

***DRAFT PROGRAM ANNOUNCEMENT
ARMED FORCES INSTITUTE OF REGENERATIVE MEDICINE***

1. Background: The U.S. Army Medical Research and Materiel Command (USAMRMC) is establishing the Armed Forces Institute of Regenerative Medicine (AFIRM) dedicated to repairing battlefield injuries through the use of regenerative medicine. Regenerative medicine is a promising field that has already achieved early success in the regeneration of several tissues and organs for repair or replacement. Regenerative medicine encompasses many novel approaches for the treatment of damaged tissues and organs by using therapies that prompt the body to autonomously regenerate, and by using the patient's own cells on biodegradable biomaterials for the creation of engineered tissues or organs for therapy. These innovations are possible because of several key advances, including the development of systems that can reliably nurture cells as they grow and divide, the discovery of growth factors that foster cell proliferation in vitro, and fabrication of biomaterial scaffolds for tissue generation in three-dimensions.

2. Sponsor's Concept for the AFIRM: The epidemiology of combat injury is well defined and presents many opportunities for the application of regenerative medicine to improve clinical outcomes after traumatic injury. The AFIRM will be a collaborative institution comprised of the US Army Institute of Surgical Research (ISR) and a non-governmental organization to address these opportunities. The sponsor anticipates that the non-governmental organization will be comprised of a management entity and several research institutions aligned as a consortium or similar partnership. It is expected that the clinical applications of this regenerative medicine effort will be conducted at the ISR and/or at the research institutions on military patients and civilian patients with similar traumatic injuries. The AFIRM will be managed by the non-governmental organization with input and coordination from the Combat Casualty Care Research Area Director at Ft. Detrick, MD, acting as the sponsor, and the ISR. The ISR has its own independent funding stream separate from the funding set aside for this effort. The AFIRM will stress the following:

- a. Most near term payoff for the service member
- b. Service member wound focus
- c. Scientific excellence and utilization of technologies at the forefront of regenerative medicine
- d. Strategic implementation of research (innovative methods for translation of research efforts into clinical practice)

3. Special Relationship. The AFIRM shall conduct its business in a manner befitting its special relationship with the Government; i.e., to operate with objectivity and be free from conflicts-of-interest, to fully disclose its affairs to its sponsor, and to serve the unique needs of its sponsor, while holding its full confidence and trust. Any subsidiary relationship the AFIRM may have with a parent organization or consortia of organizations must demonstrate and maintain strict safeguards from conflicts of interest with such parent organizations. Work performed by the AFIRM for customers other than

the sponsor (USAMRMC) may be performed only with the explicit permission of the sponsor. The sponsor will appoint an Executive Agent to represent the interests of the sponsor to the AFIRM on a day-to-day basis. The sponsor will also appoint an Executive Oversight Board, which will receive the annual, in-person, Report of the Institute.

The nature of the mission of the AFIRM requires that the AFIRM operate in a strategic relationship with its sponsor and users. This strategic relationship shall have the following characteristics and be governed as follows:

- a. The AFIRM and its sponsor commit to a stable and long-term relationship.
 - b. The AFIRM is granted access to information beyond that which is common to the normal contractual relationship, including medical intelligence data and program planning information.
 - c. The AFIRM bears a special responsibility to avoid actual and perceived conflicts of interest, and the AFIRM accepts stringent restrictions on its scope, method of operations and the kinds of efforts it can undertake either for its sponsor or for other users.
 - d. AFIRM work. The AFIRM may only perform work as defined in its core statement and in accordance with the following guidelines:
 - (1) The sponsor must approve all work.
 - (2) Work may only be accepted from the sponsor and other entities approved by the sponsor.
 - e. Non-AFIRM work performed by member, parent and affiliate organizations.
 - (1) Non-AFIRM work shall not undermine the independence, objectivity, or credibility of the AFIRM by posing an actual or perceived conflict of interest, nor shall it detract from the performance of AFIRM work.
 - (2) Non-AFIRM work shall not be acquired by taking unfair advantage of the parent institution's operation of the AFIRM or of information that is available only through the AFIRM.
4. Research objectives. Therapies are being sought for the following rehabilitation, reconstruction, problems resulting from battlefield trauma with clearly defined clinical implementation (e.g. clinical trial, evidence based change in clinical practice) of one or more technologies within five years:
- a. Compartment syndrome – therapies for repair of sequelae
 - b. Functional limb and digit salvage, reconstruction, regeneration, or transplantation
 - i. Regenerating large osseous defects
 - ii. Nerve repair
 - iii. Regrowing functional muscles and tendons
 - c. Facial reconstruction
 - d. Healing without scarring

- e. Burn repair (regeneration or replacement of skin)

5. Funding. The funding level for the AFIRM is at least \$6 million per year. Congressional supplements and work for other entities approved by the sponsor may bring AFIRM funding up to \$30 million per year. The most likely funding range will be \$10 million to \$15 million per year. The non-governmental organization managing the AFIRM must be able to effectively and meaningfully execute all AFIRM funding in support of its research objectives. The sponsor envisions that the non-governmental organization managing the AFIRM will establish flexible relationships with members, partners, and collaborators to advance the research objectives while responding to varying funding levels.

