

# Program Announcement

Department of Defense Congressionally Directed Medical Research Programs

Deployment Related Medical Research Program

Clinical Trial Award

Funding Opportunity Number: W81XWH-08-DRMRP-CTA

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## I. HELPFUL INFORMATION

### A. Contacts

**1. Program announcement, proposal format, or required documentation:** To view all funding opportunities offered by the Congressionally Directed Medical Research Programs (CDMRP), perform a Grants.gov basic search using CFDA Number 12.420. 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

Fax: 301-619-7792

Email: [cdmrp.pa@amedd.army.mil](mailto:cdmrp.pa@amedd.army.mil)

**2. eReceipt system:** Questions related to pre-application components through the CDMRP eReceipt system should be directed to the eReceipt help desk, which is available Monday through Friday from 8:00 a.m. to 5:00 p.m. Eastern time.

Phone: 301-682-5507

Website: <https://cdmrp.org>

Email: [help@cdmrp.org](mailto:help@cdmrp.org)

**3. Grants.gov contacts:** Questions related to submitting applications through the [Grants.gov](http://www.grants.gov/) (<http://www.grants.gov/>) portal should be directed to Grants.gov help desk. Deadlines for proposal submission are 11:59 p.m. Eastern time on the deadline date. Therefore, there is an approximate 3-hour period during which the Grants.gov help desk will NOT be available. Please plan ahead accordingly, as the CDMRP help desk is not able to answer questions about Grants.gov submissions.

Phone: 800-518-4726, Monday to Friday, 7:00 a.m. to 9:00 p.m. Eastern Time

Email: [support@grants.gov](mailto:support@grants.gov)

***Grants.gov will notify Principal Investigators (PIs) of changes made to this Program Announcement and/or Application Package ONLY if the PI clicks on the “send me change notification emails” link and subscribes to the mailing list on the Opportunity Synopsis Page for this announcement. If the PI does not subscribe and the Application Package is updated or changed, the original version of the Application Package may not be accepted.***

## B. National Technical Information Service

The technical reference facilities of the National Technical Information Service ([www.ntis.gov](http://www.ntis.gov)) are available for the purpose of surveying existing knowledge and avoiding needless duplication of scientific and engineering effort and the expenditure thereby represented. All other sources also should be consulted to the extent practical for the same purpose.

## C. Commonly Made Mistakes

- Not obtaining or confirming the organization's [DUNS number](https://eupdate.dnb.com/requestoptions.asp?cm_re=HomepageB*TopNav*DUNSNumberTab) ([https://eupdate.dnb.com/requestoptions.asp?cm\\_re=HomepageB\\*TopNav\\*DUNSNumberTab](https://eupdate.dnb.com/requestoptions.asp?cm_re=HomepageB*TopNav*DUNSNumberTab)) well before the proposal submission deadline.
- Not obtaining or confirming the organization's registration with the [Central Contractor Registry \(CCR\)](http://www.ccr.gov/) (<http://www.ccr.gov/>) well before the proposal submission deadline.
- Failing to request "send me change notification emails" from [Grants.gov](http://www.grants.gov/) (<http://www.grants.gov/>).
- Not contacting [help desks](#) until just before or after deadlines.
- Not completing the pre-application submission before the mandatory pre-application deadline, i.e., pre-application remains in draft status (**NOTE: "Submit" button must be pressed for pre-application to be complete**).
- Using an incorrect Grants.gov application package to submit a proposal through Grants.gov. Each Program Announcement/Funding Opportunity requires a specific application package.
- Uploading attachments into incorrect Grants.gov forms.
- Attaching files in the wrong location on Grants.gov forms.
- Submitting attachments that are not PDF documents, except for the R&R Subaward Budget Attachment(s) Form.
- Exceeding page limitations.
- Failing to submit a proposal 48-72 hours before the deadline so that Grants.gov can provide notification of errors and allow for resubmission of application package.
- Failing to submit proposal by [submission deadline](#).

## II. FUNDING OPPORTUNITY DESCRIPTION

### A. Program Objectives

The Deployment Related Medical Research Program (DRMRP) was established in Fiscal Year 2008 (FY08) to provide support for deployment health-related research of clear scientific merit. The DRMRP anticipates that approximately \$92 million (M) of the full \$273.8M of the FY08 supplemental appropriations bill, Public Law 110-252, will be available to support DRMRP

research. Other solicitations funded from the cited appropriation will be announced by organizations other than the CDMRP, potentially including organizations outside the United States Army Medical Research and Materiel Command (USAMRMC). Links to those solicitations will be placed on the CDMRP website (<http://cdmrp.army.mil/>) as they become available. The Government reserves the right to increase or decrease the DRMRP funding of \$92M to execute the program.

The vision of the FY08 DRMRP is to find and fund the best medical research to protect, support, and advance the health and welfare of deployed military personnel. The research projects should be tailored for use within a military milieu across field, shipboard, garrison, primary care, behavioral health care, or combat settings. Strategies that promote and sustain healthy adaptation to prolonged and/or adverse military operations (i.e., reset/resiliency) across the deployment lifecycle are encouraged as applicable. Other contextual factors such as, but not limited to, individual, peer, family, caregiver, community, culture, gender, personality, social, and rural settings, among military Service members and family/co-residents, that may affect the selection, implementation, and outcomes of empirically validated research should be addressed as applicable. Studies that focus on comparisons between active duty (including individual military augmentees), National Guard, and Reserve Service members are encouraged. Strategies that use innovative technology to address research gap areas are encouraged as appropriate.

The DRMRP challenges the scientific and clinical communities to develop innovative ideas that will leapfrog the delivery of emerging new approaches, technologies, and agents to the military through basic science, translational, and/or clinical research. The DRMRP seeks deployment-related proposals in clinical, cognitive/behavioral, computational, epidemiologic, laboratory and field research, as well as public health and policy, international health and humanitarian relief, environmental sciences related to optimal healing, nursing, occupational health, complementary and alternative therapies, ethics, medical safety, and economics. Interdisciplinary and integrative health approaches are encouraged.

