appropriate judgment and sound rationale. 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 Description**

The PRORP Orthopaedic Rehabilitation Clinical Consortium Award mechanism is being offered for the first time in FY10. The intent of the award is to fund clinical rehabilitation studies focused on improving functional outcomes of severe musculoskeletal injuries associated with military combat. The award is designed to bring together populations of military orthopaedic trauma patients, the combat-relevant research expertise of the specified military treatment facilities (MTFs) listed in Section B.2, and the patient populations and research expertise of highly qualified civilian rehabilitation scientists (i.e. from the fields of physical medicine, physical therapy, occupational therapy, and/or orthopaedic trauma) at outstanding organizations. It is expected that relevant clinical outcomes will require longitudinal evaluations of rehabilitation and return to optimal function. At the time of award completion, it is anticipated that the awardee will have established a strong infrastructure for continuing clinical studies on combat-relevant musculoskeletal injuries, and products (information, guidelines, validated techniques, or devices) that result in changes to, or validation of, current clinical practice that lead to better outcomes for our injured warriors. All projects should account for financial costs and provide detailed estimates of the proposed system cost if procured, so that the military and civilian medical community can conduct a cost benefit analysis with current practice alternative to distinguish the optimal cost-effective treatments.

Projects must be militarily relevant, have very defined objectives, control confounders, have a patient population that will allow for an appropriately robust sample size at each site, be of high quality, and be capable of producing results that are likely to change practice. Studies involving non-military patient populations must describe how they simulate the targeted population (i.e. Armed Forces and/or the US veteran population). While large, randomized controlled clinical studies are expected to be part of this multi-institutional consortium effort, small randomized or pilot clinical trials and observational prospective studies to develop metrics or provide proof of principle to inform future clinical studies are also appropriate. All projects shall be limited to clinical research and clinical trials. ***Animal studies are excluded from consideration.***

The Orthopaedic Rehabilitation Clinical Consortium Award resulting from this program announcement will be issued as a cooperative agreement between the recipient (Coordinating Center) and the Government (the US Army Medical Research Acquisition Activity [USAMRAA]). An appointed Government Steering Committee will review research priorities and make recommendations to the Grants Officer's Representative (GOR) for the GOR's consideration and ultimate approval decisions by the USAMRAA Grants Officer.

**1. PRORP Orthopaedic Rehabilitation Clinical Consortium Award Focus Areas:**

The goal of the PRORP Orthopaedic Rehabilitation Clinical Consortium Award is to improve rehabilitation of combat and combat-related neuromusculoskeletal injuries (including spine injuries, burns, and contractures, and excluding spinal cord injury [SCI]). To further progress toward this goal, the FY10 PRORP has established a set of rehabilitation focus areas, listed below in order of decreasing priority. Applications for the PRORP Orthopaedic Rehabilitation Clinical Consortium Award must address **at least four** of the following focus areas. Special consideration will be given to those submissions that incorporate focus areas of high priority:

- Improvement and enhancement of rehabilitative strategies for patients with severe limb trauma and amputation as measured by effectiveness and improvement of functional outcomes.
- Development and validation of novel rehabilitation approaches designed to optimize function following limb salvage and regenerative medicine interventions.
- Evaluation of the impact of exercise and fitness systems, and strategies on rehabilitation and sustainment of fitness in individuals with limb loss or limb-threatening injuries.
- Evaluation of amputee-specific technologies and rehabilitation strategies that address/assess residual limb health and/or mitigate long-term consequences of severe limb trauma such as arthritis, overuse injury, and cardiovascular disease.
- Assessment of strategies to minimize deleterious effects of contracture on function and mobility.
- Improvement and enhancement of rehabilitative strategies for spine injury (excluding SCI).
- Enhancement of the understanding of psychosocial aspects that influence rehabilitative care.
- Identification of upper extremity kinematics and kinetic variables following injury that negatively influence functional activities including mobility.
- Development of validated strategies for incorporating existing advanced technology (prosthetics, orthotics, assistive devices) for patients with severe extremity trauma, including burns, peripheral nerve injuries, joint contractures, soft tissue defects, and/or amputation.
- Development of improved rehabilitation strategies (non-pharmaceutical) for management of pain and its impact on return to function.

- Improved understanding and definitive management of severe extremity fractures which positively or negatively influence return to military duty or successful community re-integration and employment.
- Assessment of the impact of rehabilitation during the early care of patients with extremity trauma to minimize the effects of immobility and deconditioning to enhance more rapid functional return and outcomes.
- Validation of current rehabilitation strategies for individuals with limb and/or spine injury incorporating relevant outcome measures.
- Development and assessment of relevant outcome measures for tele-medicine/web-based systems used for dispersed groups (e.g., social networking style).

**All applications must have a direct relevance to orthopaedic injuries sustained during military combat or combat-related activities.**

**2. General Information:** The PRORP Orthopaedic Rehabilitation Clinical Consortium Award supports the development of a consortium that will consist of a Coordinating Center in collaboration with multiple MTFs (required) and non-military (encouraged) Clinical Study Sites. **Because this award is intended to maximally benefit wounded warriors, the Coordinating Center will be required to collaborate with the following MTFs: Naval Medical Center Portsmouth (NMCP), Naval Medical Center San Diego (NMCS), San Antonio Military Medical Center (SAMMC), and Walter Reed National Military Medical Center (WRNMMC).** In addition, collaborations with academic, VA, government, other military, industry, or non-profit organizations are strongly encouraged and should be described within the application. Applicants are also strongly encouraged to leverage existing clinical programs to enhance collaboration and educational/training opportunities for clinical researchers.

Aside from the named MTF collaborators listed above, the applicant must propose additional Clinical Study Sites to execute the mission of the Consortium. The Consortium should be comprised of existing high volume and high productivity sites that have a clinical research track record to maximize enrollment within the available funding constraints. Applicants may provide a plan for the inclusion of secondary sites to be activated as needed for study participation. See Figure 1 for a proposed structure of the PRORP Clinical Consortium.

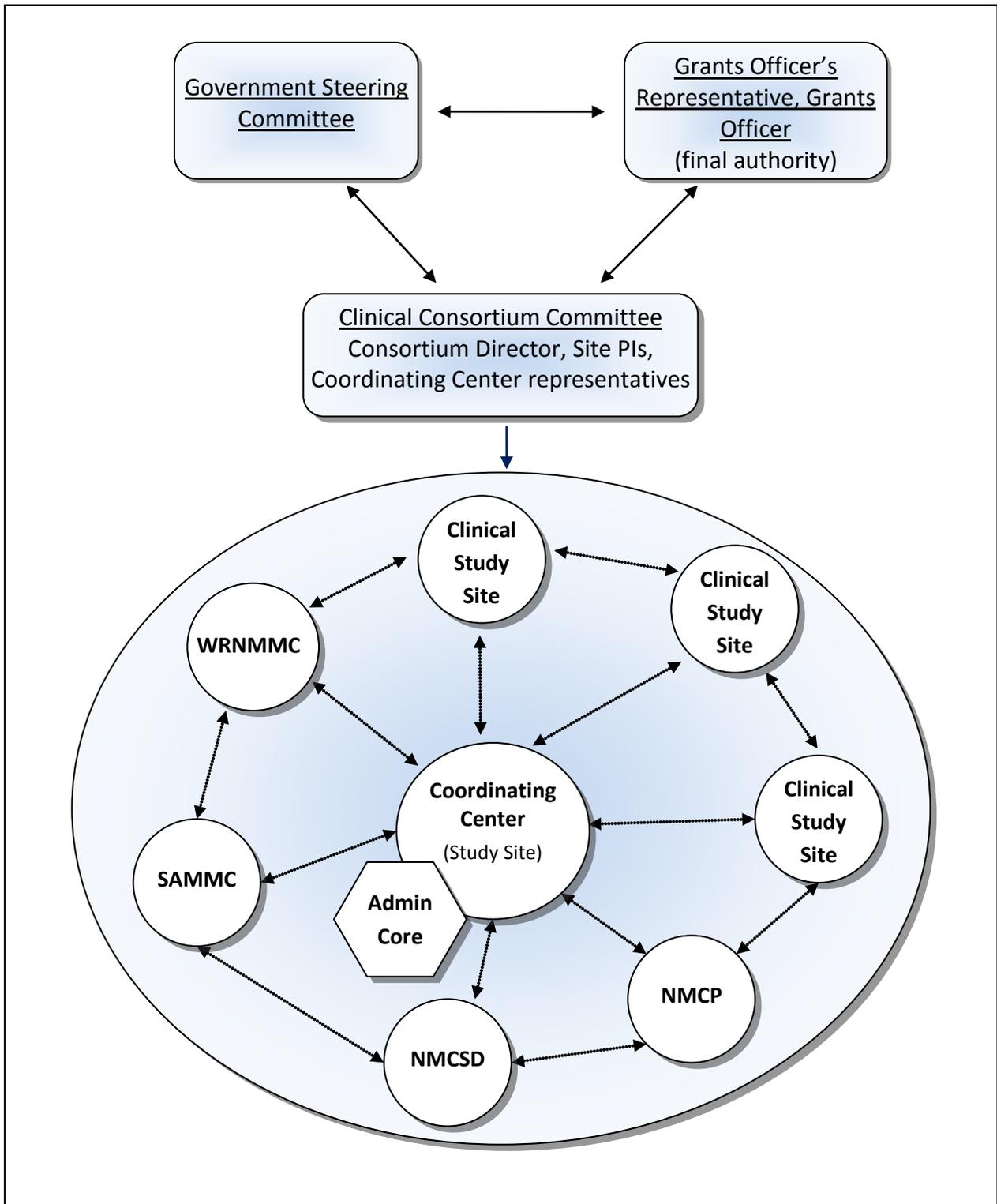
The Coordinating Center and any associated Clinical Study Sites (not including PRORP-named MTFs) must apply to this announcement through a single application. A single award will be made to the Coordinating Center, and award funds will be used to support the Coordinating Center's efforts as well as Consortium-associated studies at each of the Clinical Study Sites, including the MTFs. The Coordinating Center will provide management and funding through the appropriate instruments for the non-MTF Clinical Study Sites to conduct medical research towards improving reconstruction and rehabilitation for combat and combat-related orthopaedic injuries. The Coordinating Center will provide management and support (research personnel, supplies, etc.) to the MTFs through various appropriate means; however, no direct funds will be provided by the Coordinating Center to the MTFs.

The Consortium will conduct studies that build upon the orthopaedic research goals and patient care initiatives established by the DOD at the MTFs ([Appendix](#)) that are in alignment with the PRORP Orthopaedic Rehabilitation Clinical Consortium Award focus areas (Section B.1). It is the responsibility of the applicant to describe clearly within the proposal how the proposed Consortium will have a significant impact on the rehabilitation of combat-related orthopaedic injury.

The Coordinating Center, which may also serve as a clinical site, will facilitate the rapid selection, design, and execution of clinical studies within the Consortium, and will provide the administrative, protocol development, regulatory, statistical, resource, and data management/storage functions necessary to facilitate Consortium studies. The Principal Investigator (PI) of the Coordinating Center should provide evidence of prior experience with the design and administration of multi-institutional clinical studies. The PI must also demonstrate a broad understanding of orthopaedic injury research, including knowledge of the current state of clinical studies and clinical priorities related to the PRORP Orthopaedic Rehabilitation Clinical Consortium Award focus areas, which address critical militarily relevant issues.

The proposal should name and describe individual core facilities at member organizations that will serve as official Consortium research core facilities. Establishment of Consortium-wide core facilities will enable more consistent, high-quality, standardized data to be collected across sites for Consortium-supported studies.

Applications must include an initial set of proposed studies (minimum of 4) reflective of the overall goals of the Consortium for consideration during the review and selection process, some or all of which may be carried out if selected for funding based upon recommendations of the PRORP reviewers and Government Steering Committee. Proposed studies should include a range of scope, size, and type that is representative of the overall goals of the Consortium. Funding selection will depend upon evaluation of the proposed studies, record of productivity, available capabilities, organization of the Consortium, and feasibility of the entire group to accomplish the overall award objectives. During the performance period of the award, all Clinical Study Sites, including the MTFs, will be responsible for working collaboratively to identify new clinical studies for implementation by the Consortium. All of these studies will be subject to Steering Committee review and recommendations to the GOR and the Grants Officer for decisions prior to implementation. Collectively, the Clinical Study Site PIs will constitute the Clinical Consortium Committee, which will be responsible for proposing and conducting clinical studies focused on rehabilitative care for combat-related orthopaedic injuries, and for determining which Consortium organizations will participate in each study. The Coordinating Center will be responsible for facilitating this process, and the proposal should include a description of how the Coordinating Center plans to coordinate with the Clinical Study Sites to propose, design, externally peer review, and prioritize the most relevant clinical studies once the Consortium is established. Additional clinical studies will be presented to the government Steering Committee at a twice-yearly meeting for review and approval recommendations prior to implementation. See Section B.6 for further information regarding the Steering Committee.



**Figure 1: Proposed Consortium Structure.** Applicants may propose alternative organizations for the Consortium; however, in all configurations, a Government Steering Committee will provide consultation to the Consortium governing body on research gaps and military priorities.

