

## ***PROGRAM ANNOUNCEMENT***

### ***ORTHOPAEDIC EXTREMITY TRAUMA RESEARCH PROGRAM***

#### ***FUNDING OPPORTUNITY NUMBER: W81XWH-09-OETRP***

1. Background: As with all previous wars, the majority of the trauma that occurs in Operation Iraqi Freedom and Operation Enduring Freedom is to the extremities. Not only are they common, extremity injuries account for over two-thirds of the inpatient hospital costs and disability payments and are the largest source of long-term morbidity for injured Warriors. In an effort to provide better treatment and outcomes for these injuries, the Orthopaedic Extremity Trauma Research Program (OETRP) was created. The OETRP is part of the US Army Medical Research and Materiel Command's research program and funds peer-reviewed, competitive orthopaedic trauma research.

2. Sponsor's Concept for the OETRP: This program announcement is soliciting proposals for prospective, multi-center clinical trials; randomization of treatment is highly preferred when possible. We wish to fund one consortium that includes sufficient participating clinical sites and patient volume to conduct trials relevant to care of military extremity trauma. Only studies that have military relevance will be funded and cooperation and inclusion of capable military hospitals are requirements. We anticipate entering into a cooperative agreement to execute this research, and the US Army Institute of Surgical Research (USAISR) will serve as the technical lead in a partnership with the funded consortium to help set priorities and execute research. The design and studies may be modified after the award. **See Appendix 1, Eligibility Information, for additional information.**

3. Research objectives. Therapies are being sought for one or more of the following conditions resulting from battlefield trauma with clearly defined clinical implementation (translating research into practice):

- a. Healing open traumatic bone defects
- b. Prevention of musculoskeletal infection
- c. Prevention of heterotopic bone formation
- d. Improving standards of care with emphasis on tissue viability assessment and wound irrigation/debridement technologies
- e. Repairing massive muscle defects

For more information on defining battlefield injuries, the treatments, and the research objectives, please see the following references:

- J Am Acad Orthop Surg. 2006; 14(10 Spec No.):S1-S214.
- J Am Acad Orthop Surg. 2007 Oct;15(10):588-9.
- J Am Acad Orthop Surg. 2007 Oct;15(10):590-5
- J Am Acad Orthop Surg. 2008 Nov;16(11):626-7.
- J Am Acad Orthop Surg. 2008 Nov;16(11):628-34.

For this announcement, trials should focus on acute clinical care (first response through reconstruction). It is anticipated that future funding will be available for rehabilitation and amputee research and translational research. Therefore, research in those areas is not desired at this time.

4. Funding. The anticipated funding level is \$14 million, inclusive of direct and indirect costs, for the five year life of the cooperative agreement. The consortium should be capable of adding or deleting clinical trial centers rapidly if the funding level changes. The sponsors expect that the consortium will submit to other agencies for extra funding to increase the breadth of research and/or increase number of participating sites. Please base your proposed budget based on \$14 million and convey what additional funding would allow you to accomplish in the introduction section of your proposal. The Statement of Work should be appropriate for the \$14 million budget. The consortium must be able to effectively and meaningfully execute all OETRP funding in support of its research objectives. The sponsors envision that the awardee will establish effective working relationships with members, partners, and collaborators to advance the research objectives while responding to varying funding levels.

5. Award instrument. The award instrument will be a Cooperative Agreement which will allow full collaboration between the consortium and the USAISR and will be for a five year period with the potential for renewal after the five years based on performance, need, available funding, and budget execution. The USAISR will monitor the consortium's progress with respect to research and budget execution. The USAISR will advise the consortium on areas of military relevance and military impact of the research. Finally, the USAISR will facilitate the possible participation of Department of Defense hospitals in the study, if the Army and the consortium agree that their participation will further study objectives. A cooperative agreement is one type of assistance agreement. An assistance agreement is a legal instrument which, consistent with 31 U.S.C. 6304, is used to enter into a relationship where the primary purpose is to transfer funds to the recipient to carry out research with a public purpose. Cooperative agreements contemplate substantial involvement between the Department of Defense and the recipient when carrying out the research activity that is the subject of the agreement. For more information on Department of Defense authority, policies and procedures with respect to assistance agreements please see 10 U.S.C. 2358 and its implementing instruction, The DOD Grants and Agreements Regulations (DODGAR).