6. Contract vehicle. The contracting vehicle will be a Cooperative Agreement which will allow full collaboration between the ISR and the non-governmental organization and will be for a five year period with the potential for renewal after the five years based on performance.

PROPOSAL SUBMISSION INSTRUCTIONS

[Note: Do not submit a proposal in response to this Draft Program Announcement. See the section entitled “Comments Invited from Respondents” at the end of the Draft Program Announcement]

1. Provide a Research Plan to include for each proposed therapies:
 - a. Maturity of the proposed therapy using the following USAMRMC Technology Readiness Levels (TRLs) (full definitions can be found in Appendix X) with rationale for this assessment:
 - i. TRL 1 – Basic principles observed and reported
 - ii. TRL 2 – Technology concepts and/or application formulated
 - iii. TRL 3 – Analytical and experimental critical function and/or characteristic proof-of-concept.
 - iv. TRL 4 – Component and/or breadboard validation in laboratory
 - v. TRL 5 – Component and/or breadboard validation in a relevant environment
 - vi. TRL 6 – System/subsystem model or prototype demonstration in a relevant environment
 - vii. TRL 7 – System prototype demonstration in an operational environment
 - viii. TRL 8 – Actual system completed and qualified through test and demonstration
 - ix. TRL 9 – Actual system proven through successful implementation
 - b. Description of the regulatory pathway for implementation of regenerative medicine research efforts into clinical practice (e.g. FDA approval process or prospective clinical trials)

- c. Overall approach to move the research forward (as applicable), to include process description, outcomes by phase, and flow chart:
 - i. Into next maturity phase
 - ii. Into clinical trials
 - iii. Into sustainable production and clinical use
 - d. Schedule (Gantt format) for each proposed research project showing major tasks and key milestones, with responsible organization and people, key decision points, and key communication points (within AFIRM and between FDA)
 - e. What and how non-AFIRM resources (other research or funding) can/will be leveraged to support the AFIRM projects (this would include any matching dollars from the host institution(s) or other sources)
2. Provide a Management Plan to include:
- a. Organizational structure
 - i. Description of who and how the lead organization was selected and how it will lead the Program
 - ii. Organizational Chart with role/responsibility, name, and organization
 - b. Management approach and processes
 - i. Description of the management approach
 - ii. Description of project/research initiation approval
 - iii. Description of management processes to be implemented
 - iv. Description of lines of authority and communication within the offeror's organization and between the AFIRM
 - v. Description of reviews and working groups to include frequency by type
 - vi. Description of deliverables
 - vii. Description of process to terminate research to include:
 - 1. Criteria
 - 2. Decision process
 - 3. Final authority
 - viii. Description of Clinical Trials management
 - 1. Description of plan to meet FDA requirements, including as appropriate a description of how GLP or GMP requirements are instituted, managed and maintained
 - 2. Description of planning clinical trials
 - 3. Description of plan to gain FDA approval and ultimately licensure
 - c. Personnel
 - i. Identification of Key Personnel including:
 - 1. Role and responsibilities
 - 2. Parent organization (who they work for)
 - 3. Thumbnail of important experience (CVs to be provided in an appendix for key personnel only)
3. Provide a Commercialization Plan

- a. Description of the organizational structure and relationships between all organizations and agency. This description should include:
 - i. An organization chart
 - ii. Roles and responsibilities
 - iii. Communications process
 - b. Description of any technology transfer process (for academic institutions)
 - c. Description of the regulatory approach to ensure that all key steps, processes, and data are completed/collected to successfully gain licensure
 - d. Description of any non-traditional technology implementation approaches (such as improving functional outcome through evidence based clinical guidelines)
 - e. Description of key communications within AFIRM and between FDA
4. Clinical Transition Track Record
- a. A table showing the track record of clinical trials and other implementation methods that were submitted, underway, completed, approved. This should show:
 - i. all regenerative medicine trials
 - ii. all other trials over the past 5 years
 - b. This table should be completed for the lead and subcontractor organization/institution for trials at:
 - i. The organization
 - ii. The PI and Key Personnel
 - c. The information shall include the following information

PI/Key Personnel	Organization where PI was employed at the time of the trial	Status (i.e., submitted, underway, completed, approved)	Current Trial Phase	Start and End Dates for each Phase	Trial Name and Outcome

- 5. The offeror shall provide a description of their understanding of the problem and criticality of identifying the appropriate approval and implementation process for the proposed technology.
- 6. The offeror shall provide a description of the near and long term vision for providing products for the service member. This should include a discussion of the cutting edge technologies that may not fit in the five year window during this initial solicitation, but will have significant payoff in the 5-10 year window.
- 7. Provide a description of facilities proposed for accomplishing the proposed research, including floor plans and pictures if available.
- 8. Each offeror will provide a compliance matrix showing where each evaluation criteria and Section L requirement can be found in the proposal.
- 9. Provide a budget by quarter in a format that includes overall AFIRM 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).