## **B. FY08 DRMRP Congressionally Directed Topic Areas**

All applications for DRMRP funding must specifically and clearly address one of the deployment-related topic areas. ***If the research is not relevant to currently advertised DRMRP topic areas, the Government reserves the right to administratively withdraw the proposal.*** The Government also reserves the right to reassign the proposal's research topic area (note listed below) if the selected topic is inconsistent with the focus of the research proposal submitted. The FY08 topic areas addressed by this program announcement are listed below.

- Blood safety and blood products
- Final development of medical devices for use in-theater, including portable suction machines and EKGs for theater hospitals
- Injury prevention
- Traumatic brain injury and psychological health, including post-traumatic stress disorder
- Trauma treatment and rehabilitation, including nonsurgical orthopedic conditions
- Wound infection and healing
- Wound infection vaccines

## C. Deployment-Related Research Gaps

All applications for DRMRP funding must specifically and clearly address deployment-related research gap(s) within the chosen topic area. **Not all of the following research gaps may be applicable to this award mechanism; some gaps are relevant to other mechanisms offered by the FY08 DRMRP.** It is incumbent upon the PI to make certain that the research gaps addressed in the proposal align with the intent of the award mechanism. *If the proposed project is not relevant to specified DRMRP research topics or gaps, the Government reserves the right to administratively withdraw the proposal.* The FY08 research gaps are listed below by topic area.

### 1. Blood Safety and Blood Products

**Blood Safety:** The priority for this topic area is to eliminate infectious pathogens of all kinds in order to increase the safety of fresh blood products collected in-theater.

#### Gaps:

- a. Pathogen inactivation of platelets, or
- b. Pathogen inactivation of whole blood.

**Blood Products:** The priorities for this topic area are products that will serve as coagulation factors for the reversal of trauma-induced coagulopathy. Preference will be given to the development of products that are suitable for use by first responders in operational settings that can be evaluated in Phase II clinical trials in the shortest time possible, preferably within two years.

**Gap:** Freeze-dried plasma products with the following characteristics: Human plasma-derived, pathogen-inactivated or -free, temperature-stable, and lipid-reduced.

### 2. Final Development of Medical Devices for Use in-Theater (including portable suction machines and EKGs for in-theater hospitals)

#### Gaps:

- a. FDA-approved, rapid detection, multiplex/multi-agent, hand-held systems designed to screen whole blood pre-transfusions and accurately detect bloodborne pathogens with a high degree of sensitivity and specificity for use far-forward in a wartime environment.
  - o Primary focus is on Hepatitis B and C, followed by HIV-1, and then other bloodborne pathogens. A multiplex/multi-agent system that covers a range of naturally occurring infectious agents, and includes Hepatitis B and C, is highly desirable.
  - o Approaches could include nucleic acid testing and immunoassay techniques as well as other innovative systems.
- b. Highly portable, autonomous or semi-autonomous ventilation and resuscitation systems, including the following:

- Decision-assist and closed-loop algorithms applicable over a wide range of physiological conditions from severely wounded to maintenance during aerial transport, or
  - Signal processing technology to remove real-time noise due to movement, interference, etc., from physiological waveforms.
- c. Web-based, telemedicine modality clinical technologies

### 3. Injury Prevention

The priority for this topic area is research proposals that take an end-to-end approach that combines appropriate animal injury and/or post-mortem human subject (PMHS) studies with computational modeling, and includes model validation.

**Gap:** Biomedically valid computational models of blast-related injuries that can be used to design, build, and test personal protection systems, such as combat helmets and body armor, and combat vehicle protection systems, such as blast-attenuating seats.

- Blast-related injuries of interest include all types of extremity, head and face, and spine injuries.
- Blast-related injury mechanisms of interest include blunt force impact, blast overpressure, acceleration, force transference, and combinations of two or more of these mechanisms.
- Computational models must be biomechanically or physiologically based, and developed from a thorough understanding of the tissue-level injury mechanisms.
- Computational models must be validated using data from appropriate animal injury and/or PMHS tests.

### 4. Traumatic Brain Injury (TBI) and Psychological Health (including post-traumatic stress disorder [PTSD])

#### Traumatic Brain Injury Gaps:

- a. Epidemiology with emphasis on battle-induced mild TBI (mTBI) and PTSD analyzing the occurrence and development of symptoms including, but not limited to, repetitive injury, sleep disturbances, cognitive and emotive symptoms (e.g., risk-taking behavior, substance abuse, etc.). Effort should be directed to determining the actual incidence of mTBI on the battlefield, its effects on performance of mission, and its long-term sequelae.
- b. Clinical trial(s) Phase II or III for pharmacological treatment of TBI including single or combination therapies.
- c. Impact of patient transport (e.g., ground, rotary/fixed-wing air) on moderate and severe TBI, and techniques and/or therapies designed to reduce negative impact.
- d. A simple, quantitative, noninvasive method to diagnose mTBI that can be used for deployed troops.

- e. Sensors, including accelerometers and dosimeters, to measure blast and predict the occurrence of TBI.
- f. Efficient clinical diagnostic criteria methodologies for detecting mTBI, while distinguishing it from psychological co-morbidities (i.e., depression and PTSD).
- g. Pain management to improve short-term outcomes and reduce the risk of long-term opioid dependence and/or abuse.
- h. Innovative therapies for TBI, including hyperbaric oxygen therapy, complementary and alternative medicine, etc.
- i. Impact of rehabilitation strategies on neural plasticity and neurogenesis following TBI, using imaging, neurobiological, cognitive, and pharmacotherapeutic approaches. The desired outcome of these approaches is an improved quality of life or an improved ability to function in home and community life.
- j. Projects aimed at providing conclusive data on the existence and tissue-level mechanisms of non-impact, blast-induced mTBI to support the development of effective preventive measures, diagnostic tools, and treatments. Priority will be given to proposals that take an end-to-end approach (i.e., animal injury tests to clinical observations) to developing a validated computational model of non-impact, blast-induced mTBI.