### ***PROPOSAL SUBMISSION INSTRUCTIONS***

**See Appendix 2, Grants.gov Instructions, for additional information.**

Proposals must be submitted electronically by the Authorized Organizational Representative (AOR) through Grants.gov ([www.grants.gov](http://www.grants.gov)). No paper copies will be accepted. Pages in excess of page limitations specified in this Program Announcement will not be reviewed. Minimum font size is 12 point for text and 10 point for tables.

Please note, submission of a proposal requires institutional registration with the Central Contractor Registry (CCR). Please note that CCR registrations have expirations. Plan accordingly and allow several weeks for these registration processes. Grants.gov will not allow proposals to be submitted unless all of the registration steps have been completed.

#### A. Proposal Components Summary

Each proposal submission must include the completed Grants.gov application package of forms and attachments identified in [www.grants.gov](http://www.grants.gov) for the US Army Medical Research Acquisition Activity (USAMRAA) program announcement. The package includes:

1. SF-424 (R&R) Application for Federal Assistance Form. This form is part of the application package in Grants.gov. This form is required for each application. All appropriate information must be entered into this form to allow for auto-population of all subsequent forms in this application package. The form is self-explanatory, with the following exceptions:

- Applicant Identifier box should be filled in with the submitting Institution's Control Number.
- State Application Identifier is not applicable.
- Block 1 – Type of Submission. For all submissions the “Application” box should be chosen. For substantial changes that must be made after the original submission, the complete application package must be resubmitted. In these cases, the “Changed/Corrected Application” box must be checked and the Grants.gov tracking number must be entered in Block 4 - Federal Identifier.
- Block 3 – Date Received by State is not applicable
- Block 4 – Federal Identifier Box. This box will be populated by Grants.gov for an original application, but the Grants.gov tracking number (i.e., the Federal Identifier Number assigned to the original application) must be manually entered for changed or corrected applications.
- Block 13 – Proposed Project. Patient accrual date should be 9 months to a year from the deadline for proposal submission for this award mechanism.
- Block 14 – Congressional Districts Of. If applying from a foreign institution enter “00-000” for both applicant and project.
- Block 17 – Is Application Subject to Review by State Executive Order 12372 Process? Choose option, b. NO, program is not covered by E.O.12372.
- Block 19 – Authorized Representative. The “signature of AOR” is not an actual signature and is automatically completed upon submission of the electronic application package. *Hard copies of applications will not be accepted.*

2. Attachment Form. This form is part of the application package in Grants.gov. Use the Attachment Form to submit the following Attachments. Save each

attachment as a .PDF file, using the attachment number as the name. For example, save the Executive Summary as “attachment1.pdf.”