EVALUATION PROCESS

The sponsor intends to utilize a Source Selection Board comprised of experts in the fields of research and management to review proposals and make a source selection recommendation to the Grants Officer. The Grants Officer will be the final authority for source selection.

Proposals will be evaluated using the criteria below. Criteria 1 is of greatest importance, followed by criteria 2. Criteria 3 and 4 are of equal importance and of greater value than 5 and 6. Criteria 5 and 6 are of equal importance (1>2>3,4>5,6). Proposals will be evaluated using a color coded ranking process. These color codes are listed here in order of importance:

Blue – Exceptional, proposal/section exceeds requirements as stated in RFP

Green – Adequate, proposal/section meets requirements as stated in RFP

Yellow – Deficient, proposal/section meets some of the requirements as stated in the RFP and potentially can be made Green or Blue with some additional material

Red – Not acceptable, proposal/section does not meet requirements as stated in the RFP

Source selection will be conducted using a four step process.

1. Initial screening. The Grants Officer and the chair of the Source Selection Board will screen all proposals to see if they meet the minimum requirements of the Program Announcement. Those proposals not meeting the minimum requirements will not be evaluated, and those offerors 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 offerors will be notified immediately.
3. The Source Selection Board and the Grants Officer will conduct a site visit at one or more of the facilities of each of the most highly ranked offerors. The site visits will have two purposes. First, the Source Selection Board will review the facilities to gain a more in-depth perspective of each offeror's capabilities. Second, the Source Selection Board and the Grants Officer will conduct discussions with each offeror to gain a greater understanding of all aspects of the offeror's proposal.
4. At the conclusion of site visits/discussions, each remaining offeror will be permitted to make final revisions to its proposal. Final revisions will be evaluated by the Source Selection Board, which will make a recommendation to the Grants Officer.

Evaluation Criteria

1. Technical Research Plan

- a. Discussion of maturity (using USAMRMC modified TRL scale and definitions) and feasibility of each research project and the overall research approach, including approval and technical process to move steps forward.
 - b. Schedule (Gantt format) for each proposed research project showing major tasks and key milestones, with responsible organization and people, key decision points, and key communication points (within AFIRM and between FDA)
 - c. How any non-AFIRM resources can/will be leveraged to support the AFIRM projects
2. Management Plan
 - a. Organizational structure
 - b. Management approach and processes
 - i. Description of the management approach
 - ii. Description of project/research initiation approval
 - iii. Description of management processes to be implemented
 - iv. Description of process to terminate research to include:
 - v. Description of Clinical Trials management
 - c. Personnel
 3. Commercialization Plan
 - a. Description of the organizational structure and relationships between all organizations and agency. Description of any technology transition and technology transfer process (for academic institutions).
 - b. Description of the regulatory approach to ensure that all key steps, processes, and data are completed/collected to successfully gain licensure
 - c. Description of key communications within AFIRM and between FDA
 4. Clinical Trials Track Record
 5. Facilities
 6. Offeror's ability to leverage non-AFIRM resources (research or funding, or both)

COMMENTS INVITED FROM RESPONDENTS

Do not submit a proposal in response to this Draft Program Announcement. Please consider the following questions and provide your response. To be of greatest value, your response should be submitted not later than 4 May 2007. Please contain your comments to 10 pages or less. Electronic submissions only, please via ASFI/FedBizOps or e-mail to christopher.gloyd@det.amedd.army.mil.

1. Your comments are invited on the Sponsor's Concept of the AFIRM. Is this an effective way to organize and execute this vital initiative?
2. Your comments are invited on the special relationship envisioned between the USAMRMC and the organization that will manage the AFIRM. The Army's objective is to have control and collaboration to a greater extent than that which exists normally in a cooperative agreement. Our notional concept is to employ a sponsorship model, using a

sponsorship agreement, executive agent, and executive oversight board. Is there a better way to accomplish the Army's objectives? Is this process too restrictive?

3. Your comments are invited on the research objectives. Are they defined well enough to develop a comprehensive proposal?

4. Your comments are invited on the Army's expectations with respect to the execution of varying funding levels. What problems does this present for the organization managing the AFIRM and how might those problems be addressed?

5. Your comments are invited on the appropriateness of a cooperative agreement as the vehicle of choice to execute the AFIRM. Would a contract be better? If so, why?

6. Your comments are invited on the proposal submission instructions and evaluation process. Are these instructions clear? Are they fair? Are they designed to produce the desired result? Can they be improved?