**Psychological Health Gaps (including PTSD):** The priorities for this topic area are interventions across the deployment lifecycle for Service members and their immediate families (spouses, children), particularly those at risk for mental disorders and psychosocial problems. Suicide-focused proposals are not appropriate for this topic area.

**a.** Clinical trials focused on universal and selective interventions (i.e., products, pharmacologic agents (drugs or biologics), cognitive/behavioral interventions, devices, clinical guidance, and/or emerging approaches and technologies) for prevention of combat deployment-related mental health and post-deployment reintegration concerns. These trials may include comparisons of existing evidence-based programs or involve enhancement and validation of novel and existing programs. Randomized controlled trials are encouraged. Priorities include, but are not limited to:

- Addressing stigma and barriers to care (i.e., individual and social),
- Resiliency skill building and reset strategies,
- Misconduct, anger and aggression,
- Substances of misuse and abuse (i.e., prescription, illicit, licit, over-the-counter),
- Stress and coping,
- Individual, family, and social context,
- Improving and sustaining family/co-resident wellness and resiliency, or
- Leader/facilitator fidelity guidelines.

**b.** Clinical trials for the treatment (i.e., products, pharmacologic agents [drugs or biologics], cognitive/behavioral interventions, devices, clinical guidance, and/or

emerging approaches and technologies) of combat-related psychological health problems, including PTSD and depression, and co-morbid psychosocial disturbances among Operation Iraqi Freedom and Operation Enduring Freedom (OIF/OEF) Veterans.

Randomized controlled trials are encouraged. Priorities include:

- Treatment approaches in primary care to reduce physical and emotional morbidity associated with psychological health problems, including PTSD and depression,
- Evidence-based strategies to enhance engagement, retention, compliance, and return-to-duty performance of Service members,
- Delivery formats (group, individual, couples),
- Clinical competencies and treatment fidelity guidelines, or
- Evidence-based clinical guidelines

**c.** Evidence-based screening, brief interventions, and referral for treatment (SBIRT) among Service members that can be employed across levels of care, care providers, and deployment cycle, with particular emphasis placed on post-deployment. Priorities include:

- Reduction of alcohol use as a coping mechanism for pain, psychosocial distress, or other mental health/life problems associated with combat deployment,
- Reduction and prevention of abuse of substances other than alcohol (e.g., nutritional supplements, illicit drugs, prescribed medication, etc.), or
- Modification of existing evidence-based SBIRTs for military relevance.

**d.** Clinical rehabilitative-treatment trials (i.e., products, pharmacologic agents [drugs or biologics], cognitive/behavioral interventions, devices, clinical guidance, and/or emerging approaches and technologies) to treat and manage Service members with combat-related persistent or chronic post-concussive symptomology, or co-occurring physical and mental health symptoms. Randomized controlled trials are encouraged. Priorities include, but are not limited to:

- Sleep disturbances,
- Cognitive dysfunction,
- Mood and anxiety disorders,
- Affective dysregulation, or
- Chronic pain.

**e.** Evidence-based interventions to provide “care for the caregiver” focusing on reducing physical and psychological stress among primary care providers, nurses, mental health providers, and chaplains involved in the care of OIF/OEF Service members.

**f.** The impact of military life on quality of life/health indices among spouses, partners, caregivers, and/or co-resident family members. Priorities include:

- Deployment-related family/co-resident separation,
- Deployment-related family/co-resident injury and/or death,

- Long-term outcome of post-deployment family/co-resident adjustment,
- Family violence and its relationship with other health/life stressors (deployment, alcohol, physical disability, mental health, etc.),
- Caregiver burden and psychosocial support needs,
- Barriers to accessing services to support psychological health, particularly in areas remote to military installations, with special emphasis on gaps in the continuum of care, or
- Child/adolescent reactions to parent separation, combat deployment, and reintegration.

## **5. Trauma Treatment and Rehabilitation, Including Nonsurgical Orthopedic Conditions**

The priorities for this topic area are research proposals with the greatest potential for improvement in activities of daily living and typical warfighter tasks, to include improved treatment, product, or clinical treatment guidelines. Additional preference will be given to the near-term availability of these products.

### **Gaps:**

#### **a. Prosthetics including the:**

- Advancement of powered prosthetic technologies for use in extreme environments,
- Development of a neural interface for powered lower limb prostheses,
- Improvement of foot prosthetics,
- Improvement of knee prosthetics with better knee control,
- Improved haptic feedback technologies and integration with orthopedic prosthetics, or
- Assessment of functional outcomes (i.e., energy efficiency, dynamic stability, gait and other movement mechanics) using advanced prosthetic technologies to optimize prosthetic prescription.

#### **b. Prevention and rehabilitation strategies designed to minimize bone loss and prevent heterotopic ossification following amputation.**

#### **c. Assessment tools that incorporate simultaneous physical and cognitive demands for use in monitoring clinical performance outcomes and return-to-duty status.**

#### **d. Comparison of the effect of known resuscitation adjuncts, drugs, and biologics via a realistic animal model of hemorrhage and tissue injury with the goal of getting a life-saving, non-coagulopathic drug into clinical trials and through FDA certification quickly.**

#### **e. Characterization of oral, maxillofacial, and craniofacial injuries including treatment needs, prosthetic replacements required, treatment costs, and long-term patient morbidity**

from combat injuries; and biocompatible craniofacial implant for use in craniofacial reconstruction due to combat trauma.