**3. Required MTF Collaboration:** Military relevance is a key element of the PRORP Orthopaedic Rehabilitation Clinical Consortium Award. As such, it is expected that Consortium-proposed studies will align closely with the research goals of the MTFs that are in alignment with PRORP Orthopaedic Rehabilitation Clinical Consortium Award focus areas (Section B.1 and [Appendix](#)). Submitting an application to the PRORP Orthopaedic Rehabilitation Clinical Consortium Award is considered an implicit commitment to collaborate with NMCP, NMCSA, SAMMC, and WRNMMC in the Clinical Consortium. Applicants should provide a plan to ensure that the MTFs have input on and participation in all Consortium activities, equivalent with other Clinical Study Sites. The plan should also outline a strategy to develop the necessary research capabilities at the MTFs, including educational and training opportunities as appropriate. The Coordinating Center must plan to provide resources to the MTFs for their role in Consortium-supported studies, including supplies and research personnel support as necessary. ***Funds provided through this award may not be used to support government salaries, but may be used to support contract research personnel.*** It is expected that exact MTF requirements will change based on the type and number of studies conducted by the Consortium. Suggestions of the types of research personnel support that may be needed at the MTFs include clinical research nurses, Ph.D./M.D.-level researchers, physical/occupational therapists, technicians to support Computer-Assisted Rehabilitation Environments (CAREN), physiatrists, and clinical research assistants. Exact personnel support and effort levels should be determined by the applicant as appropriate for the proposed studies. It is anticipated that the MTF interface with Consortium-supported personnel will be provided by an active duty, doctoral-level research director assigned to the MTF.

Applicants should utilize the information papers provided by each MTF ([Appendix](#)) to work within existing MTF capabilities and determine potential MTF needs within the Consortium. In addition, a Question and Answer (Q&A) informational meeting prior to the application submission deadline is scheduled for September 13, 2010, in the Washington, DC metro area. Applicants will be invited to meet with representatives of the PRORP Integration Panel (IP) and the MTFs to discuss the intent of this funding opportunity and the research needs in the field of physical medicine and rehabilitation as it relates to combat injury. Details and registration information for the Q&A informational meeting will be included in an invitation to submit a full application following the pre-application screening process outlined in Section III.A. Only those applicants invited for full application submission will be invited to the Q&A informational meeting. Travel expenses for invited applicants will be reimbursed by the Office of the Congressionally Directed Medical Research Programs (CDMRP).

A summary of the Q&A informational meeting will be posted on the CDMRP eReceipt website, <https://cdmrp.org>. In addition, questions about the PRORP Orthopaedic Rehabilitation Clinical Consortium Award may be sent to [cdmrp.prorp@amedd.army.mil](mailto:cdmrp.prorp@amedd.army.mil). Questions will be accepted until October 15, 2010. Questions and answers will be posted on the CDMRP eReceipt website, <https://cdmrp.org>.

**As the MTFs (NMCP, NMCSA, SAMMC, and WRNMMC) are named collaborators for this Program Announcement/Funding Opportunity, no discussion between MTF personnel and the applicant regarding this Program Announcement/Funding Opportunity is permitted during proposal preparation and review outside of the Q&A**

**informational meeting.** Once award selection is complete, there will be an opportunity to refine MTF needs and resources with appropriate MTF input prior to issuance of the award.

#### **4. Summary of Responsibilities:**

- **Responsibilities of all Consortium Participants:** Procedures for the Consortium, while proposed by the Coordinating Center, will be fully developed and agreed upon by all participants working collaboratively at a pre-award planning meeting hosted by the US Army Medical Research and Materiel Command (USAMRMC) to be held in March or April, 2011, and attended by representatives of the Coordinating Center, Clinical Study Sites (including the MTF sites), Steering Committee, and USAMRMC. The process shall be codified in a Standard Operating Procedure (SOP), which will be provided to the GOR and Steering Committee within 6 months of the Consortium pre-award planning meeting, or 90 days from award execution, whichever comes later.
- **Consortium Coordinating Center**
  - Coordinating Center PI will serve as the Director of the Consortium, Chair of the Clinical Consortium Committee, and the primary liaison with the GOR;
  - Ensure that a minimum number of clinical studies, as agreed upon by the Steering Committee, Clinical Consortium Committee, and USAMRMC during the pre-award planning meeting, are initiated by the start of the second year of the award;
  - Ensure that the Consortium adheres to the planned timeline and milestones for overall study execution;
  - Develop and maintain the Consortium organizational structure;
  - Manage Consortium-developed procedures for external scientific review, prioritization, and implementation of clinical studies proposed by or through Consortium members;
  - Establish a mechanism to provide MTFs with resources necessary for participation in the Consortium;
  - Establish and manage procedures to ensure that all sites maintain compliance with local Institutional Review Boards (IRBs) and the Army Surgeon General's Human Research Protection Office (HRPO) for the proper conduct of clinical studies and the protection of human subjects;
  - Provide a Consortium Clinical Research Manager who will oversee the efforts of the Clinical Research Coordinators at the Clinical Study Sites. The Consortium Clinical Research Manager will be responsible for coordinating and facilitating clinical protocol approval, patient accrual, and study activities across all sites;
  - Establish and manage procedures for ensuring compliance with US Food and Drug Administration (FDA) requirements for investigational agents, devices, and procedures;
  - Establish and manage a communications plan and a real-time communications system between the Coordinating Center and Clinical Study Sites, including the purchase of multi-site licenses, if necessary;

- Ensure the standardized analyses of specimens, imaging products, and other data through the establishment of scientific core facilities;
- Manage Consortium-developed quality assurance and quality control mechanisms for study monitoring, including but not limited to:
  - On-site monitoring program, to include safety
  - Management plan for the handling, distribution, and banking of specimens and imaging products generated from Consortium studies
  - Registration, tracking, and reporting of participant accrual
  - Timely medical review, rapid reporting, communication of adverse events, and data management/coordination among all sites
  - Interim evaluation and consideration of measures of outcome
- Manage Consortium-developed comprehensive data collection and data management systems that address the needs of all Clinical Study Sites in terms of access to data, data security, and data integrity measures;
- Implement statistical execution plans/support for all Consortium clinical studies;
- Manage costs to support the Clinical Study Sites, including provision of personnel, equipment, and materials required to conduct approved clinical studies;
- Manage Consortium-developed intellectual and material property issues among organizations participating in the Consortium;
- Manage Consortium-developed procedures for the timely publication of major findings and other public dissemination of data;
- Attend a pre-award planning meeting, hosted by the USAMRMC, with all Consortium members to develop the operational features of the Consortium, the requirements for progress and evaluation, and the award negotiations process;
- Coordinate the preparation of written and oral twice-yearly briefings to the Steering Committee and USAMRMC staff at 1-day meetings to be held in a centralized location to be determined by USAMRMC;
- Develop, organize, and submit quarterly written progress reports, annual reports, and a final written comprehensive report to the USAMRMC.
- **Clinical Study Sites**
  - Participate fully in the Clinical Consortium Committee;
  - During the performance period of the award, identify potential studies and develop proposals in accordance with the Consortium SOP for presentation to the Steering Committee;
  - Integrate with clinical studies at other Clinical Study Sites;
  - In accordance with Consortium-developed guidelines, maintain a minimum combined accrual across all Consortium-associated studies as well as a maximum contributed percentage for each individual study;

- Provide a Clinical Research Coordinator who will interact with the Clinical Research Coordinators of other Clinical Study Sites and the Consortium Clinical Research Manager at the Coordinating Center to expedite and guide clinical protocols through regulatory approval processes and to coordinate patient accrual and study activities across sites;
- Implement the Consortium's core data collection methodology and strategies;
- Comply with Consortium-developed quality assurance and quality control procedures, as appropriate, including:
  - Participate in an on-site monitoring program to be managed by the Coordinating Center
  - Implement the Consortium-developed management plan for acquisition and aggregation of protocol-specified specimens, biological fluids, and relevant clinical data to the appropriate laboratories for testing or storage necessary for the conduct and analyses of clinical studies during the performance period of the award
  - Submit appropriate data and materials to allow for verification and review of protocol-related procedures (e.g., pathology, imaging techniques, surgical methods, and therapeutic use)
- Implement procedures established by the Coordinating Center for ensuring compliance with FDA requirements for investigational agents, as appropriate;
- Implement procedures established by the Coordinating Center to meet the local IRB and the Army Surgeon General's HRPO requirements for the conduct of clinical studies and the protection of human subjects;
- Serve as a resource or core for the conduct of protocol-specified laboratory projects (including correlative studies), as appropriate;
- Participate in Consortium-developed procedures for the timely publication of major findings;
- Participate in Consortium-developed procedures for resolving intellectual and material property issues among organizations participating in the Consortium;
- Attend a pre-award planning meeting with all Consortium members to develop the operational features of the Consortium, outline the requirements for progress and evaluation, identify target initial clinical studies, align selected studies with appropriate Clinical Study Sites, and facilitate the award negotiations process (to be held in March or April, 2011);
- Participate in the preparation of written and oral twice-yearly briefings to the Steering Committee and USAMRMC staff at 1-day meetings to be held in a centralized location to be determined by USAMRMC;
- Assist with the preparation of quarterly written progress reports and a final written comprehensive report;
- Prepare for a site visit audit, if applicable.

**5. Performance Metrics:** Applicants should lay out a plan for the number and types of clinical studies the Consortium expects to execute. As a preliminary guideline, the Consortium should be prepared to complete between 8 to 15 clinical studies during the performance period of the award, depending upon the size and complexity of each study. By the start of the second year of the performance period, a minimum number of clinical studies, as agreed upon by the Clinical Consortium Committee, the Steering Committee, and USAMRMC, shall be initiated. A timeline outlining the overall plan for study initiation, performance, and analyses shall be developed, with clear milestones to which the Consortium will be held accountable. The Clinical Consortium Committee will determine appropriate overall minimum and maximum accrual metrics for the Clinical Study Sites as part of the Consortium SOP, with input from the Steering Committee. For individual clinical studies, the Coordinating Center should ensure the maintenance of overall patient accrual per year, appropriate for the target population. The Consortium SOP should also contain a plan to address underperforming sites. Accrual metrics for the MTFs are expected to differ, and will be determined at a later date by USAMRMC staff and the Steering Committee. The Coordinating Center will be required to submit quarterly written reports that outline accrual and retention statistics, any problems with study execution, and actions to disseminate study results. It is expected that the Consortium will submit to other agencies for additional funding in order to increase the breadth of research and create a self-sustaining entity that will continue functioning beyond the five-year performance period of the award.

**6. Oversight of the Consortium:** A Steering Committee comprised of government personnel will be established by USAMRMC. The Steering Committee will review progress, and it will provide advice and guidance on scientific and military relevance and on the coordination of proposed projects with other military relevant initiatives. The Steering Committee will provide approval recommendations regarding proposed Consortium studies prior to implementation, and will recommend areas of future study to the Consortium. Consortium PIs must present written and oral briefings to the Steering Committee and USAMRMC staff at twice-yearly 1-day meetings to be held in a centralized location. Based on these reports and presentations, the Steering Committee and USAMRMC staff will evaluate progress, provide feedback, and invoke modifications as needed to facilitate the success of the Consortium. The Clinical Consortium Committee, through the Coordinating Center PI, is expected to maintain monthly or more frequent contact with a government appointed GOR, who will maintain full documentation of interactions. The USAMRAA Grants Officer will issue the final approval of any proposed projects and/or studies.

**7. Use of Human Subjects and Human Biological Substances:** All Department of Defense (DOD)-funded research involving human subjects and human biological substances must be reviewed and approved by the USAMRMC Office of Research Protections (ORP), HRPO, in addition to local IRBs. The HRPO is mandated to comply with specific laws and directives governing all research involving human subjects that is conducted or supported by the DOD. These laws and directives are rigorous and detailed, and will require information in addition to that supplied to the local review board. Allow a minimum of 6 months for regulatory review and approval processes for studies involving human subjects. Refer to General Application Instructions, Appendix 5, for detailed information.

## **8. Department of Veterans Affairs (VA) Medical Centers Patient Populations:**

Applicants are encouraged to include collaborations with VA organizations. Access to patient populations from VA Medical Centers or use of information from VA data systems must be coordinated by the PI. PIs who submit a research project designed to recruit patients from a VA Medical Center or use information from VA data systems, and those who do not have an appointment at one of the VA Medical Centers must include a collaborator with a VA appointment. This collaborator must be willing to assume the role of PI for the VA component of the research. IRB approval from all participating VA clinical sites will be required.

### **C. Eligibility**

Coordinating Center PIs must be independent investigators at or above the level of Associate Professor (or equivalent) at an eligible organization. Refer to General Application Instructions, Appendix 1, for general eligibility information.

### **D. Funding**

A single award will be made to support the FY10 PRORP Orthopaedic Rehabilitation Clinical Consortium. The award will be made to the Coordinating Center applicant selected for funding. The Coordinating Center will provide funding support for the selected Clinical Study Sites as subawards.

All applicants are requested to propose a minimum of four studies that may be initiated in the first year of the award. Proposed studies should include a range of scope, size, and type that is representative of the overall goals of the Consortium. Budget out-years should be projected based on the proposed costs of the initial studies, with appropriate escalation factors included. Following award, a budget for each study will be negotiated individually once study selections are made.

- The maximum period of performance is **5** years.
- The maximum allowable funding for the entire period of performance is **\$19.5M** in total (direct plus indirect) costs.
- The applicant may not exceed the maximum allowable funding. In addition to direct costs, indirect costs may be proposed in accordance with the organization's negotiated rate agreement.