- a. Attachment 1: Executive summary (limit 2 pages)
- b. Attachment 2: Introduction: Understanding the problem/vision, near and long term, discussion of what additional funding may buy (to include more sites and other clinical trials). (limit 10 pages)
- c. Attachment 3: The Over Arching Research Plan (limit 10 pages)
- d. Attachment 4: Provide a Research Plan, Part B, for each proposed clinical trial or study (limit 15 pages each). Save each therapy as an increment of Attachment 4. For example, save as “attachment4.1.pdf,” “attachment4.2.pdf,” etc.
- e. Attachment 5: The submitters may wish to propose pre-clinical studies or auxiliary work. This should focus on bringing a promising therapy into the clinic or provide an understanding of clinical observations. This work must be kept at a minimum and may not be funded.
- f. Attachment 6: Description of the regulatory pathway for implementation of Extremity Injury research efforts into clinical practice, if applicable (e.g. FDA approval process or prospective clinical trials of non-FDA approved drugs, devices, or biologics) (limit 10 pages).
- g. Attachment 7: Schedule (Gantt format) for each proposed clinical trial or study.
- h. Attachment 8: Explain what and how non-OETRP resources (other research or funding from Federal or private sources) can/will be leveraged to support the OETRP projects. (limit 5 pages)
- i. Attachment 9: Provide a Management Plan to include (limit 15 pages):
  - (1) Organizational structure
    - a) Description of who and how the lead organization was selected and how it will lead the Program
    - b) Organizational Chart with role/responsibility, name, and organization
  - (2) Management approach and processes
    - a) Description of the management approach
    - b) Description of project/research initiation approval
    - c) Description of management processes to be implemented
    - d) Description of reviews and working groups to include frequency by type
    - e) Description of the financial reporting to be provided.
    - f) Description of deliverables
    - g) Description of process to terminate research to include:
      - i. Criteria
      - ii. Decision process
      - iii. Final authority

- h) Description of Clinical Trials management
  - i. Description of plan to meet FDA requirements, including as appropriate a description of how GLP or GMP requirements are instituted, managed and maintained (if applicable)
  - ii. Description of planning clinical trials
  - iii. Description of plan to gain FDA approval and ultimately licensure (if applicable)

j) Process for Handling Intellectual Property Issues: Questions regarding intellectual property rights in technical data, computer software, copyrights, and patents, and the protection of those rights, will arise. The proposal must therefore address how the consortia propose to handle such issues with the various entities with which it interfaces: industry, academia and government. Since the specifics of any technological transfer or collaboration is not yet known, it is sufficient to explain what issues would be considered and the mechanism for resolving disputes and protecting sensitive information. The Army reserves the right to a royalty-free license to all developed intellectual property, it does not ask for first patent rights.

(3) Personnel (limit 15 pages)

Identification of Key Personnel including:

Role and responsibilities

Parent organization (who they work for)

Thumbnail of important experience (CVs to be provided in an appendix for key personnel only)

j) Attachment 10: Clinical Trials/Studies Track Record (limit 10 pages)

A table showing the track record of clinical trials and other implementation methods that were submitted, underway, completed, approved.

k) Attachment 11: Provide a description of facilities proposed for accomplishing the proposed research, including floor plans and pictures subject to page limitations (limit five pages).

l) Attachment 12: Each offeror will provide a compliance matrix showing where each evaluation criteria proposal submission requirement is addressed in the proposal.

3. Research and Related Budget Form. This form is part of the application package in Grants.gov. Provide a budget by year in a format that includes overall OETRP consortia program management, and each of the proposed projects to match the schedule(s) provided in the Research Plan. The budget for the research project(s) will include the major tasks and milestones provided in the schedule, and show proposed individuals by name (if possible), and role (or labor category). **See Appendix 3, Budget Forms, for more information.**

4. R&R Subaward Budget Attachment(s) Form (optional form; use if applicable). This form is part of the Grants.gov application package. **See Appendix 3, Budget Forms, for more information.**

**See also Appendix 4, Formatting Guidelines**

### ***EVALUATION PROCESS***

The sponsors intend to utilize a Peer Review Evaluation Board comprised of experts in research and clinical management of trauma patients to review proposals and score the proposals according to the criteria below. The scored proposals will then be sent to a Program Review Board comprised of senior leaders in military combat casualty care and orthopedic research, orthopedic consultants to the service Surgeons General, and the OETRP program manager. The Director, US Army Medical Research and Materiel Command, will appoint the chair of the Program Review Board. The Program Review Board will make a funding recommendation to the Grants Officer.