- f.** Characterization of physical, mechanical, and aesthetic properties of human skin in the subject population ages 17-45.
- g.** Treatments and techniques to prevent and treat penetrating eye injuries, particularly:
  - For use in the deployed healthcare environment to include use by non-expert providers (medics, physician assistants, nurses, and physicians without advanced training in ophthalmology),
  - For use in more traditional healthcare facilities by eyecare experts to improve outcomes and limit loss of sight,
  - Novel low-vision rehabilitation techniques, including vision prostheses, vision augmentation technologies, etc., or
  - Novel approaches to splint and repair of retina damage.
- h.** Novel rehabilitation techniques, including virtual reality, nonsurgical treatment of extremity injuries (e.g., novel physical therapy techniques), etc., for the mental and physical rehabilitation of other than amputees to facilitate recovery and return to duty.
- i.** Novel approaches for repair and treatment of nerve damage, including nerve regeneration, nerve grafting, etc.
- j.** Surgical and nonsurgical approaches to the treatment of combat-related middle and inner ear trauma, including reconstruction, replacement, or augmentation of hearing structures.

## **6. Wound Infection and Healing**

The priorities for this topic area are the prevention and acceleration of healing from blast-induced wounds and the reduction of wound-related infections. Focus will also be placed on those proposals with technologies having the greatest impact and that can be moved rapidly into U.S. military wartime medical practice. The proposed measures to prevent and control wound infections could also prevent transmission of antimicrobial-resistant bacteria to other Service members and civilians in hospital facilities.

### **Gaps:**

- a.** Improve wound healing and clinical outcomes by evaluating the role of topical nitric oxide and hyperbaric oxygen to disinfect blast wounds.
- b.** New treatment protocols, drugs, biologics, and devices to reduce wound-related infections and accelerate wound healing.
- c.** Approaches to prevention or treatment of bone infections.
- d.** Methods and technologies for prevention of the formation of bacterial biofilms in wounds and colonization of orthopedic devices.

- e. Evaluation of oral and topical nutritional supplements and over-the-counter products (such as zinc, silver, and lysine) to accelerate wound healing and enhance the patient's immune status.
- f. Methodologies that will predict clinical outcomes of blast-induced wound infections. Approaches of interest include methodologies to assess total bacterial load in wounds and identification of critical biomarkers that predict outcomes related to wound infection.

## 7. Wound Infection Vaccines

The priority for this topic area is the development of vaccines to prevent bacterial infections caused by wounds.

### Gaps:

- a. FDA-approved vaccines to prevent sepsis caused by gram-negative bacteria.
- b. FDA-approved vaccines to prevent *Staphylococcus aureus* infection. Priority will be given to those vaccines that also include protection against methicillin-resistant strains.
- c. Others as appropriate.

## D. Award Description

The DRMRP Clinical Trial Award mechanism is being offered for the first time in FY08.

This award supports rapid implementation of clinical trials with the potential to have a significant impact on a disease or condition addressed in one of the FY08 DRMRP topic areas. All proposed clinical trials must be responsive to the healthcare needs of deployed members of the Armed Forces and may address prevention, detection, diagnosis, treatment, and/or quality of life. The clinical trial may be designed to evaluate promising new products, pharmacologic agents (drugs or biologics), cognitive/behavioral interventions, devices, clinical guidance, and/or emerging approaches and technologies. ***Funding from this award mechanism cannot be used for preclinical research studies.*** PIs seeking funding for a preclinical research project should apply to the Advanced Technology/Therapeutic Development Award mechanism.

Each proposal should contain only one clinical trial with a distinct study design. Investigational New Drug (IND) or Investigational Device Exemption (IDE) applications should be submitted or approved prior to proposal submission. The Government reserves the right to withdraw funding if IND/IDE approval is not received within 6 months of the award date. Principal Investigators (PIs) must clearly specify in the Clinical Protocol (main body of the proposal) which type of clinical trial is being proposed: Phase 0, Phase I, Phase II, or Phase III or a combination. For descriptions of each type of clinical trial, please refer to [www.fda.gov/cder/guidance/6384dft.htm](http://www.fda.gov/cder/guidance/6384dft.htm) and <http://www.clinicaltrials.gov>. Refer to the Application Instructions, Appendix 6, for helpful information about distinguishing clinical trials and clinical research. The proposed clinical trial is expected to begin within 12 months of the award date.

The following are important aspects of the Clinical Trial Award submission:

- Demonstrate availability of, and access to, a suitable patient population that will support a meaningful outcome for the study.
- Describe clearly defined and appropriate endpoints for the proposed clinical trial.
- Clearly articulate the statistical analysis plan.
- Discuss the potential impact of the study results for patients with the specified disease/condition.
- Include a named study coordinator(s) who will guide the clinical protocol through Institutional Review Board (IRB), Human Subjects Research Review Board, and other regulatory approval processes, coordinate activities from all sites participating in the trial, and coordinate participant accrual.
- Demonstrate institutional support.

Military relevance is a key feature of this award. Therefore, PIs are strongly encouraged to collaborate and integrate their projects with military and/or Veterans Affairs (VA) research laboratories and programs. Each PI must provide a transition plan (including funding and resources) showing how the product will progress to the next clinical trial phase and/or delivery to the military market after the successful completion of this DRMRP award.

***Proposals must include preliminary and/or published data relevant to the topic area and the proposed project.***

**Partnering PI Option:** As a method to support an accelerated assessment of promising new products, pharmacologic agents (drugs or biologics), cognitive/behavioral interventions, devices, clinical guidance, and/or emerging approaches and technologies in clinical research or clinical trials, the FY08 DRMRP is offering a Partnering PI option for this award mechanism. Development of the research plan should involve a reciprocal flow of ideas and information with equal intellectual input from all partners into the design of a single research project. For example, a proposed project in which a partner merely supplies support services, tissue samples, or access to patients will not meet the intent of this option.

One Initiating and up to two Partnering PIs will each be designated a PI, and a separate award will be made to each PI's institution. Additional collaborators may be included, but will not be designated PIs. Multidisciplinary and multi-institutional projects are allowed.

**Multi-institutional Clinical Trials:** If the proposed clinical trial is multi-institutional, plans for communication and data transfer between the collaborating institutions, as well as how specimens and/or imaging products obtained during the study will be handled, should be included in the appropriate sections of the Clinical Protocol. A separate intellectual and material property plan agreed upon by all participating institutions is also required for multi-institutional clinical trials.