Within the guidelines provided in the General Application Instructions, funds can cover:

- Salary support for personnel needed to meet the goals of the Clinical Consortium, such as the PIs, Consortium Core personnel, Consortium Clinical Research Manager, Physical/Occupational Therapists, Psychiatrists, Financial Officer, Program Coordinator, Administrative Assistant(s), Research Nurse(s), Statistician(s), Database Manager, and Informatics Manager;
- Implementation of Consortium-developed standardization plan, data management program, real-time communications system, and administration plans for the Consortium;

- Support of Consortium-related meetings, teleconferences, and travel among participating investigators;
- Costs associated with the external scientific peer review of clinical studies/research;
- Purchase of computers, specialized software, and specialized software licenses for Clinical Study Sites when required to fulfill Coordinating Center-specific tasks;
- Purchase of minor equipment necessary for specimen and data storage and transfer;
- Costs associated with coordination of informed consent/assent form preparation and other IRB-required materials among different organizations;
- Reimbursement of organizations for additional costs associated with using Consortium Core facilities;
- Reimbursement of organizations for costs associated with conducting the IRB review of the clinical protocols and informed consent/assent forms;
- Costs associated with management of intellectual property resolution and material rights resolution among organizations;
- Clinical costs;
- Research-related subject costs;
- General research costs;
- Costs associated with development of sources for intervention supply or availability;
- Other costs directly associated with planning and developing the consortium;
- Travel costs of up to \$3,600 per year to attend scientific/technical meetings;
- Other direct costs as described in the General Application Instructions for the Detailed Budget and Justification.

In addition, travel funds must be requested for the Coordinating Center PI and each Clinical Study Site PI to attend one DOD military research-related meeting per year, to be determined by the Government during the award performance period. The PI must also include funds for travel to twice-yearly 1-day briefings with the Steering Committee and USAMRMC staff.

Direct transfer of funds to a government organization or agency is not allowed except under very limited circumstances and as subject to prior Grants Officer approval. The Coordinating Center is expected to provide a mechanism to transfer resources such as supplies and support as necessary to the MTFs to support their participation in Consortium studies. **Funds provided through this award may not be used to support government salaries.** Details on exceptions to the prohibition of direct fund transfer to government entities can be found in Section II.B.2 (Federal Financial Plan) of the General Application Instructions.

*The CDMRP expects to allot approximately \$19.5M of the \$22.5M FY10 PRORP appropriation to fund approximately 1 Orthopaedic Rehabilitation Clinical Consortium Award application, depending upon 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.*

## **E. Award Administration**

The Coordinating Center of the PRORP Clinical Consortium Award cannot be transferred to another organization.

The awardee will be required to submit three quarterly written progress reports per year, a written annual report, and a final written comprehensive report.

In addition to written progress reports, awardees may expect requests for formal progress presentations in clinical symposia to accelerate transition into clinical practice.

Awards will be made approximately 4 to 6 months after receiving a funding notification letter, but no later than September 30, 2011. Refer to the General Application Instructions, Appendix 4, for general award administration information.

## **II. TIMELINE FOR SUBMISSION AND REVIEW**

- **Pre-application Submission Deadline: 5:00 p.m. Eastern time (ET), July 16, 2010**
- **Invitation to Submit an Application: August 2010**
- **Q & A Informational Meeting: September 13, 2010**
- **Application Submission Deadline: 11:59 p.m. ET, October 29, 2010**
- **Scientific Peer Review: December 2010**
- **Programmatic Review: February 2011**

*Application submissions will not be accepted unless the pre-application process is completed by the pre-application deadline.*

## **III. SUBMISSION PROCESS**

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/>). *Applications will be invited based on pre-application screening.*

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

PIs and organizations identified in the application should be the same as those identified in the pre-application. If a change in PI or organization is necessary after submission of the pre-application, the PI must contact the eReceipt help desk at [help@cdmrp.org](mailto:help@cdmrp.org) or 301-682-5507.

### **A. Step 1 – Pre-Application Components**

All pre-application components must be submitted through the CDMRP eReceipt system by **5:00 p.m. ET on the deadline**. 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.

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 for additional information on pre-application submission):

- **Proposal Information – Tab 1**
- **Proposal Contacts – Tab 2**
- **Collaborators and Conflicts of Interest (COI) – Tab 3**
- **Required Files – Tab 4**

**Preproposal Narrative (five-page limit):** The Preproposal Narrative is inclusive of any figures, tables, graphs, photographs, diagrams, chemical structures, pictures, pictorials, and cartoons.

The Preproposal Narrative should include the following:

- **Overarching Goals:** Provide a brief description of the overall goals of the consortium in the field of rehabilitative medicine for combat or combat-related orthopaedic injuries.
- **Consortium Structure:** Outline the organizations that will participate in the consortium. Briefly discuss the qualifications of key personnel in the administration and conduct of multi-institutional clinical studies. Discuss potential core facilities, shared resources, and other elements of the Consortium that will promote synergy.
- **Research Plan:** Provide a brief description of the initial clinical studies to be proposed. Identify the PRORP Orthopaedic Rehabilitation Clinical Consortium Award focus area(s) relevant to each study. Describe the reasoning on which the studies are based, the target patient population(s), and the outcomes to be measured.
- **Military Relevance:** Describe how the Consortium will have an impact on the lives of individuals recovering from combat-relevant orthopaedic injuries, and the evaluation and/or acceleration of promising rehabilitation treatments into clinical practice.

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

- **References Cited:** 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)**
- **Submit Pre-application – Tab 5**
- **Other Documents Tab**

Not applicable.

**Pre-Application Screening:** Pre-applications will be screened by the PRORP IP based on the following criteria:

- **Consortium Structure:** How well the outlined consortium structure will support timely and efficient multi-institutional clinical studies of varying scope and size. The

appropriateness of the administrative and research teams' background and expertise with respect to their ability to oversee rehabilitative medicine clinical studies.

- **Military Benefit:** The degree to which the proposed research, if successful, will have a significant clinical impact to innovate and/or improve clinical care for warfighters who have sustained combat-relevant orthopaedic injury.
- **Research Plan:** How well the proposed initial studies align with the PRORP Orthopaedic Rehabilitation Clinical Consortium Award focus areas. The degree to which the proposed studies address important questions that will further clinical rehabilitative research and treatment of musculoskeletal injury.

Following the pre-application screening, PIs will be notified of whether or not they are invited to submit an application; however, they will not receive feedback (e.g., strengths and weaknesses) on their pre-application.

## **B. Step 2 – Application Components**

*Applications will not be accepted unless the PI has received a letter of invitation.*

Applications are submitted by the Authorized Organizational Representative (AOR) through Grants.gov (<http://www.grants.gov/>). Applications must be submitted **by 11:59 p.m. ET on the deadline.**

Each application submission must include the completed application package of forms and attachments identified in Grants.gov for this Program Announcement/Funding Opportunity.

The Grants.gov application package consists of the following components (Refer to the General Application Instructions, Section II.B., for additional information on application submission):

**1. SF 424 (R&R) Application for Federal Assistance Form:** Refer to the General Application Instructions, Section II.B., for detailed information.

### **2. Attachments Form**

- **Attachment 1: Project Narrative (70-page limit):** Upload as “ProjectNarrative.pdf.” Describe the qualifications of the group and the key features of the Consortium using the following general outline:
  - Outline the structure of the proposed Consortium and identify key personnel.
  - Describe the previous experience of the PI and other key personnel within the Coordinating Center with the design and administration of multi-institutional musculoskeletal rehabilitation clinical studies. Reference relevant publications and submit reprints with the proposal supporting documentation (Attachment 2).
  - Describe the previous experience of key personnel at each Clinical Study Site with the development and conduct of musculoskeletal rehabilitation clinical studies. Reference relevant publications and submit reprints with the proposal supporting documentation (Attachment 2).

- Describe the traumatic orthopaedic injury patient populations at each Clinical Study Site and provide evidence of the ability to enroll adequate patient numbers into Consortium-sponsored studies. Provide an estimate of case enrollment/patient load and the track record of research in this area for each Clinical Study Site and each Site PI.
- Describe the resources and facilities available within each Clinical Study Site for the care and rehabilitation of orthopaedic trauma patients.
- Describe the resources and expertise in each participating Clinical Study Site for data management and maintenance of data security/confidentiality.
- Provide evidence of organizational commitment for the Coordinating Center and each participating Clinical Study Site for the use of facilities and resources in the conduct of Consortium operations.
- Describe any plans to leverage existing clinical or translational funding programs and infrastructure for the proposed Consortium.

### **Plan of Operations**

- **Government Coordination:** Describe plans to communicate and partner with the named MTFs. Explain how the MTF Clinical Study Sites will provide input on all Consortium procedures and studies to a level commensurate with all other Clinical Study Sites. Outline a plan for providing resources to the MTFs and establishing the research capabilities needed at the MTFs for full Consortium participation.
- **Study Identification:** Outline a plan for the proposal, design, and prioritization of potential future Consortium studies for presentation to the Steering Committee following initial study implementation. Include a mechanism for determining Clinical Study Site participation.
- **Study Management and Monitoring:** Describe plans for real-time communication among all organizations participating in the Consortium (including the rapid dissemination of adverse events). Include a named Consortium Clinical Research Manager who will interact with other individual site clinical coordinators to guide clinical protocols through the regulatory approval processes, coordinate participant accrual, and coordinate study activities across sites. Outline procedures for quality assurance, quality control, safety and study monitoring.
- **Core Facilities:** Outline essential cores and other facilities to be shared that will be necessary for facilitation of Consortium success. Discuss how the core facilities will be utilized and integrated across all Clinical Study Sites.
- **Clinical Protocol Development and Human Subjects Protection:** Describe plans for coordinating the development of clinical protocols and associated clinical documents that include HRPO-prescribed content. Outline a plan for the external peer review of all Consortium clinical protocols, and the coordination of IRB submissions and approvals. Describe the development of a plan for addressing human subjects protection requirements as outlined by HRPO at [https://mrmc.detrack.army.mil/index.cfm?pageid=research\\_protections.hrpo](https://mrmc.detrack.army.mil/index.cfm?pageid=research_protections.hrpo). Outline plans for developing procedures to ensure compliance with FDA requirements for investigational agents, as appropriate.

- **Data Management:** Outline a strategy for the development and implementation of a Consortium-wide data management plan, including: (1) Descriptions of the overall approach to data collection and management, (2) a statistical plan that includes methods to monitor quality and consistency of data collection and methods to measure outcomes, (3) a plan for real-time data transfer, and (4) data security measures.
- **Specimen Handling and Distribution:** Describe plans for the development of methods for the handling, distribution, analysis, banking, and security of any specimens and/or imaging products generated from Consortium-sponsored studies. Include a named coordinator responsible for managing and resolving material and intellectual property issues among Consortium organizations.
- **Information Technology (IT) Resources:** Since the Consortium will rely heavily on information technology, provide the name of the individual who will be responsible for database and information infrastructure. Describe relevant personnel and organizational experience with implementing multi-institutional real-time communications.
- **Publication and Data Dissemination:** Describe plans for ensuring rapid publication and other public dissemination of data while maintaining participant privacy. Include a plan to provide for open architecture of any prosthetic or orthotic development that results from Consortium studies.
- **Fiscal and Legal Administration:** Describe the fiscal organization necessary for the proper distribution of funds between Clinical Study Sites for performance of clinical studies.
- **Research Plan:** The narrative should include a projection of the types of clinical trials and clinical research to be conducted by the Consortium over the entire award period. Applicants must provide a description of a minimum of four clinical studies in sufficient detail to allow for evaluation of the group's capabilities, study design expertise, and research interests. The described research should address a minimum of four of the PRORP Orthopaedic Rehabilitation Clinical Consortium Award focus areas (see page 6). Animal studies are not allowed. Information about the proposed studies should include:
  - **Overall Focus:** Identify the major gaps in the field of rehabilitation of combat-related orthopaedic injury that the Consortium seeks to address. Describe the broad research goals of the Consortium, and the types of clinical trials and studies to be conducted. Outline a plan for the estimated number and types of studies to be conducted over the five-year performance period.
  - **Research Idea:** For each proposed study, describe the ideas and reasoning on which it is based, and how the study addresses a central problem in the rehabilitation of combat-relevant orthopaedic injuries. Provide preclinical evidence to support the rationale for each study. Identify the PRORP Focus Area(s) each study addresses.
  - **Research Strategy:** Concisely state each study's objectives and specific aims. Describe the patient populations and study sites that will be utilized for each study. Provide sufficient information on the methods, metrics, and statistical power for each study to allow for an evaluation of the proposed budget.

- **Military Benefit:** Describe how the proposed studies build on the research goals of the named MTF collaborators in order to maximally benefit wounded warriors. Describe how the studies will have impact on accelerating the movement of promising treatments for orthopaedic injury into a military combat-relevant application.
- **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. *Each component has no page limit unless otherwise noted.*
  - **References Cited:** List all 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 Acronyms and Symbols:** Provide a list of acronyms and symbols (e.g., PCR = polymerase chain reaction).
  - **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 (ten-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 (two-page limit per letter):** Provide a letter (or letters if applicable), of organizational support for the Coordinating Center and each Clinical Study Site (with the exception of the PRORP-named MTF Clinical Study Sites), signed by the Department Chair or appropriate organizational official. Letters should reflect resources available to the Coordinating Center PI or Clinical Study Site PIs for this project. The letters should also indicate the extent to which the PI or Clinical Study Site PIs will be relieved of academic or administrative responsibilities and allowed to pursue his/her research goals.
  - **Letters of Collaboration (if applicable) (two-page limit per letter):** Provide a signed letter from each collaborating individual or organization (not including the MTFs) demonstrating access to the resources necessary for participation in the proposed effort, including but not limited to the availability of and access to appropriate orthopaedic injury patient populations.
  - **Intellectual and Material Property Plan (if applicable):** Provide a plan for resolving intellectual and material property issues among participating organizations and how any conflicts will be resolved.