**The evaluation will be conducted using a five step process.**

1. Initial screening. The Grants Officer and the chair of the Peer Review Evaluation Board will screen all proposals to see if they meet the minimum requirements of the Program Announcement (must have more than one institution, must have performed a successful clinical trial in orthopaedic trauma, and must have thorough technical, management plans). Those proposals not meeting the minimum requirements will not be evaluated, and those respondents will be notified immediately.
2. Written proposal evaluation. Those proposals meeting the minimum requirements of the Program Announcement will be evaluated, rated, and ranked using the criteria in this section. Those proposals not among the most highly ranked will be eliminated, and those respondents will be notified immediately.
3. The Grants Officer will invite the remaining respondents to present their plans to the Peer Review Evaluation Board in person. This will allow the Peer Review Evaluation Board to gain a greater understanding of all aspects of the offeror's proposal and to answer any questions that might have arisen during the review of the written proposals. If this step or step four is not required make the determination, it will not be used.
4. At the conclusion of these discussions, each remaining respondent will be permitted to make final revisions to its proposal. Final revisions will be evaluated by the Peer Review Evaluation Board, which will send its evaluation to the Program Review Board.
5. The Program Review Board will review the evaluations from the Peer Review Evaluation Board and make a funding recommendation to the Grants Officer.

### **Review Criteria**

1. **Peer Review:** All proposals will be evaluated according to the following criteria, which are listed in order of importance:

- **Impact**
    - How the project may lead to an original and important contribution to orthopedic extremity trauma care
    - What impact this study may have on the concepts or methods that drive the field of orthopedic extremity trauma research
  - **Research Strategy**
    - How the scientific rationale and logical reasoning support the project and its feasibility
  - **Budget**
    - How the budget is appropriate for the proposed research.
2. **Programmatic Review:** Criteria used by the Program Review Board to make funding recommendations include:
- **Military Relevance.** The successful proposal must address the clinical issues of high energy orthopaedic trauma. The successful proposal will use the appropriate civilian trauma patients to reduce infection, delayed unions, length of stay in hospital, and morbidity associated with extremity trauma.
  - **Military Impact.** This will be determined by comparing the proposed trials with the number of battlefield injured Warriors that had similar injuries and the morbidity associated with the injury. Military impact will also consider the improvement in care that might come from the trial.
  - **Scientific Merit.** Ratings and evaluations of peer reviewers will be considered.
  - **Proposed Clinical Action Plan**
    - Infrastructure for coordinating multi-center clinical trials
    - Prior experience in clinical research, especially orthopaedic trauma research
    - Consortia member institutions' history of orthopedic trauma patient volume

**Post Award Information. See Appendix 5, Award Administration Information, Appendix 6, Regulatory Requirements and Reviews, and Appendix 7, Reporting Requirements.**

#### **Identifying Potential Conflicts of Interest**

Investigators are required to disclose to the Grants Officer any Significant Financial Interests (and those of his/her spouse and dependent children) that would reasonably

appear to be affected by the research proposed for funding under this Program Announcement. The Grants Officer will review those disclosures and determine whether any of the reported financial interests could directly and significantly affect the design, conduct, or reporting of the research and, if so, the Grants Officer may require an acceptable conflict of interest mitigation plan before approving the funding recommendation.

#### **Timeline for Submission and Review**

- **Proposal Submission Deadline:**      **11:59 p.m. Eastern time, 01 May 2009**
- **Peer Review:**                              **June 2009**
- **Programmatic Review:**                **July 2009**

A single award will be made no later than September 30, 2009.

You may be able to submit a proposal to Grants.gov after the deadline and you will receive a message that your application is being processed. You will, however, receive at a later date notification that your proposal was late and will not be accepted.

You may email questions about OETRP to Kathryn McCune at [kathryn.mccune@us.army.mil](mailto:kathryn.mccune@us.army.mil). Questions will be accepted until 15 April 2009. Questions and answers will be posted on the USAMRAA home page, [www.usamraa.army.mil](http://www.usamraa.army.mil).