**Encouraged DOD Collaboration and Alignment:** Alignment with current DOD research and collaboration with military researchers and clinicians is encouraged. The following websites

may be useful in identifying information about ongoing DOD areas of research interest within the FY08 DRMRP topic areas:

Defense Technical Information Center  
<http://www.dtic.mil>

Congressionally Directed Medical  
Research Programs  
<http://cdmrp.army.mil>

U.S. Army Medical Research and Materiel  
Command  
<https://mrmc.amedd.army.mil>

Air Force Research Laboratory  
<http://www.wpafb.af.mil/afrl>

Navy and Marine Corps Public Health  
Center  
[www-nmcphc.med.navy.mil/main.htm](http://www-nmcphc.med.navy.mil/main.htm)

U.S. Department of Veterans Affairs,  
Office of Research and Development  
[www.research.va.gov](http://www.research.va.gov)

Office of Naval Research  
<http://www.onr.navy.mil/>

U.S. Army Research Laboratory  
<http://www.arl.army.mil>

U.S. Naval Research Laboratory  
[www.nrl.navy.mil](http://www.nrl.navy.mil)

Defense Advanced Research Projects  
Agency  
<http://www.darpa.mil/>

U.S. Army Medical Research Acquisition  
Activity  
<http://www.usamraa.army.mil>

Naval Health Research Center  
<http://www.nhrc.navy.mil/>

Office of the Under Secretary of Defense  
for Acquisition, Technology and Logistics  
<http://www.acq.osd.mil/>

**Use of Military Populations:** Describe the military population(s) to be used for the proposed study, if applicable. Coordination of access to various military populations is described below.

**1. Active Duty, National Guard, Reserve troops, and/or military patient populations** (not CENTCOM Area of Responsibility): Unless the PI has an already established Service member population, access to Active Duty, National Guard, or Reserve troops must be coordinated through the CDMRP. *PIs who do not have a previously established study population should not contact unit Commanders at this time or during preparation of the proposal submission. If selected for funding, the PI will be provided guidance on how to obtain access to the appropriate population.*

**2. CENTCOM Area of Responsibility military populations:** Access to military populations in these areas is very limited and will be coordinated through the CDMRP as described above.

Research conducted using military populations in Iraq is conducted solely by select elements of the Multi-National Corps-Iraq (MNC-I). PIs who are outside of this system and submit a research proposal designed to recruit patients within MNC-I must be working in collaboration with an in-theater military investigator, undergo an in-theater review, and be approved by the MNC-I Command and the MNC-I designated IRB. Given the constraints of wartime operations, investigators without an ongoing collaboration with an appropriate military investigator should strongly consider alternatives to conducting in-

theater research. DOD-supported human subjects research can only be conducted by institutions (including those in-theater) with approved Federal Assurances of Compliance from the Human Research Protection Office. It is strongly suggested that clinical trials necessitating the use of this population involve civilian and non-deployed military populations as an alternative.

At present there is no ability to conduct research using military populations in Afghanistan.

**3. Department of Veterans Affairs (VA) Medical Centers patient populations:** Access to patient populations from the Department of Veterans Affairs (VA) Medical Centers or use of information from VA data systems must be coordinated by the PI. PIs who submit a research proposal 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.

**Use of Human Subjects and Human Biological Substances:** All DOD-funded research involving human subjects and human biological substances must be reviewed and approved by the USAMRMC Office of Research Protections (ORP), Human Research Protection Office (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 Application Instructions, Instructions and Guidelines for Regulatory Requirements, Appendix 6, for detailed information.

## **E. Eligibility**

PIs must be independent investigators at any academic level (or equivalent). Eligible institutions include for-profit, nonprofit, public, and private organizations, such as universities, colleges, hospitals, laboratories, and companies. Refer to Application Instructions, Appendix 1, for general eligibility information.

## **F. Funding**

No more than \$5M total costs (direct costs and indirect costs) will be awarded in any single year, **to ALL PIs COMBINED** during the lifetime of the award. Proposals may be submitted for up to a 5-year period of performance. Overall total costs (direct costs plus indirect costs) may not exceed \$25M. Programmatic priority will be given to smaller-scale, cost-efficient projects with well-defined endpoints, that address highly relevant and scientifically meritorious program needs. In addition, travel funds must be requested by each PI, whether applying as a single PI or through the Partnering PI option, to attend one Department of Defense military research-related meeting to be determined by the CDMRP during the award performance period.

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

- Salary
- Research supplies
- Equipment
- Clinical costs
- Research-related subject costs
- Travel to scientific/technical meetings
- Travel between collaborating institutions
- Other direct costs as described in Application Instructions for the Research & Related Budget Form Section F – Other Direct Costs

**Partnering PI Option:**

No more than \$5M in total direct and indirect costs will be awarded in any single year **to ALL PIs COMBINED**, during the lifetime of the award, and all research should be completed within 5 years. Programmatic priority will be given to smaller-scale, cost-efficient projects with well-defined endpoints, that address highly relevant and scientifically meritorious program needs. In addition, travel funds must be requested by each PI, whether applying as a single PI or through the Partnering PI option, to attend one Department of Defense military research-related meeting to be determined by the CDMRP during the award performance period.

Within the guidelines provided in the Application Instructions, funds for the Partnering PI option can cover:

- Salary
- Research supplies
- Equipment
- Clinical costs
- Research-related subject costs
- Travel to scientific/technical meetings
- Travel between collaborating institutions
- Other direct costs as described in Application Instructions for the Research & Related Budget Form Section F – Other Direct Costs

*The CDMRP expects to allot approximately \$42M of the \$92M FY08 DRMRP appropriation to fund approximately 2 to 7 Clinical Trial Award proposals, depending on the quality and number of proposals received. Funding of proposals received in response to this Program Announcement/Funding Opportunity is contingent upon the availability of Federal funds for this program. If the DRMRP appropriation is either increased or decreased in order to*

*execute the program, the Government reserves the right to adjust the funding levels and number of awards accordingly.*

## **G. Award Administration**

At the Government's discretion and expense, the PI(s) and Clinical Study Coordinator(s) may be requested to participate in a pre-award meeting.