- **Attachment 3: Technical Abstract (one-page limit):** Upload as “TechAbs.pdf.”
  - Background: Describe the general management and organizational structure of the consortium. Outline the management and clinical expertise of consortium personnel at the Coordinating Center and Clinical Study Sites.
  - Objectives: Describe the consortium’s overall clinical research goals and agenda.
  - Research Plan: Briefly describe the clinical studies the consortium plans to pursue during the performance period. State how the proposed projects address the PRORP Orthopaedic Rehabilitation Clinical Consortium Award focus areas.
  - Military Benefit: Briefly describe how the expected results will impact the rehabilitative care, and ultimately the lives, of individuals with combat or combat-related orthopaedic injuries.
- **Attachment 4: Public Abstract (one-page limit):** Upload as “PublicAbs.pdf.”
  - Describe the clinical objectives and rationale for the proposal in a manner readily understandable by non-scientists.
    - Do not duplicate the technical abstract.
  - Describe the ultimate applicability of the consortium’s 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 time it may take to achieve a clinically relevant outcome?
  - What are the likely contributions of this study to advancing the field of research?
- **Attachment 5: Statement of Work (SOW) (ten-page limit):** Upload as “SOW.pdf.” Refer to the General Application Instructions, Section II.B., for detailed information.
- **Attachment 6: Detailed Budget and Justification (no page limit):** Upload as “Budget.pdf.” Use the Detailed Budget and Justification form (available for download on the Full Announcement page in Grants.gov). Refer to the General Application Instructions, Section II.B., for detailed information.
- **Attachment 7: Subaward Detailed Budget and Justification (if applicable) (no page limit):** Use a separate Detailed Budget and Justification form for each subaward budget. Combine into a single file and upload as “SubBudgets.pdf.” Refer to the General Application Instructions, Section II.B., for detailed information.

**Attachment 8: Military Benefit Statement (two-page limit):** Upload as “MilBen.pdf.” State explicitly how the proposed work, if successful, will have an impact on accelerating the evaluation and movement of promising rehabilitation treatments into clinical practice. Further, describe the impact of the Consortium studies 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.

Describe how the proposed studies are responsive to the health care needs of the Armed Forces and/or the US veteran population. Describe the military or veteran population(s) that are to be utilized, and their appropriateness for the proposed studies. If non-military populations will be used for the proposed research, explain how the

populations simulate the targeted population (i.e., Armed Forces and/or the US veteran population). Show how the proposed studies complement ongoing DOD areas of orthopaedic research interest. Describe how the studies build upon research initiatives ongoing at the named MTF Clinical Study Sites.

**3. Research & Related Senior/Key Person Profile (Expanded) Form:** Refer to the General Application Instructions, Section II.B., 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. Project/Performance Site Location(s) Form:** Refer to the General Application Instructions, Section II.B., for detailed information.

#### **IV. INFORMATION FOR APPLICATION REVIEW**

##### **A. Application Review and Selection Overview**

All applications are evaluated by scientists, clinicians, and consumer advocates using a two-tier review process. The first tier is a scientific peer review of applications against established criteria for determining scientific merit. The second tier is a programmatic review that compares applications to each other and makes recommendations for funding to the Commanding General, USAMRMC, based on scientific merit, the overall goals of the program, and 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 may be found at <http://cdmrp.army.mil/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, it is a crime for Federal officials to disclose confidential information of one party to another third party (Title 18 United States Code 1905).

## **B. Review Criteria**

**1. Peer Review:** All applications will be evaluated according to the following criteria, which are of equal importance:

- **Consortium Expertise**
  - To what extent the Coordinating Center personnel's background, track record, and expertise are appropriate with respect to the ability to manage and oversee multi-institutional musculoskeletal rehabilitation clinical studies.
  - To what extent the research teams' background, track record, and expertise at each Clinical Study Site is appropriate with respect to the successful conduct of orthopaedic injury-related rehabilitation studies and participation in multi-center clinical studies.
  - To what extent the levels of effort are appropriate for successful conduct of the proposed work.
  - The degree to which the level of organizational information technology experience in implementing multi-institutional real-time communications is appropriate.
  - How the specific abilities and experience possessed by the named information technology lead will enable him/her to quickly and efficiently implement the electronic communications required by the Consortium.
  - The degree to which the ability and experience of the organization with the financial management of multi-institutional research studies is appropriate.
- **Coordination of Consortium Components**
  - To what extent the proposed overall organizational structure of the Consortium is appropriate.
  - How well the Coordinating Center addresses a plan to oversee and coordinate all Consortium Sites.
  - How well the plan for the establishment and maintenance of core facilities will effectively support Consortium activities.
  - How well each Consortium Site will function as an integrated unit.
  - How well the proposed Consortium structure and research integrates the MTFs and their stated research goals.
  - To what degree the appropriate resources are provided for full participation at each Consortium Site.
- **Study Management and Monitoring**
  - How the plans for real-time communication among all organizations participating in the Consortium, including complete and timely reporting of adverse events, are appropriate to facilitate Consortium activities.
  - The extent of the named Consortium Clinical Research Manager's experience with guiding clinical protocols through the regulatory approval processes, coordinating participant accrual, and coordinating study activities across sites.

- How the outlined procedures for quality assurance, quality control, safety and study monitoring are adequate for conducting multi-institutional clinical studies.
- How the plans for specimen handling, distribution, analysis, banking, and security are appropriate to facilitate Consortium activities.
- **Data Management**
  - The degree to which the overall approach to data collection, management, analysis, and security measures is appropriate.
  - How clearly the effective application of methods to monitor quality and consistency of data collection and methods to measure outcomes in previous trials conducted have been demonstrated by the PI and key personnel.
  - How the plan for real-time data transfer is adequate for supporting the Consortium-associated activities.
  - The degree to which plans for the publication and other dissemination of data are appropriate.
- **Clinical Protocol Development and Human Subjects Protection**
  - The degree to which plans for the proposal, development, and external peer review of clinical protocols and associated clinical documents within the performance period are appropriate.
  - To what extent the plans for addressing human subjects protection requirements as described by HRPO and coordinating IRB submissions and approvals at participating sites are appropriate.
  - How well appropriate plans for developing procedures to ensure compliance with FDA regulations for investigational agents are considered.
- **Organizational Resources and Commitment**
  - The degree of organizational commitment for the use of facilities and resources in the conduct of Consortium operations.
  - Whether the organizations have demonstrated access to appropriate patient populations for conduct of Consortium clinical studies.
  - How the facilities and resources within each Clinical Study Site are appropriate for the rehabilitative care of orthopaedic trauma patients.
  - How the resources and expertise at each organization are appropriate for coordinating specimen collection and processing.
  - How the resources and expertise at each organization are appropriate for data management and maintaining security/confidentiality.
  - The degree to which each organization demonstrates a willingness to resolve intellectual and material property issues with other organizations in the Consortium.
  - The extent to which the intellectual and material property plan is developed and appropriate.

- How well the commitment of the organizations to work with all Consortium sites, including the MTFs, is demonstrated.
- **Research Plan**
  - The extent to which the plan for the estimated number and types of studies to be conducted during the duration of this award is appropriate and feasible.
  - How well the scientific rationale and preliminary data support each proposed initial study's design and objectives.
  - The degree to which the patient populations and sample size are appropriate for each proposed initial study.
  - The degree to which proposed methods and outcome measures are appropriate for the purposes of each proposed initial study.
- **Military Benefit**
  - The degree to which the proposed research, if successful, will have a significant impact on the rehabilitative care of combat-relevant orthopaedic injuries.
  - How the proposed research will make original and important contributions towards the goal of advancing treatment and/or recovery from musculoskeletal injuries sustained during combat or combat-relevant activities.
  - How well appropriate studies were proposed to resolve gaps related to the PRORP Orthopaedic Rehabilitation Clinical Consortium Award focus areas.

The following will not be individually scored, but may impact the overall evaluation of the application:

- **Application Presentation**
  - How the writing and components of the application influenced the review.
- **Budget**
  - Whether the budget is appropriate for the proposed research and within the limitations of the award mechanism.

**2. Programmatic Review:** The following criteria are used by programmatic reviewers to make funding recommendations.

- Adherence to the intent of the award mechanism
- Programmatic relevance in relation to PRORP ORCCA focus areas
- Ratings and evaluations of the peer reviewers
- Relative translational potential and military benefit
- Program portfolio composition

## **V. 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.
- Page size is larger than 8.5 inches x 11.0 inches (approximately 21.59 cm x 27.94 cm).

The following will result in administrative rejection of the application:

- Project Narrative exceeds page limit.
- Project Narrative is missing.
- Budget is missing.
- Page size is larger than 8.5 inches x 11.0 inches (approximately 21.59 cm x 27.94 cm).
- Submission of an application for which a letter of invitation was not received.
- Pre-application is not submitted.

### **B. Modifications**

- 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, you may be contacted by CDMRP via email with a request to provide certain missing supporting documents (excluding those listed above in Section V-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 application:

- FY10 PRORP IP member(s) is found to be involved 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 FY10 PRORP IP members may be found at <http://cdmrp.army.mil/prorp/panel10>
- Submission of the same research project to different funding opportunities within the same program and fiscal year.
- 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 detailed budget form exceed maximum allowed by this Program Announcement/Funding Opportunity.
- Inclusion of URLs with the exception of links to published references.

#### **D. Withhold**

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

### **VI. CONTACT INFORMATION**

**A. CDMRP Program Announcement Help Desk:** Questions related to Program Announcement/Funding Opportunity content or submission requirements should be directed to the CDMRP Program Announcement help desk, which is available Monday through Friday from 7:30 a.m. to 4:00 p.m. ET. Submit questions as early as possible. Response times will vary depending upon the volume of inquiries. Every effort will be made to answer questions within 5 working days.

Phone: 301-619-7079  
 Email: [cdmrp.pa@amedd.army.mil](mailto:cdmrp.pa@amedd.army.mil)

**B. CDMRP eReceipt System Help Desk:** Questions related to the submission of the pre-application through the eReceipt system should be directed to the CDMRP eReceipt system help desk, which is available Monday through Friday from 8:00 a.m. to 5:00 p.m. ET.

Phone: 301-682-5507  
 Email: [help@cdmrp.org](mailto:help@cdmrp.org)

**C. Grants.gov Contact Center:** Questions related to application submission through the Grants.gov portal should be directed to Grants.gov help desk, which is available 24 hours a day, 7 days a week. Please note that the CDMRP Program Announcement/Funding Announcement and eReceipt system help desks are unable to provide technical assistance regarding Grants.gov submissions.

Phone: 800-518-4726  
 Email: [support@grants.gov](mailto: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

<b>Grants.gov Application Components</b>	<b>Action</b>	<b>Completed</b>
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 Public Abstract (PublicAbs.pdf) as Attachment 4	
	Upload Statement of Work (SOW.pdf) as Attachment 5	
	Upload Detailed Budget and Justification (Budget.pdf) as Attachment 6	
	Upload Subaward Detailed Budget and Justification (SubBudgets.pdf) as Attachment 7	
	Upload Military Benefit Statement (MilBen.pdf) as Attachment 8	
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	
Project/Performance Site Location(s) Form	Complete form as instructed	

**APPENDIX**  
**INFORMATION ON MILITARY TREATMENT FACILITIES**

**Naval Medical Center Portsmouth**  
**Department of Orthopaedic Surgery**

**Orthopaedic Research Goals:** The goals of our research program are essentially two-fold: to address gaps in orthopaedic literature or clinical practice (including surgical techniques) that are military relevant and to provide an environment of scientific inquiry with hands-on experience for our resident staff. We are especially interested in improving the care of the injured active duty member, prevention of injuries, performance enhancement, and biomechanics. Many of the projects under this area are applicable to the civilian population.

More recently, we have focused on collaborations to complement our resources and to expand our research. We applied for six major grants and were awarded four. We plan to perform more prospective studies (including multicenter, multiyear), more biomechanical studies, and more studies with living models. One of our staff has experience with cadaveric biomechanical models, ballistics, and efficacy testing of personal protective equipment (PPE, body armor). Another has expertise in lower extremity amputation in combatants.

Our ultimate goal is to have self-sustaining funding and to be a center for injury prevention and performance enhancement. We plan to be a military center for performance and injury prevention with emphasis on early intervention (including surgery) and rapid rehabilitation. Included in this goal is the improvement in PPE, development of appropriate models (anthropomorphic and physiological) to test PPE, and the refinement of PPE requirements. We also plan to evaluate non-battle musculoskeletal injury, including the burden of disease, type, and severity of diagnosis and its effect on readiness.

**History of Orthopaedic Research:** The Department has focused on military and clinically relevant topics with the majority of the effort in Sports Medicine, Spine, and Upper Extremity. More recently, effort has been focused on Performance and Injury Prevention. Several basic science studies in biomechanics have also been conducted. Our productivity and depth of research have increased with our recent affiliation with Old Dominion University. We have a mix of clinical and basic science research combined with current concept and evidenced-based research. We now have over 30 active studies.

**Funding:** Support for clinical and laboratory research is derived from multiple intra- and extramural sources.

**Intramural funds:**

Commander's Grant (annual competition, variable): \$2000 to \$6800 per protocol.

Clinical Investigation and Research Department (CIRD): Travel for 1 author for 1 presentation per project per year.

Other departments: Variable, significant amount of personnel support and resources for studies at the discretion of the individual departments (e.g., Radiology) conducting the research or are impacted by the research (e.g., Pharmacy, Laboratory).

**Extramural funds:** We have greatly increased the amount and breadth of sources in the last three years through Cooperative Research and Development Agreements (CRADA) and Memorandums of Understanding (MOU):

**1) American Orthopaedic Society for Sports Medicine - \$900,000.** No direct funds; one FTE research associate for the first orthopaedic study of its kind on knee pain and arthritis (IRB

approved). Evaluates clinical outcomes in patients receiving two different hyaluronic acid injections. Data: Patient-based scores, CARTIGRAM MRI, gait analysis, numerous validated outcome measures; serially collected to document the natural history of arthritis and to determine a treatment algorithm. The CARTIGRAM MRI is the only one in the DOD, including the VA system.

**2) Henry M. Jackson Foundation - \$90,000.** No direct funds; two FTE research assistants for two different IRB-approved protocols. One evaluates the effect of a pharmaceutical additive to knee irrigation for arthroscopically assisted anterior cruciate ligament injury; additive designed to decrease post-operative pain and improve rehabilitation. Second study critically evaluates two different non-operative treatments of low back pain.

**3) Office of Naval Research - \$1.5 million.** Two multiyear projects, no direct funds to NMCP. Collaboration with Old Dominion University (ODU), NMCP is developing a performance prediction model and comparing two types of exercise programs (Cross-Fit and a specially designed military training program). Data collection and exercise physiology applied to develop a validated model for injury prediction. Second project evaluates effect of personal protective gear weight and configuration on performance, fatigue, balance, physiologic measures of fitness, and function. A part of this protocol evaluates training with and without gear.

**4) Vice Chief of Naval Operations - \$500,000.** Program to compare fitness training for PRT failures in the Fitness Enhancement Program to a specially designed program for each individual. Funding for fitness equipment, body composition measurement devices, and contracts.

**5) Pentagon - \$390,000.** Collaboration with New York University to critically evaluate two different non-operative comprehensive treatments of low back pain employing multi-disciplinary treatment.

**6) American Orthopaedic Foot and Ankle Society- \$2000.** One time grant with ODU, for evaluation and quantification of subtalar instability in a cadaveric model. Goal is subtalar joint arthrometer.

**7) Health Science Education and Training Command.** Travel grants are offered to the primary investigators of projects that are approved through our IRB; for a single presentation annually.

**Current Focus Areas of Basic and Clinical Orthopaedic Research:** We are examining our outcomes for commonly performed procedures on active duty. Further, we have attempted to study biomechanics and injury prevention, focusing on improving surgical reconstruction and optimizing physical performance. We are modeling data from the performance studies to better understand and prevent injury. Our approach has been by topic, areas of expertise, and resource availability.

#### **Ongoing Research Projects:**

- 2003.0064 Anterior Cruciate Ligament Reconstruction in Active Duty Military Personnel: A Medical Board Analysis Comparing Multiples Variables for Returning Patients to Full Duty vs. Medical Discharge (expedited-retrospective)
- 2005.0013 Clinical Results of Surgical Repair for Pectoralis Major Muscle Tears (prospective series)

- 2005.0014 Apical Pedicle Screw Fixation: Analysis of Curve Correction Using Hybrid Fixation with Pedicle Screw to the Curve Apex (exempt-retrospective)
- 2005.0040 Accuracy and Reliability of Digital Templating in Primary Total Hip Arthroplasty (exempt-retrospective)
- 2005.0017 Vertical Expandable Prosthetic Titanium Rib (VEPTR) (prospective series)
- 2006.0043 The Management of contaminated Open Fractures: A Comparison of Two Types of Irrigation in a Porcine Model (basic science)
- 2007.0006 Basic Microsurgical Course (basic science)
- NSWG-2. Naval Special Warfare Injury Prevention and Human Performance Initiative  
2007.0017 (prospective)
- 2007.0021 Development and Validation of a Subject Specific Model of the Hindfoot to Improve the Treatment of Hindfoot Disorders (exempt-basic science)
- 2007.0022 Clinical and Radiological Results with the Charite Disc in Military Personnel (expedited-retrospective)
- 2007.0069 Development of a Method to Quantify Subtalar Joint Instability (exempt-basic science)
- 2008.0002 Prediction of Response to Intra-articular Injections of Hyaluronic Acid for Knee Osteoarthritis (prospective, double blinded, randomized clinical trial)
- 2008.0023 Development and Validation of a Physical Performance Prediction Model (prospective)
- 2008.0029T A Double-Blind, Multi-center, Phase 3 Study Comparing the Efficacy and Safety of OMS103HP with Vehicle in Patients Undergoing Autograft and Allograft ACL Reconstruction (prospective, double-blinded, randomized clinical trial)
- 2008.0063 A Multi-Center Randomized Study to Evaluate Conventional posterior Lumbar Microdiscectomy vs. Microdiscectomy using the SpineJet Hydrosurgery System (prospective)
- 2008.0067 The Effects of Personal Protective Equipment on Functional Performance (prospective)
- 2008.0070 Proximity of Brachial Artery to Anterior Humerus at the Elbow (exempt-basic science)
- 2008.0077 Non-anatomic Reconstruction of the Coracoclavicular Ligaments: A Retrospective Review and Technique Article (retrospective)
- 2009.0008 Research to Limit Attrition of DoD Service Personnel Due to Episodes of Non-Specific Low Back Pain (prospective, randomized clinical trial)
- 2009.0039 Comparison of Two Exercise Programs (Fitness Enhancement Program/FEP vs Individualized Enhancement Program/IEP) for Remediation of Navy Sailor Physical Assessment Failures (prospective, randomized clinical trial)
- 2009.0045 The Effects of Localized Hypothermia on Bacterial Colony Counts in Soft Tissue Infection in Rats (randomized treatment, basic science)
- 2009.0047 Biomechanical and Motion Analysis of Transverse Olecranon Fractures: Is Tension Band Wire Fixation Adequate? (exempt-basic science)

**Research Teams and Laboratory Capabilities:** We have on-site and local research laboratories. On base: Hospital facility, CIRD. Nearby clinic: Fitness lab. As part of a CRADA, we have laboratory space with Old Dominion University's Mechanical Engineering Lab and Human Movement Sciences Lab.

**NMCP on Site:** Our hospital is a 300-bed teaching facility with a complement of specialty and subspecialty services. Orthopaedics has 18 surgeons and podiatry has 3 surgeons.

**Bioskills Lab:** Dedicated space for biomechanical, cadaveric studies. Deep freezers, instrumentation, overhead video system, arthroscopic gear. Four work stations, large dissection table, fluoroscopy.

**Clinical Investigation/Research Department (CIRD):** Staff of 15, support for both animal and clinical research. Two IRBs and IACUC. Animal facility is AAALAC-accredited with a full-time veterinarian, vet technicians, facility manager, and animal technicians; capability for major and microscopic surgery, full anesthesia, histopathology, and an operational small animal hyperbaric chamber. Clinical side: Biostatistician, two basic science Ph.D. administrators, medical editor, CRADA manager, research training, and protocol processing; 3 research assistants assigned as needed.

**Pharmacy:** Clinical support, 1 FTE pharmacist with extensive experience in randomized, clinical trials.

**Physical Therapy; Occupational Therapy:** Multicervical unit (BTE), Primus (BTE), Isokinetic dynamometer, treadmills, weights (free and resistance), stair climber, balance training, local modalities, EMG, bicycles (upright and recumbent), SwimEx, 50 meter 6 lane pool, outdoor track, numerous grass fields, upper extremity ergometer, custom splints.

**Radiology:** Two MSK radiologists. 2 MRIs, Cartigram MRI for articular cartilage (the only one in the DOD), high resolution CT scan, conventional radiology, fluoroscopy, ultrasound, fast scans. MSK fellowship to start July 2010.

**Simulation Laboratory:** State-of-the-art patient simulation center, two full-time staff. Occupies almost one entire floor, over \$300,000 of equipment (including two adult, one infant, and two neonatal human patient computerized simulators). Three patient examination rooms (audio and video recording); virtual reality training with laparoscopic, bronchoscopic, and endoscopic simulators. Two computer-supported basic laparoscopic trainee simulators. Training for high-risk scenarios.

**Medical Library:** Two medical librarians. Extensive orthopaedic, medical, and surgical materials (textbooks, orthopaedic journals); interlibrary loan. Available 24 hours a day. Literature searches.

### **NMCP Off-Site Assets and Capabilities**

**Norfolk Naval Base Fitness Lab:** VO2 max, BTE equipment, air displacement body composition assessment, isokinetic dynamometer, multicervical unit.

**Old Dominion University:** Core staff collaborating with NMCP are in the Departments of Mechanical Engineering, Human Movement Science, Physical Therapy, and Mathematics

and Statistics. Virginia Modeling, Analysis and Simulation Center affiliation from core staff. Contribution to projects is from 5-50% effort.

**Human Movement and Exercise Science Laboratory:** Motion analysis lab (8 camera Vicon system, 10 camera Vicon system, 6 camera Motion Analysis, 4 channel polhemus liberty, EMG, force plates), BTE Primus dynamometer, postural control lab (Neurocom, Balance Error Scoring system, STAR excursion balance test, dynamic force plate measurements of postural sway), upper and lower body strength assessments, functional movement screen, metabolic cart (VO2 max capabilities), and body composition measurement (air displacement, skin calipers). Capabilities for in vitro testing, including sensors to measure contact pressure in the knee, ankle, and subtalar joint (Novel), differential variable reluctance transducers (to measure ligament strain), and a positioning and loading device that is CT and MRI compatible for data collection in the lower extremity.

**Patient Population:** Our patient population comprises active duty, retirees, their dependents, and multinational eligible beneficiaries. The majority of our surgical cases are on active duty members with non-battle-related conditions. Although we have the capability, we do not routinely care for combat injured. Patients transfer here for reconstruction (revision of amputation) and bone tumors. However, the majority of patients specifically sent here are those with non-battle-related injuries sustained in the combat zone, though the data are not well documented. The only data from FY05 to FY09 (through August 2009) are as follows:

Combat-related inpatients: 17

Combat-related outpatients: 111

Total number of orthopaedic and podiatry clinic encounters (all patients and providers):

FY 2008	76,117
FY 2007	76,896
FY 2006	79,508

The number of surgical cases performed for all orthopaedic and podiatry during the last three fiscal years is below. Most of our procedures are on active duty. These data do not include cases for minor procedures done in the clinic.

	<b>Main OR</b>	<b>Same Day</b>
FY 2008	3,901 (2,579 active duty)	1,972
FY 2007	~3,800	1,125
Jan-Sept 2007	3,080 (1,973 active duty)	Not available
FY 2006	~3,250	1,837
Jan-Dec 2006	1,917 2,569 procedures	2,138 2,643 procedures

The Navy Surgeon General has informed our facility that our numbers of combat-wounded patients would increase. A “Wounded Warrior Center” was constructed to address in anticipation of this change in patient demographic. However, to date, the numbers and types of patients remain fairly constant.

**Future Studies of Interest:** As stated above, our ultimate goal is to have self-sustaining funding and to be a center for injury prevention and performance enhancement. Injury prevention and studies focusing on improving physical performance in collegiate athletes and military, *in vivo* and *in vitro* kinematics studies to improve our understanding of injury and musculoskeletal disease, musculoskeletal modeling with the goal of optimizing treatment and virtual reality-based rehabilitation in stroke patients and patients with mild TBI are currently ongoing.

**Extension of Ongoing Research:**

- Performance optimization
- Risk screening for injury (acute, overuse) by occupation, history and exam, deployment duties
- Training to decrease non-battle-related musculoskeletal injury during deployment
- Development of weight and configuration requirement of PPE
- Randomized multicenter study on hyaluronic acid
- Cooling of the injured extremity after injury and bacterial contamination
- Identification of the optimal irrigant for penetrating blast injury to the lower extremity
- Refinement of PPE requirement
- Develop arthrometer for the subtalar joint
- Knee kinematics

**New Research Areas:**

- Performance and injury prevention
  - Emphasis on early intervention (including surgery)
  - Rapid rehabilitation
  - Biomarkers
- Improvement in personal protective equipment (PPE)
- Development of an anthropomorphic and physiological model for blast research
- Enhancement of bony healing in bone defects
- Evaluation of non-battle musculoskeletal injury
  - Burden of disease
  - Type and severity of diagnosis
  - Effect on readiness
- Biomechanics, need to purchase materials testing device
- Registries for total joint arthroplasty, spine disc arthroplasty, allografts

**Naval Medical Center San Diego**  
**Orthopaedic Surgery and Rehabilitation Services**

**Mission:** The NMCSO Orthopaedic Surgery and Rehabilitation Services Departments are dedicated to the treatment of the wounded warrior and maintenance of the deployable fighting force in the Global War on Terrorism. To this end, our departments currently have several ongoing research projects that deal with the clinical aspects of trauma care as it relates to the wounded warrior acute management, definitive treatment, bench research, and rehabilitation.