Quarterly updates regarding study progress will be required.

The transfer of an award to another institution is strongly discouraged. A transfer will not be allowed for any institution that includes a study site/clinical trial at its location. Approval of a transfer request from an institution that does not include a study site at its location will be at the discretion of the Grants Officer. Refer to Application Instructions, Appendix 5, for general award administration information.

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

Proposal submission is a two-step process consisting of (1) pre-application submission and (2) proposal submission. *Pre-application submission is a required first step.*

- **Pre-application Submission Deadline: 5:00 p.m. Eastern time, October 1, 2008**
- **Proposal Submission Deadline: 11:59 p.m. Eastern time, October 15, 2008**
- **Scientific Peer Review: December 2008**
- **Military Relevance Review: December 2008**
- **Gap Alignment Peer Review January 2009**
- **Programmatic Review: February 2009**

Awards will be made approximately 4 to 6 months after receiving the funding notification letter, but no later than September 30, 2009.

## **IV. SUBMISSION PROCESS**

Proposal submission is a two-step process consisting of (1) a pre-application submission through the [CDMRP eReceipt system \(https://cdmrp.org/\)](https://cdmrp.org/) and (2) a proposal submission through [Grants.gov \(http://www.grants.gov/\)](http://www.grants.gov/). The Clinical Trial Award is structured to support the assessment of promising new products, pharmacologic agents (drugs or biologics), cognitive/behavioral interventions, devices, clinical guidance, and/or emerging approaches and technologies by either one PI or up to a maximum of three PIs through the Partnering PI option.

PIs and Organizations identified in the proposal submitted through Grants.gov should be the same as those identified in the pre-application. If there is a change in PI or organization 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.

Submission of the same research project to different award mechanisms within the same program or to other CDMRP programs is discouraged. The Government reserves the right to reject duplicative proposals.

### **Partnering PI Option:**

One partner will be identified as the Initiating PI, who will be responsible for the majority of the administrative tasks associated with proposal submission. The other partners will be referred to as Partnering PIs. *The Initiating PI must begin the pre-application process and submit contact information for each Partnering PI.*

#### **A. Step 1: Pre-Application Components and Submission**

The pre-application consists of the components discussed below. All pre-application components must be submitted electronically through the [CDMRP eReceipt system](#) by **5:00 p.m. Eastern time on the deadline date**. Refer to the Application Instructions for detailed information.

1. Proposal Information
2. Proposal Contacts
3. Collaborators and Conflicts of Interest (COI)
4. Letter of Intent Narrative

### **Partnering PI Option:**

- The Initiating PI must complete the pre-application components listed above.
- The Initiating PI must enter the contact information for up to two Partnering PIs in the “Partnering PI” section.
- Each Partnering PI will be contacted via email by the CDMRP eReceipt system and provided the information necessary to begin proposal submission through Grants.gov. Please note that each Partnering PI must follow the link in this email and register with CDMRP eReceipt in order to associate his or her grant application package with that of the Initiating PI.

#### **B. Step 2: Proposal Components and Submission**

**Proposal submission will not be accepted unless a pre-application was submitted by the pre-application deadline.** Proposals must be submitted electronically by the Authorized Organizational Representative through Grants.gov ([www.grants.gov](http://www.grants.gov)). No paper copies will be accepted.

Each proposal submission must include the completed Grants.gov application package of forms and attachments identified in Grants.gov for the US Army Medical Research Acquisition Activity (USAMRAA) Program Announcement. In addition to the specific instructions below, please refer to the Application Instructions for detailed requirements of each component.

## **Proposal Submission Components:**

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

#### **2. Attachments Form**

- Attachment 1: Clinical Protocol: No-page limit.

The Clinical Protocol is the main body of the proposal and must address the required components described in Application Instructions (Appendix 8).

- Attachment 2: Supporting Documentation
  - References Cited
  - Acronyms and Symbol Definitions
  - Facilities & Other Resources
  - Description of Existing Equipment
  - Publications and/or Patent Abstracts (Five-document limit)
  - Letters of Institutional Support (Three-page limit per letter)

If the PI is a practicing clinician, the institution must clearly demonstrate a commitment to the clinician's research.

- Intellectual and Material Property Plan (If applicable)
- Letters of Collaboration (If applicable; no page limit)
- Attachment 3: Technical and Public Abstracts: (One-page limit per abstract)
- Attachment 4: Statement of Work (SOW) (Three-page limit)
- Attachment 5: Impact Statement (One-page limit)

State explicitly how the proposed clinical trial will have an impact on the prevention, detection, diagnosis, or treatment of the specified disease/condition, if successful. Explain the potential clinical applications, benefits, and risks.

- Attachment 6: Military Relevance Statement (Two-page limit)

Demonstrate how the proposed study is responsive to the healthcare needs and quality of life of members of the Armed Forces who are deployed, including family members. If a military population(s) will be used in the proposed project, describe the population(s), the appropriateness of the population for the proposed research, and the feasibility of using the population. Explain how the proposed research study is aligned with the military research gap(s) appropriate for the topic area address. Describe how the study design will replicate field conditions for the selected topic area. Discuss how the new product, pharmacologic agent (drug or biologic), cognitive/behavioral intervention, device, clinical guidance, and/or emerging approach and technology is suitable for operation in a field environment.

- Attachment 7: Transition Plan (One-page limit)

Provide information on the methods and strategies proposed to move the product, pharmacologic agent, behavioral intervention, device, clinical guidance, and/or emerging approach and technology to the next clinical trial phase and/or military field deployment after the successful completion of the DRMRP award. The plan should include details of potential funding sources, collaborations, other resources that will be used to provide this continuity of development, a potential timeline for field deployment, the involvement of appropriate intellectual property, licensing and/or business professionals, and plans for the further development and successful transition of the product or intervention.