**Stated Problem Areas:**

1. Reconstruction of bone and soft tissue defects continues to be problematic for the wounded warrior: Continued research toward better methods for reconstituting these defects while limiting morbidity is needed.
2. Infection: Acute and chronic musculoskeletal infections as a result of war time trauma continues to be one of the top contributors toward prolonged time to return to duty, and the inability to return to duty (need for medical discharge). The cost in dollars, health care resources, and individual suffering is high, and thus is a potential area for intervention where further research can make an impact.
3. Optimization of treatment protocols: Which patients are best served with primary amputation? Which implants/techniques are best for which injuries? How valuable is it to preserve amputation length and levels (AKA vs. BKA) and at what cost to the patient?
4. Heterotopic Ossification: Ectopic bone formation, bone that forms in muscles, tendons, and bridges joints is seen in high numbers among wounded warriors. It has been particularly high among high-energy penetrating trauma victims such as those who are blast injured. Contemporary methods of treatment are both unreliable and have undesirable side effects, while not taking into account the pathophysiology of the disease. Though significant research is ongoing to address this condition, more is needed, and the DOD has a potentially concentrated patient population with which to investigate new strategies for prevention and treatment.
5. Articular reconstruction and recovery of limb function: Current methods for restoring lost segments of joints include allograft reconstruction and arthroplasty. Both techniques have limited longevity in a young and highly active patient population. Likewise, lost functional units (such as complete loss of a quadriceps) are common in this patient population. Current treatment involves tendon transfers that are not previously well described. Further research is needed to optimize these techniques which are used in lieu of regenerative medicine, which is only in its infantile stages.
6. The value of focused, multidisciplinary rehabilitation: The DOD established three centers of excellence for rehabilitation: Walter Reed Army Medical Center (east coast), Brooke Army Medical Center (midwest), and NMCSO (west coast). These three centers were designed with the wounded warrior in mind by combining Orthopaedic, General and Plastic Surgery, Neurology, Physical/Occupational therapy and Prosthetics – all joined by case management. The goal is for rehabilitation of the wounded warrior to occur in a controlled, managed, and well equipped environment that is located near the infrastructure (command or family) for the individual casualty. Many of these wounded warriors pass through these centers of excellence, but only minimal research has been done to document the value of these centers for overall return of function, for return to duty, and for the ultimate goal of being a productive member of society. Improvements in the quality of rehabilitation would also be expected with further research in this arena.

**Broad Research Goals:** The NMCSO Orthopaedic Surgery and Rehabilitation Services Departments are working toward establishing projects in all the areas of interest to improve casualty care, which includes clinical, laboratory (bench research), and rehabilitation. The ultimate goal is to limit patient morbidity, achieve maximum functional outcomes, and optimize return to duty.

**Current Focus Areas:**

1. Prevention and treatment of infection
2. Amputee care
3. Methods to promote and optimize limb salvage
4. Articular reconstructions
5. Longitudinal assessment of wounded warriors
6. Functional outcomes of amputee rehabilitation

**Multi-disciplinary Research Teams:** Currently there are ongoing research projects within the Department of Orthopaedic Surgery at Naval Medical Center, San Diego, with multi-disciplinary collaboration with both medical professionals and non-medical scientific teams. Medical profession collaborations include partnerships with Infectious Disease, Musculoskeletal Imaging, General/Trauma Surgery, Physical Medicine and Rehabilitation, Neurosurgery, and Plastic Surgery. Non-medical profession collaborations include partnerships with gait mechanical engineers at the Naval Medical Center San Diego Gait Analysis Laboratory, chemists at both San Diego State University and HT Laboratory Inc., and biomechanical engineers at the San Diego Orthopaedic Biomechanical Research Laboratory. The NMCSO Gait Laboratory has ongoing collaboration with Biomechanical and Biomedical engineers from the Mayo Clinic, UCLA, and University of Illinois, Chicago.

**Research Laboratory Capabilities:**

**Clinical Investigations Department Core Laboratory:** The Clinical Investigation Department (CID) possesses a core laboratory which is available for use by the department. This core laboratory is designed to be a “common access” facility open to all departments at NMCSO. Funding for the laboratory originates from the Clinical Investigation Department, and researchers are not charged rental or use fees to utilize the space and equipment. Additional equipment or resources unavailable in the core laboratory are supplied and funded by individual researchers through CID sponsored grants. The core laboratory has a full-time research assistant skilled in the use of the available equipment whose services are available at no charge to the Department of Orthopedic Surgery as funding of this individual is through the NMCSO Clinical Investigation Department. The core laboratory research assistant provides assistance with research protocols and teaches researchers the skills needed to operate available equipment for research endeavors. Approximately 7500 square feet of research space is available and divided into several rooms to allow for segregation of research efforts. The laboratory has Bio-Safety Level 2 ratings. The core laboratory is currently being utilized by researchers from the Department of Orthopaedic Surgery, and the Department has contributed equipment to the lab via research awards.

Major equipment available in the core laboratory includes but is not limited to:

- Laboratory benches with equipment necessary for sterile and non-sterile endeavors
- Sterile and non-sterile exhaust hoods

- Multiple CO2 and O2 incubators for cell, bacterial, viral, and fungal storage, growth, and passage
- Specimen Freezers
- Electron Microscopy
- RNA Analysis capability
- Spectroscopy Analysis capability

**Surgical Training Laboratory:** A Surgical Training Laboratory is available for Command-wide research efforts and is currently being utilized by the Orthopaedic Department for anatomical and basic biomechanical cadaveric research endeavors. The Surgical Training Laboratories Division is located within the Clinical Investigation Department and consists of a space of approximately 1500 square feet. The Surgical Training Laboratories Division and its resources are funded by the Clinical Investigation Department. A full-time Surgical Training Laboratory staff member is employed by the Clinical Investigation Department to run and maintain the facility. The Surgical Training Laboratories Division is designed to provide intense, multidisciplinary research opportunities and training experiences. The Surgical Training Laboratories provide the following resources:

- Two lab venues for cadaveric research with free-standing cadaveric work stations
- Seven teaching microscope stations
- Counter space adequate for 12 participants in smaller dissection and procedure labs
- Walk-in refrigerator for cadaver storage only
- Freezer dedicated to long-term storage of specimens
- Resources and materials requested for each scheduled research or procedure lab
- General Surgery and Neuro-Ortho Instruments in quantity
- Scrubs and other required apparel
- Intubation supplies; needles/catheters; syringes; drapes; gloves; sutures; various consumables appropriate to surgical and research lab venues
- Full capacity arthroscopic stations including towers, cameras, light sources, and shaver/electrocaudery capabilities

**San Diego Orthopaedic Biomechanical Research Laboratory:** Biomechanical research resources are available through a relationship with the San Diego Orthopaedic Biomechanical Research Laboratory (OBRL) at Rady Childrens' Hospital. While this facility is not directly located at Naval Medical Center San Diego, the NMCSO Orthopaedic Department is currently collaborating with the lab on numerous research endeavors. Major equipment available at the OBRL includes but is not limited to:

- MTS 858 bi-axial servo-hydraulic materials testing machine with two load ratings. For testing at lower loads with high precision, the lab employs a 2.5kN load cell and 25Nm torque cell. For testing at higher loads, the lab utilizes a 10kN load cell and 100Nm torque cell. In addition, the machine has a variety of Sensotec tension/compression load cells that can be used for customized testing or off-line measurements of load.

- A six degree of freedom Stewart Platform has recently been integrated for particular interest in spinal biomechanics. A six-axis AMTI load cell is of particular importance to hip and spine research.
- Two Medical Measurements high-pressure needle-mounted pressure transducers are used for in vitro pressure measurement.
- A four-camera 60Hz Qualisys three-dimensional motion measurement system for non-contact kinematics analysis.
- A four-channel Measurements Group strain gage amplifier for assessment of rod/screw strain for spinal constructs.
- Two 6mm and two 3mm soft tissue strain gages for use in sports medicine applications. A data logger/oscilloscope/signal generator is hard-wired to a customized PC laptop for off-line usage.
- An array of customized fixation rigs for use in all types of testing.
- A portable radiographic machine, 4 cassettes and 3 viewing boxes.
- Two standing freezers (approximately 75 cubic feet each) and one refrigerator (approximately 35 cubic feet) for storing specimens.
- Basic machine shop capabilities with drill presses, grinders, band saws, and a mitre saw.
- Five desktop PCs and two laptops function for all aspects of data collection and processing.
- Surgical sets for use in research regarding spinal instrumentation, complex joint deformity, and trauma fixation.

**Patient Population:** NMCS D has a local catchment area of 500,000 within San Diego County alone. The local and extended referral base includes the 1st Marine Expeditionary Force (Camp Pendleton, 29 palms, Marine Corps Air Station Miramar), the Naval Base, the West Coast Special Operations Units at the Naval Amphibious Base (SEAL Teams 1,3 &5, Special Boat Units and EOD), Marine Corps Recruit Depot, Edwards Air Force Base and Ft. Irwin in Barstow, California. These units constitute 20% of all active duty assets stationed in CONUS, all of which use NMCS D as its tertiary referral center. Over the past four years, we have had priority for rapid transfer of patients to our facility who are either stationed within our catchment or have a local family support network in order for them to have continuity of care. The number of cases and surgical procedures has followed a series of peaks and valleys dependent upon the operational tempo, and which units are currently deployed (the East and West Coast Marine units alternate years in Operation Iraqi Freedom [OIF] and Operation Enduring Freedom [OEF], though there is always significant overlap). Our current database represents 1400 combat casualties and 60 patients currently undergoing intensive rehabilitation. The capacity at the Medical Holding Company (those casualties receiving outpatient care) is often full requiring dispositioning of Marines with lower acuity to the Wounded Warrior Battalion at Camp Pendleton, but with coordinated follow-up care at NMCS D.

**Research Personnel:** The Department of Orthopaedic Surgery at NMCS D has a dedicated research assistant who works part-time to support the needs and demands of resident research efforts. Outside of the Department, there are personnel within the Clinical Investigation Department to support research activity in the NMCS D Core Research Laboratory and Surgical Training Laboratory. Furthermore, there is a biostatistician available within the Clinical Investigation Department and a Gait Analysis engineering team available at the NMCS D Gait Analysis

Laboratory. The NMCS D Physical and Occupational Therapy Department is collocated with the Comprehensive Combat and Complex Casualty Care (C5) program. This state of the art facility includes the Gain Analysis Laboratory. Additional research collaboration is provided by the Warfighter Performance Branch of the Naval Health Research Center in San Diego, California.

**Gait and Motion Analysis Lab:** The Gait Analysis/Biomechanics Laboratory at NMCS D is a 720-square foot motion capture space with an adjacent examination room, office and workspace. It is located within the Physical and Occupational Therapy Department, and is a part of the Comprehensive Combat and Complex Casualty Care (C5) program. The technology includes a computerized video motion analysis system utilizing 12 infrared cameras (Motion Analysis Corporation, Santa Rosa, California), four AMTI force platforms (AMTI, Watertown, Massachusetts.) embedded in the floor, and two Canon XHA1 video cameras placed orthogonal to the walkway. These systems provide the capability to collect three-dimensional kinematic and kinetic data and video images all synchronized in real time. Data processing and analysis are performed via proprietary Motion Analysis Corp. software or high-powered and multifunctional Visual3D (C-Motion, Inc.). The laboratory is also equipped with a 16-channel telemetered kinesiological electromyography system (Motion Lab Systems, Inc) and an ActiveStep Dynamic Gait Simulator (Simbex, LLC).

**Computer Assisted Rehabilitation ENvironment (CAREN):** The CAREN is housed in the Human Performance Laboratory (HPL) at the Naval Health Research Center (NHRC) in San Diego, California. A state-of-the-art performance analysis system called the Computer Assisted Rehabilitation Environment or CAREN (Motek BV, Amsterdam, Netherlands). The CAREN system is a fully immersive VR environment for the patient /subject including visual, auditory, vestibular, and tactile sensory inputs. The system consists of a six-degree-of-freedom (yaw, pitch, and roll by 25°), hydraulically actuated platform that can be programmed to move in any of its degrees of freedom (independently or simultaneously). At the center of the CAREN platform is a dual-belt treadmill that runs the length of the platform and has integrated force plates under each belt. The two side-by-side belts can run at the same or different speeds. The platform is surrounded by a 180-degree screen, whose images are synchronized with movement of the platform and the actions of the user. The CAREN system immerses the subject in a variety of VR environments. The system is also capable of recording kinematic and kinetic data, allowing motion analysis of the person's movements while performing an activity. A full-body harness system is worn by the user and is attached to a safety support system on the CAREN platform.

Kinematic and Kinetic data can be collected in the CAREN environment utilizing a 12-camera Vicon Motion Capture System (Oxford Metrics Group Plc, Oxford, UK) and the force plates imbedded in the treadmill. Video is simultaneously recorded to document the activity of the subject during testing for comparisons with the marker data. Kinetic measurements are collected from two force plates situated under each belt of the split belt treadmill. Ground reaction forces as well as joint moments and powers can be calculated from the force plate and marker data.

**Prosthetic Service:** Prosthetics is staffed by two full-time American Board Certified prosthetists and one full-time prosthetic technician. NMCS D Prosthetics specializes in custom prosthetic limbs that are designed and fabricated for each individual patient.

Each team prosthetist is certified and credentialed in the advanced microprocessor knee, foot, and bionic technologies for lower extremity amputees. Advanced understanding in both socket interface designs and alignments for running and cycling is commonly used to achieve the goals of each patient. Prosthetics also services upper limb amputees with several types of advanced elbow and

hand units. Myoelectric, conventional, and cosmetic prosthetic limbs are available for each of our patients that experienced an upper limb loss.

The prosthetic facility at NMCS D has the ability to design, fabricate, and fit prosthetic limbs on site. The department houses an advanced CAD/CAM computer system (Biosculptor, Hialeah, FL) a lamination and thermoplastics facility for fabrication of all upper and lower extremity prosthetics, and a heavy machine lab. All prosthetic adjustments and final alignments are finished onsite.

**Ongoing and Completed Projects:** Currently, there are over two dozen ongoing active research protocols ongoing within the Department of Orthopaedics. Ongoing and completed projects that are most in line with the CDMRP Peer Reviewed Orthopaedic Research Program include:

- Expanded Antibiotic Impregnated Bone Cement Options for the Treatment of Osteomyelitis and Severe Open Fractures
- A Prospective, Randomized Trial of the Saline Load Test With and Without Methylene Blue Dye in the Diagnosis of Traumatic Knee Arthrotomies
- Field Tourniquet Use in Combat Casualty Care
- Gait Analysis of Ertl Below Knee Amputees Compared to Traditional Trans-tibial Amputees
- Resource Utilization, Injury Patterns, and Associated Morbidity of Operation Iraqi Freedom Casualties Received at NMCS D over a Two-Year Period
- The Military Extremity Trauma and Amputation/Limb Salvage (METALS) Study
- Characterizing and Treating Dizziness Associated with Amputees
- Design of Virtual Reality-Based Therapy to Restore the Whole Body Coordination Deficits Following Deployment-Acquired Traumatic Brain Injury
- Development of an Improved Training Method for Rapid Rehabilitation of Patients with Lower Extremity Amputations
- A Pneumatic Balloon-Based Haptic Feedback System for Prosthetic Rehabilitation-Biomechanical Analysis

**Future Studies of Interest:**

- In Vivo Analysis of Antibiotic Bone Cement Combinations for Treatment of Multidrug Resistant Bacteria (an animal model)
- Evaluation of the Bioelectric Effect on the Formation of Antibiotic Biofilm
- A Prospective Longitudinal Study of the Effect of Deployment on the Musculoskeletal Health of the U.S. Marine
- Mechanical Work Load Variations for Lower Extremity Amputees at Different Levels
- Functional Outcome of Delayed Amputations (Failed Limb Salvage)

**San Antonio Military Medical Center**  
**Department of Orthopaedics and Rehabilitation**

Brooke Army Medical Center Department of Orthopaedics and Rehabilitation places a premium on three pillars of academic medicine. These are direct clinical **care**, scientific **inquiry**, and **education**. The Department comprises every aspect of musculoskeletal injury and is the focal point of research in acute and definitive surgical management, and subsequent return to optimal physical performance. The Department is unique among all Department of Defense Medical Treatment Facilities due to our proximity and close partnership with the Institute of Surgical Research, our own Center for the Intrepid, housing the only research laboratory directly managed within a clinical facility, and Brooke's status as a Level I Trauma Center. These unique qualities create an environment where scientific inquiry is not only a natural consequence, but a mandate to further our understanding of outcomes. This response to a request for information about the Department, and supporting facilities will address capabilities of Brooke Army Medical Center (BAMC), our research vision and future direction, and the specific capabilities and efforts of the CFI and the ISR Extremity Trauma and Regenerative Medicine Task Area.

**Problem Statement:** Due to the nature of current conflicts in Iraq and Afghanistan, the widespread use of body armor and improved medical management, Warriors are now surviving wounds that would have proven fatal in previous conflicts. As a result, the number of severely wounded Warriors receiving prolonged medical and rehabilitative care is larger than in previous conflicts. Evidence from several studies performed by our team here in San Antonio demonstrated that extremity injuries account for more than half of all battlefield wounds, and require more than two thirds of the resources for care of these Warriors. These severe injuries have rare parallels in civilian orthopaedic trauma. The most severe injuries, including segmental bone, muscle, nerve loss, infections, and wound healing remain as clear and present obstacles to optimum outcomes. In spite of the importance of optimizing rehabilitative practices for civilian and military patients following severe traumatic events, there is limited scientific literature to guide the physical and psychological rehabilitation process. In particular, there is a paucity of information to guide rehabilitation aimed at returning young, severely wounded patients to advanced functional activities.

### **San Antonio Military Medical Center**

Brooke Army Medical Center (BAMC) is a 450-bed echelon V military treatment facility that is also the only American College of Surgeons verified Level I trauma center in the Army. BAMC is located on Fort Sam Houston, and has standing agreements with the South Texas Regional Trauma Consortium to accept up to one half of the civilian trauma for this region, in addition to serving over 400,000 military beneficiaries. The surgical services provide more than 9000 cases, and over 1200 trauma resuscitations annually. As one of three primary receiving facilities for returning wounded Warriors, Brooke has performed over 5000 surgical cases for more than 1000 injured Warriors in the past five years. Brooke Orthopaedic Surgery has 12 assigned surgeons, and performs over 2500 surgical cases per year, of which approximately 750 are related to the overseas conflicts. The residency program is fully accredited and trains 21 residents with a dedicated one-year research fellowship option, and has a 100% first-time pass rate for the American Board of Orthopaedic Surgery for the past 8 years. BRAC 2005 law requires the combination of BAMC with Wilford Hall Medical Center by 2011, which will create the largest medical treatment facility in the Department of Defense, and double the load described above. This union is occurring now, and is referred to as the San Antonio Military Medical Center (SAMMC).

## Center for the Intrepid

The mission of the Combat Trauma Rehabilitation Research Program (CTRRP) at the Center for the Intrepid is to identify evidence-based rehabilitation solutions to *optimize physical performance capabilities in wounded Warriors, with the intent to maximize their opportunity to return to full function within both civilian and military settings*. This research plan was specifically developed to address the need for a systematic evidence-based approach to the provision of post-injury care to combat wounded Warriors. Target patient populations include individuals with amputation, limb salvage, complex musculoskeletal trauma, mild Traumatic Brain Injury (mTBI), PTSD, and/or burns. The ultimate goal is to “reset” the soldier, acknowledging a holistic treatment concept that extends beyond rehabilitation to include all activities necessary to return injured service members to duty or to productive civilian life.

**Broad Research Goals:** The CTRRP will provide scientific evidence regarding the effectiveness of advanced technologies and rehabilitation approaches in an effort to improve clinical management of patients with injuries related to operations in a deployed environment in three broad areas:

**Respond:** Respond to the acute care needs of wounded Warriors following injury through epidemiological surveillance, and the study of innovative medical management solutions.

**Rehabilitate:** Develop evidence-based treatment strategies to optimize recovery of function.

**Reintegrate:** Assess program success in returning Warriors to a full and productive life, to include return to duty, competitive sports, or a new vocation.

### Current Focus Areas:

**Military Amputee Research Program (MARP):** Optimize clinical care through studies that assess functional outcomes following innovative surgical approaches, pain management techniques, advances in socket design and fit, weight management intervention, and the use of advanced rehabilitation technologies to hasten and/or maximize functional performance.

**War-Related Extremity Injury and Rehabilitation Program:** Develop studies designed to minimize or reverse impairments associated with extremity trauma and maximize functional outcomes following burn injury, limb salvage, and other complex deployment-related musculoskeletal trauma.

**TBI Research Program:** Define the patient population, identify and investigate field-expedient screening methods for mTBI, and explore use of advanced technologies to assess performance.

**Research Laboratory Capabilities:** The Center for the Intrepid (CFI), located on the BAMC campus, is a multi-disciplinary outpatient rehabilitation facility dedicated to providing advanced rehabilitative care for Wounded Warriors. The CFI houses full-service physical therapy and occupational therapy clinics, and a prosthetic fabrication laboratory. Also housed within the CFI is the Military Performance Laboratory, a state-of-the-art research and clinical care facility. The 5,300 square foot lab includes nearly 3,500 square feet of data collection space designed for the scientific assessment of activity performance and advanced rehabilitation training.

**Gait and Motion Analysis Lab:** Laboratory equipment in the Gait and Motion Analysis area includes: 26-camera optoelectronic motion capture system, 8 force plates (AMTI, Inc.), an instrumented dual-belt treadmill (AMTI, Inc.), an instrumented staircase and adjustable inclining walkway (AMTI, Inc.), a 16-channel electromyography system, (Motion Lab Systems, Inc.), two digital video cameras (Panasonic), and a metabolic testing system (Cosmed, Ltd.). The combination

of an 18-meter walkway, two terrain pits (turf and gravel), a treadmill, a full flight of stairs, and a set of inclining parallel bars afford a unique opportunity to test patients' physical function across a wide range of basic to advanced activities.

**Computer Assisted Rehabilitation ENvironment (CAREN):** The CAREN system is a virtual reality-based training system that allows real-time feedback while patients perform a range of physically challenging tasks. Its 21-foot diameter dome, eight-projector visualization system, and instrumented treadmill mounted on a motion platform provide the ability to fully immerse patients in a virtual world. This first-of-its-kind system creates exciting opportunities for rehabilitation, testing, and research. Virtual reality training-based environments can be selected to match an individual's unique needs and level of function, allowing the opportunity to effectively challenge patients in a safe and controlled environment. Performance assessment and patient feedback can be provided through the use of a 24-camera optoelectronic motion capture system (Vicon), an integrated heart rate monitoring system, as well as electromyographic and metabolic testing equipment.

To maximize lab utilization, the Military Performance Laboratory also has over 1600 square feet of office space for 13 full-time personnel and students, two meeting spaces, and an examination room for subject preparation and physical evaluation.

**Research Personnel:** One full-time researcher is assigned to BAMC as the Military Performance Laboratory director, and an active-duty scientist assigned to the Medical Research and Materiel Command is on-site to facilitate and guide the rehabilitation science initiatives being undertaken by both clinical and research staff. One virtual reality specialist is employed to support the CAREN system. The majority of research efforts ongoing at the Center for the Intrepid are currently supported by contract personnel funded through the congressionally-directed Military Amputee Research Program as follows:

1 Ph.D. physical therapist (exercise physiologist), specialized in amputee research

5 full-time research assistants (biomechanics background)

1 full-time research physical therapist

1 full-time protocol coordinator (recruiting, approvals, etc.)

Pending hires: One Ph.D./TBI clinician (PT or OT), and one research assistant (TBI)

### **Ongoing and Completed Projects:**

#### *Military Performance Laboratory*

- Trans-tibial Amputations: Reliability of Kinetic and Videofluoroscopic assessment in Global War on Terrorism Veterans
- Effects of Walking Speed and an Uneven Surface on Dynamic Stability in Young Adults With and Without Amputation
- Relationships between shank angular velocity and linear acceleration and ankle angle
- Dynamic stability of walking during platform and visual field oscillations in the Computer Assisted Rehabilitation ENvironment (CAREN) system
- Amputee Gait Training Using Virtual Reality and Real-Time Feedback
- The Effect of Gait Training Using Virtual Reality and Real-Time Feedback on Physiological and Functional Gait Performance in Persons with a Traumatic Lower Extremity Amputation

- Microprocessor-controlled ankle system for stair and slope ambulation following trans-tibial amputation
- Factors influencing rehabilitation effectiveness in the restoration of physical function in the military amputee
- Microprocessor vs. Hydraulic Controlled Prosthetic Knee in Early Stage Rehabilitation for Trans-femoral Amputees: A Pilot Study
- Residual Limb Health in Response to Active Vacuum vs. Suction Socket Designs. The effect of vacuum assisted suction suspension on limb-socket dynamics, ambulation on uneven terrain, and response time in traumatic below knee amputees
- The effect of a new microprocessor-controlled prosthetic knee on physical performance following transfemoral amputation
- Improving Dynamic Walking Stability in Traumatic Amputees
- Novel methods for identification of concussion-associated impairment in blast-exposed service members
- Maximizing Function Following Transfemoral Amputation: Assessment of a Technologically Advanced High-Performance Prosthetic Knee

#### *Clinical Research Program*

- Effect of Upper Extremity Prostheses type on Functional Activity
- Measurement of Community Reintegration of Wounded Warriors
- Targeted Muscle Reinnervation Rehabilitation project
- Comparison of the Functional Performance and User Satisfaction of a Standard
- Myoelectric Hand with the I-Limb in Upper Extremity Amputees
- Investigation of Emerging Technologies for Use in Screening for Traumatic Brain Injury
- Development of an Amputee Mobility Functional Outcomes Predictor
- Efficacy of mirror-box and mental visualization treatments on phantom limb pain

### **Extremity Trauma and Regenerative Medicine**

The majority of battlefield wounds occur to the extremities (55%) and head/neck region (30%). Penetrating soft tissue wounds and open fractures account for the majority of the wounds in the extremities. Infection, nonunion, and impaired/loss of muscle function are common outcomes. The Extremity Trauma and Regenerative Medicine task area is addressing these problems several different ways, with the goal of returning the injured Warrior to full function.

#### **Current Focus Areas:**

**1. Warriors' injuries and clinical outcomes are being defined:** To help direct research efforts, retrospective studies were conducted to determine the incidence, rate, and qualitative outcomes of extremity injuries in the Iraq and Afghanistan conflicts. A database of over 200 type 3 open tibia fractures to determine what causes poor clinical outcomes is being investigated. It has become apparent that skeletal muscle injury is the main reason why many injured Warriors never fully

recover. An orthopaedic registry that has data elements specific to extremity injuries has been created and will work in conjunction with the JTTR.

**2. Pre-clinical studies to determine which therapies have the greatest clinical potential:**

Various pre-clinical animal models are utilized to evaluate potential therapies for infection and soft tissue and bone injury. We strive to evaluate the most advanced and promising technologies using the most clinically relevant and stringent animal models possible. Clinical practice guidelines for irrigation of contaminated wounds were created based on studies that we conducted in animals. Other notable efforts include developing animal models for compartment syndrome, massive contaminated defects, and large volumetric muscle loss. Relevant animal models have been created and collaborations with academic institutions have been initiated to develop innervated and vascularized muscle constructs to solve this volumetric muscle loss problem. The concept of a dual-purpose bone implant (promotes regeneration and prevents infection) was developed and is being evaluated by us. The ability to utilize stem cells as a therapy for skin, muscle, and bone injuries has been established. Regenerative medicine studies have been initiated, and outside collaborations are being leveraged to make a wide variety of biomaterials readily available for evaluation in soft tissue and bone defects.

**3. Prospective clinical trials aimed at improving outcomes of extremity wounds:** These have been initiated. The Department of Orthopedics and rehabilitation at Brooke Army Medical Center has initiated several clinical trials in the areas of combat casualty care, and several more are planned for next year. A multi-center clinical trials consortium through a cooperative agreement with Orthopaedic Extremity Trauma Research Program (OETRP) has been created. Capable military orthopaedic departments (to include Brooke), along with thirteen clinical centers, will be members of this consortium; this will further develop needed infrastructure, allow military personnel to gain expertise, and will further solidify a research culture within these orthopaedic departments.