- Attachment 8: Request for Information (If applicable; four-page limit)
- Attachment 9: Federal Agency Financial Plan (If applicable)

**3. Research & Related Senior/Key Person Profile (Expanded Form)**

- PI Biographical Sketch (Four-page limit)
- PI Current/Pending Support
- Key Personnel Biographical Sketches (Four-page limit each)
- Key Personnel Current/Pending Support

**4. Research & Related Budget Form**

- Budget Justification

**5. Research & Related Project/Performance Site Location(s) Form**

**6. R&R Subaward Budget Attachment(s) Form (If applicable)**

**Proposal Submission Components for the Partnering PI Option:**

The CDMRP eReceipt system assigns a unique and separate log number to each PI (Initiating and Partnering) that must be used when submitting the Grants.gov application package. To obtain his or her unique log number, before submitting the proposal application to Grants.gov, each Partnering PI must associate him- or herself with the Initiating PIs proposal by accepting the link sent by the CDMRP eReceipt system.

**Proposal Components for the Initiating PI:**

The Initiating PI must submit components 1-6 from the numbered list above.

**Proposal Components for the Partnering PI:**

The proposal submission process for each Partnering PI uses an abbreviated application package of forms and attachments from Grants.gov.

Each Partnering PI package includes only the following from the numbered list above:

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

- Attachment 4: SOW: The Initiating and Partnering PIs must create a joint SOW
- Attachment 9: Federal Agency Financial Plan (If applicable)

#### **4. Research & Related Budget Form**

- Budget Justification

#### **5. Research & Related Project/Performance Site Location(s) Form**

#### **6. R&R Subaward Budget Attachment(s) Form (If applicable)**

### **V. INFORMATION FOR PROPOSAL REVIEW**

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

Proposals are evaluated by scientists, clinicians, and consumer advocates using a two-tier review process. For purposes of this solicitation, the first tier is conducted in two phases. Phase one includes a scientific peer review of proposals against established criteria for determining scientific merit and a military relevance review of proposals against established criteria for determining the military relevance. Phase two involves a gap alignment review of proposals against established criteria for assuring optimal alignment of funding priority recommendations with the deployment-related research gaps listed above. The second tier is a programmatic review that compares submissions to each other and recommends proposals for funding based on scientific merit, military relevance, and overall goals of the program. Additional information about the two-tier review process used by the CDMRP may be found at <http://cdmrp.army.mil/fundingprocess.htm>.

The scientific peer, military relevance, gap alignment, and programmatic review processes are conducted confidentially and anonymously to maintain the integrity of the merit-based selection process. Each tier review requires panelists to sign a nondisclosure statement attesting that proposal and evaluation information will not be disclosed outside the panel. Violations of the nondisclosure statement can result in the dissolving of a panel(s) and other corrective actions. Institutional personnel and PIs are prohibited from contacting persons involved in the proposal review process to gain protected evaluation information or to influence the evaluation process. Likewise persons involved in the proposal review process are prohibited from communicating the program priorities, other than what is listed in this program announcement, to PIs and/or also are prohibited from being involved in the proposal development (including the pre-application process, concept design, budget, and supporting documentation). Violations of these prohibitions will result in the administrative withdrawal of the institution's proposal. Violations by panelists or PIs that compromise the confidentiality or anonymity of the scientific peer, military relevance, gap alignment peer, and programmatic review processes may also result in suspension or debarment of their employing institutions 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).

The Government reserves the right to review all proposals based on one or more of the required attachments or supporting documentation (e.g., Impact Statement, Transition Statement, etc.).

## B. Review Criteria

### 1. First Tier of Review

#### a. Phase One

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

- **Study Design**
  - How the scientific rationale and preliminary data, including critical review and analysis of the literature, and laboratory and preclinical evidence support the proposed clinical trial and its feasibility.
  - How the aims, hypotheses or objectives, experimental design, methods, data collection procedures, and analyses are developed.
  - How the logistical aspects of the proposed clinical trial (e.g., communication plan, data transfer and management, and standardization of procedures) meet the needs of the proposed clinical trial.
  - How the recruitment, informed consent, and screening processes for volunteers will be conducted to meet the needs of the proposed clinical trial.
  - How the inclusion, exclusion, and randomization criteria meet the needs of the proposed clinical trial.
- **Impact**
  - How the results of the proposed clinical trial will affect the magnitude and scope of potential clinical applications (e.g., prevention, detection, diagnosis, treatment, management, and/or quality of life).
  - How the proposed clinical trial addresses one of the FY08 DRMRP topic areas.
- **Intervention, Drug, or Device**
  - How the intervention, drug, or device to be tested is appropriate for the proposed clinical trial.
  - How the availability and purity of the substance to be used in the clinical trial is appropriate for the proposed clinical trial.
  - Whether there is documentation that an IND/IDE application has been submitted.
- **Feasibility**
  - The evidence that the proposed clinical trial is feasible.
  - How the plan for addressing unanticipated delays (e.g., slow accrual) is likely to lead to success in completing the proposed clinical trial within the performance period.

- How the proposal addresses the availability of volunteers for the clinical trial, the prospect of their participation, and the consideration of likelihood of volunteer attrition.
- The evidence that the PI will have access to any military populations required for the clinical study, if applicable.
- **Statistical Plan (as appropriate to phase of study)**
  - How the statistical plan, including sample size projections and power analysis, is adequate for the study and all proposed correlative studies.
  - How the data analysis plan is consistent with the study objectives.
- **Personnel**
  - How the clinical study team's background and expertise are appropriate to accomplish the proposed work (i.e., statistical expertise, expertise in the disease, and clinical studies).
  - How the levels of effort of the clinical team are appropriate for successful conduct of the proposed trial.
- **Environment**
  - How the evidence indicates an appropriate scientific environment, clinical setting, and the accessibility of institutional resources to support the clinical trial at each participating center (including collaborative arrangements).
  - The evidence for appropriate institutional commitment from each participating institution.
  - How the intellectual and material property plan that is agreed upon by each participating institution is appropriate for the proposed clinical trial.
- **Ethics and/or Regulatory Issues**
  - How the ethical considerations, information privacy, and assessment of risks and benefits of participation in the clinical trial will be addressed.
  - Evidence that an appropriate plan for dealing with adverse events, which should include named agencies or offices to be notified in this event, and point of contact information has been prepared.
  - How plans for data disposition during and after the clinical trial are appropriate for the proposed clinical trial.
  - How the procedures for protocol modifications during the course of the clinical trial have been addressed.
  - How the plans for data and safety monitoring are appropriate for the proposed clinical trial.