**4. External research programs are being actively leveraged:** The USAISR manages the OETRP and is an active partner in the Armed Forces Institute of Regenerative Medicine (AFIRM). The OETRP focuses on improving outcomes of extremity injuries within the next 5 years. This is accomplished by funding translational research projects that are evaluating new and emerging therapies and by conducting clinical trials that evaluate current standards of care and available treatments. To date, 26 preclinical and clinical studies have been funded as well as the aforementioned consortium. AFIRM is a collaboration between the military and two civilian research consortia; it is focused on utilizing regenerative medicine to improve outcomes on injured Warriors who have sustained extremity, craniomaxillofacial, and burn injuries. Most of the immediate clinical efforts from AFIRM will be in skin replacement and scar mitigation along with composite tissue allografts.

**Institute of Surgical Research Capabilities:** The U.S. Army Institute of Surgical Research (USAISR) is part of the U.S. Army Medical Research and Materiel Command and is collocated with Brooke Army Medical Center. The USAISR is dedicated to both laboratory and clinical trauma research. Its mission is to provide requirements-driven combat casualty care medical solutions and products for injured soldiers, from self-aid through definitive care across the full spectrum of military operations.

The USAISR occupies 94,206 square feet within the three-story research facility. The building includes the Command Suite, Budget Division, Information Management Division, Personnel Division, Laboratory Support Division, Combat Casualty Care Division, the USAISR Library a dedicated Trauma Research Branch and Combat Casualty Care Division. The lower level houses a distinct Pathology branch, imaging, animal research surgery suites, and a joint use vivarium. In

addition to the current capabilities of the ISR, it is also the site for the Joint Center of Excellence for Battlefield Health and Trauma Research (BHTR), which is currently under construction. The BHTR is a \$92 million (M), 150,000 square foot research facility that will house DOD researchers from the Army, Navy, and Air Force. The objective is to establish an entity that integrates all Services' combat casualty care research missions/functions into a multi-faceted synergistic research capability with a clinical foundation. The BHTR will be the definitive focal point for all future Combat Casualty Care Research, a critical factor to the Department of Orthopaedics and Rehabilitation research vision.

**Research Personnel:** The Orthopaedic Trauma and Regenerative Medicine Task Area has a \$5.2M budget for intramural research and receives approximately \$1M per year from grants, contracts, and other funding sources. Part of this budget covers salaries of research and support personnel.

- 6 research Principal Investigators
- 2 clinician scientists
- 4 Ph.D. Post-Doctoral Fellows
- 2 research residents
- 1 graduate student
- 10 research technicians
- 1 program assistant
- 1 administrative assistant
- 1 computer programmer
- 3 research nurses

**Research Support Unit:** As an integrated Department with multidisciplinary collaboration and diversity, Brooke Army Medical Center Department of Orthopaedics and Rehabilitation is uniquely positioned to be the Premier Department of Defense Center of Excellence for Extremity Injury and Amputee Care. We have proven record of high performance in direct care, scientific inquiry, and education at all levels and specialties. The future will require sustained operations and a coherent selective approach to research. To this end, a dedicated research support unit is being constructed. While the capabilities of this unit are being defined, this is an essential part of our future organization and will contribute to capabilities for future collaboration.

### **Summary**

Brooke Department of Orthopaedics and Rehabilitation has firmly established excellence in clinical care, scientific inquiry, and education. This information paper has focused on the specific capabilities of the available patient population, research capabilities, and personnel to support these. While this is a concise snapshot of capability, the fact that a pending merger with the largest medical center of the US Air Force, and the pending completion of the Department of Defense Battlefield Health and Trauma Research Center on the same site will greatly expand this capability. Additionally, standing agreements in effect between the institution and the Department of Veteran Affairs make longitudinal studies beyond active duty military service a reality. The multi-disciplinary nature of the Department of Orthopaedics and Rehabilitation make meaningful clinical trials from the injury through final outcome our expectation.

**Walter Reed National Military Medical Center**  
**Department of Orthopaedics and Rehabilitation**

The research mission of Integrated Department of Orthopaedics & Rehabilitation at Walter Reed Army Medical Center and the National Naval Medical Center at Bethesda is to identify evidence-based orthopaedic treatment and rehabilitation solutions to optimize physical performance capabilities in wounded Warriors, with the intent to maximize their opportunity to return to full function within both civilian and military settings. This research plan was specifically developed to address the need for a systematic evidence-based approach to the provision of post-injury care to combat wounded Warriors. Target patient populations include individuals with amputation, limb salvage, complex musculoskeletal trauma, full spectrum of TBI, and/or PTSD. The ultimate goal is to “reset” the soldier, acknowledging a holistic treatment concept that extends beyond rehabilitation to include all activities necessary to return injured service members to duty or to productive civilian life.

**Problem Statement:** Due to the nature of current conflicts in Iraq and Afghanistan, the widespread use of body armor, and improved medical management, Warriors are now surviving wounds that would have proven fatal in previous conflicts. As a result, the number of severely wounded Warriors receiving prolonged medical and rehabilitative care is larger than in previous conflicts.

The use of improvised explosive devices against US soldiers has resulted in an increased number of patients with both severe musculoskeletal and psychological injuries. In spite of the importance of optimizing orthopaedic treatment and rehabilitative practices for civilian and military patients following severe traumatic events, there remain gaps in the scientific literature to guide the treatment process. In particular, there is a paucity of information to guide rehabilitation aimed at returning young, severely wounded patients to advanced functional activities.

**Research Products:** Integrated Department of Orthopaedics & Rehabilitation at Walter Reed Army Medical Center and the National Naval Medical Center at Bethesda will provide scientific evidence regarding the effectiveness of advanced technologies, treatment approaches, and rehabilitation approaches in an effort to improve clinical management of patients with traumatic extremity injuries.

### **Broad Research Goals:**

**Respond:** Respond to the acute care needs of wounded Warriors following injury through epidemiological surveillance, and study of innovative medical management solutions.

**Rehabilitate:** Develop evidence-based treatment strategies to optimize recovery of function.

**Reintegrate:** Assess program success in returning Warriors to a full and productive life, to include return to duty, competitive sports, or a new vocation.

### **Current Focus Areas:**

**Military Amputee Research Program (MARF):** Optimize clinical care through studies that assess functional outcomes following innovative surgical approaches, pain management

techniques, advances in socket design and fit, weight management intervention, and the use of advanced rehabilitation technologies to hasten and/or maximize functional performance.

**War-Related Extremity Injury and Rehabilitation Program:** Develop studies designed to minimize or reverse impairments associated with extremity trauma and maximize functional outcomes following burn injury, limb salvage, and other complex deployment-related musculoskeletal trauma.

**TBI Research Program:** Define the patient population, identify and investigate field-expedient screening methods for the full spectrum of TBI, and explore use of advanced technologies to assess performance.

### **Multi-disciplinary Research Teams:**

Dept. of Orthopedics and Rehabilitation (orthopedic surgeons, physiatrists, physician assistants)

Military Performance Laboratory, Walter Reed AMC (biomechanists and physiologists)

Clinical Teams (physical therapists, occupational therapists, prosthetists, dietitians)

Traumatic Brain Injury Service (physicians and psychiatrists)

**Research Laboratory Capabilities:** Walter Reed Army Medical Center and the National Naval Medical Center at Bethesda are modern, technologically-advanced health care facilities that provide full-spectrum medical care to military service members, veterans, and their families. The Military Advanced Training Center (MATC), located on the WRAMC campus, is a multi-disciplinary outpatient rehabilitation facility dedicated to providing advanced rehabilitative care for Wounded Warriors. The MATC houses full-service physical therapy and occupational therapy clinics, and a prosthetic fabrication laboratory. Also housed within the MATC is the Military Performance Laboratory, a state-of-the-art research and clinical care facility. The 2,250 square foot lab includes nearly 1,630 square feet of data collection space designed for the scientific assessment of activity performance and advanced rehabilitation training.

**Gait and Motion Analysis Lab:** Laboratory equipment in the Gait and Motion Analysis area includes: 23-camera optoelectronic motion capture system, 6 force plates (AMTI, Inc.), an instrumented dual-belt treadmill (AMTI, Inc.), a 16-channel electromyography system, (Motion Lab Systems, Inc.), two digital video cameras (Panasonic), and a metabolic testing system (Cosmed, Ltd.). An instrumented staircase and adjustable inclining walkway (AMTI, Inc.) are located within the MATC and utilized by the lab staff. The combination of a 25-meter walkway, a treadmill, a full flight of stairs, and a set of inclining parallel bars afford a unique opportunity to test patients' physical function across a wide range of basic to advanced activities.

**Computer Assisted Rehabilitation Environment (CAREN):** The CAREN system is a virtual reality-based training system that allows real-time feedback while patients perform a range of physically challenging tasks. Its curved display screen, two-projector visualization system, and instrumented treadmill mounted on a motion platform provide the ability to fully immerse patients in a virtual world. This first-of-its-kind system creates exciting opportunities for rehabilitation, testing, and research. Virtual reality training-based environments can be selected to match an individual's unique needs and level of function, allowing the opportunity to effectively challenge patients in a safe and controlled environment. Performance assessment and

patient feedback can be provided through the use of a 12-camera optoelectronic motion capture system (Vicon), an integrated heart rate monitoring system, as well as electromyographic and metabolic testing equipment. Our CAREN operator has developed over 50 unique environments for clinical applications for our patients.

**Prosthetics and Orthotics Service:** Our in-house prosthetics and orthotics service is intimately involved in numerous research efforts to advance patient care. Led by a Department Chief who is a Ph.D. candidate currently defending his thesis, this service has the full spectrum of prosthetics and orthotics services, to include CAD-CAM capabilities.

**Spine Research Center (Orthopaedic Biomechanics Lab):** The Spine Research Center is engaged in translational biomechanics/basic science research of the vertebral column reconstruction and spinal cord regeneration after injury. Translational aspect of the research involves biomechanical evaluation of implantable devices/prostheses using in vitro cadaveric models. In vivo surgical studies investigate the biology of bone formation in the spine and the regenerative processes in the spinal cord.

**Patient Population:** Walter Reed Army Medical Center and the National Naval Medical Center at Bethesda have cared for over 650 patients with major limb loss over the past five years. Over 21% have upper extremity involvement, and over 25% of those treated at Walter Reed have multiple limb involvement. On an average week, Walter Reed has 135 patients with major limb loss actively undergoing treatment.

**Research Personnel:** One full-time physical therapist/researcher is assigned to WRAMC as the Military Performance Laboratory director, and one biomechanical engineer/virtual reality specialist is employed to support the CAREN system. Both Orthopaedic Residency Program Physicians and Physical Medicine and Rehabilitation Residency Program Physicians are required to complete research projects as a portion of their training. The orthotics and prosthetics department provides on-site personnel to assist in a wide range of research efforts focusing on advancing technologies in this field. The majority of research efforts ongoing at the Center for the Intrepid are currently supported by contract personnel funded through the congressionally directed Military Amputee Research Program, as follows:

- 1 Ph.D. biomedical engineer specializing in amputee research
- 5 full-time research assistants (biomechanics background)
- 1 full-time research physical therapist
- 1 full-time protocol coordinator (recruiting, approvals, etc.)

### **Ongoing and Completed Projects:**

#### *Military Performance Laboratory*

- Factors influencing rehabilitation effectiveness in the restoration of physical function in the military amputee
- Body composition and metabolic changes over time in traumatic amputees – a pilot study
- The Effects of Amputation Level, Time to Closure, and Ability to Perform Myodesis on Trans-femoral Amputee Function

- Transfemoral Amputee Activity Level in Response to Microprocessor vs. Mechanical Hydraulic Controlled Knee Joints
- Biomechanical and Metabolic Analysis of Amputees Carrying Military Loads to Meet Return to Duty Requirements
- Functional and Clinical Assessment of the POWER Knee™: A Case Series of Young, Adult, Traumatic, Transfemoral Amputee, US Military Service Members
- Vanderbilt Knee: Testing of a Powered Knee and Ankle Prosthesis with Transfemoral Amputees at Walter Reed Army Medical Center
- Pre- and Post-Surgical Evaluation of Gait in Patients with Spinal Column Injury
- A Simple Model Using Gait Analysis to Determine Amputee Lordosis

#### *Clinical Research Program*

- The CAREN and NeuroCom EquiTest as augmentative tools in balance retraining in service members with mild traumatic brain injury
- Core Strengthening Regimen Effect on the Spinal Column of Uninjured Military Personnel
- Targeted Muscle Reinnervation Rehabilitation project
- Comparison of the Functional Performance and User Satisfaction of a Standard
- Development of an Amputee Mobility Functional Outcomes Predictor
- Efficacy of mirror-box and mental visualization treatments on phantom limb pain

#### **Future Projects:**

- Determination of optimal frequency and duration of rehabilitation following major limb loss
- Assessment of capabilities with a militarized/hardened microprocessor knee
- Functional and Clinical Assessment of the POWER Knee™ with bilateral above knee amputees
- Impact of body armor on physical work performance in TTA during simulated operational conditions
- The effect of a custom molded foot orthosis on plantar pressures and vertical ground reaction forces in Service members with unilateral lower extremity amputation
- Use of Visual Feedback in Normalizing Trunk Lateral Flexion in Amputees
- Weight Distribution Training of Lower Extremity Amputees using the CAREN
- Training Attention and Working Memory in a Virtual Environment Setting
- Rapid Prototyping of Prosthetic Feet that are mathematically “tuned” to individual patient specifications