- **Transition Plan**
  - How the transition plan describes field deployment of the product, pharmacologic agent, cognitive/ behavioral intervention, device, clinical guidance, and/or emerging approach and technology.
  - Whether there is evidence that the PI has or can secure additional funding, or whether the PI has clearly described potential options to secure the additional funding needed to bring the product, pharmacologic agent, cognitive/behavioral intervention, device, clinical guidance, and/or emerging approach and technology to a clinical trial phase and/or field deployment.
  - How the proposed resources will be used to provide continuity of development/deployment and support the likelihood of success.
  - How appropriate intellectual property, licensing, and/or business professionals have been included or engaged.
  - How well the plans are described for further development of the product or intervention, and how well the plan completes development of the product or intervention to ensure a successful transition.
- **Budget**
  - How the budget is appropriate for the proposed research.

## **b. Phase Two**

**Military Relevance Review:** All proposals will be evaluated according to the following criteria, which are listed in order of decreasing importance:

- **Alignment with Gaps**
  - How the proposed study aligns with identified gap(s) in the topic area addressed.
- **Military Benefit**
  - How the proposed study may benefit the identified military population, if successful.
- **Field Deployability**
  - How the transition plan addresses the deployability of the product, pharmacologic agent, cognitive/behavioral intervention, device, clinical guidance, and/or emerging approach and technology.
  - Whether the product, pharmacologic agent, cognitive/behavioral intervention, device, clinical guidance, and/or emerging approach and technology may be suitable for operation in the field environment.
  - How well the transition plan addresses a timeline for field deployment of the product, pharmacologic agent, cognitive/behavioral intervention, device, clinical guidance, and/or emerging approach and technology.

- **Study Population**

- How well the research design will replicate field conditions for the selected topic area.
- How the plan to study military populations, if applicable, is appropriate and feasible.

**Note:** The results of scientific peer review and the military relevance review are of equal importance.

**c. Phase Three**

**Gap Alignment Review:** All proposals will be evaluated according to the following criteria, which are of equal importance:

Criteria used by the Joint Program Alignment Peer Review Panel (JPAPRP) to assess the degree to which each proposed research project will fill target gap(s).

- Ratings and evaluations by military relevance reviewers and scientific peer reviewers, to include scientific risk.
- How well the proposed study will close the identified gap(s) in the topic area addressed, if successful.
- How much the proposed project will accelerate fulfilling deployment-related military requirements, if successful.
- Whether the proposed research is a duplication of effort funded by DOD or other agencies.

**2. Second Tier of Review**

**Programmatic Review:** Criteria used by the Joint Senior Leadership Integration Panel (JSLIP) members are of equal importance. They include:

- Responsiveness to FY08 DRMRP topic areas and gaps,
- Ratings and evaluations of the scientific peer and military relevance reviewers,
- Analyses by the JPAPRP of the scientific peer review and the military relevance review of each proposal as it relates to the deployment-related military medical needs,
- Programmatic relevance,
- Program portfolio balance, and
- Adherence to the intent of the award mechanism.

Scientifically sound proposals that best fulfill the above criteria and most effectively address the unique focus and goals of the program will be identified by the JSLIP members and recommended for funding to the Commanding General, USAMRMC.

## VI. COMPLIANCE GUIDELINES

Compliance guidelines have been designed to ensure the presentation of all pre-applications and proposals in an organized and easy-to-follow manner. Scientific peer and military relevance reviewers expect to see a consistent, prescribed format. Failure to adhere to formatting guidelines makes documents difficult to read, may be perceived as an attempt to gain an unfair competitive advantage, and may result in pre-application or proposal rejection. **Pre-applications or proposals missing required components as specified in the Program Announcement/Funding Opportunity may be administratively rejected.**

*If the research is not relevant to specified DRMRP topic areas, the Government reserves the right to administratively withdraw the proposal at any stage from proposal receipt through proposal review.*

The following will result in administrative rejection of the entire proposal:

- Clinical protocol is missing.
- Military Relevance Statement is missing.
- Margins are less than specified in the formatting guidelines.
- Print area exceeds that specified in the formatting guidelines.
- Spacing is less than specified in the formatting guidelines.
- Budget is missing.
- FY08 DRMRP scientific peer and/or military relevance reviewer(s) have not declared a Conflict of Interest (COI) but are found to have involvement with the applicant prior to or during the review.
- FY08 JSLIP member(s) are named in the proposal.
- FY08 JSLIP member(s) are found to be involved in any capacity in the pre-application and proposal processes including, but not limited to, concept design, proposal development, budget preparation, and the development of any supporting document.
- FY08 JSLIP member(s) communicated program priorities prior to the release of this program announcement.

A list of the FY08 JSLIP members may be found at <http://cdmrp.army.mil>.

For any other sections of the pre-application or proposal with a defined page limit, pages exceeding the specified limit will be removed and not forwarded for scientific peer review or military relevance review.

Material submitted after the submission deadline, unless specifically requested by the Government, will not be forwarded for scientific peer review or military relevance review.

Proposals that appear to involve any allegation of research misconduct will be administratively withheld from further consideration pending institutional investigation. The institution will be

requested to perform an investigation and provide those findings to the Grants Officer for a determination of the final disposition of the application.