

Program Announcement

Department of Defense Congressionally Directed Medical Research Programs

Multiple Sclerosis Research Program

Metric Development and Validation Award

Funding Opportunity Number: W81XWH-09-MSRP-MDVA

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I. FUNDING OPPORTUNITY DESCRIPTION

A. Program Objectives

The Multiple Sclerosis Research Program (MSRP) was established in fiscal year 2009 (FY09) to promote innovative research focused on multiple sclerosis (MS). The FY09 appropriation is \$5 million (M).

The MSRP challenges the scientific community to design innovative and integrated research that will enhance knowledge relevant to understanding the etiology and pathogenesis of, and to quantifying and treating, MS. The vision of the MSRP is to prevent the occurrence, reverse or slow the progression and disability, and lessen the impact of MS.

B. FY09 MSRP Focus Areas

The FY09 MSRP specifically encourages applications that address critical needs of the MS community through understanding the genetic, biological, and environmental factors that contribute to any of the following:

- **Etiology:** The search for the cause or trigger of MS
- **Population subgroups:** Elucidate the causes of differences in incidence and severity that are attributable to race and gender, which could be relevant to an understanding of the disease process
- **Primary progressive MS:** The events that lead to primary progressive disability, and identifying ways to stop and reverse disease progression
- **Relapse-remitting MS:** Define key processes that are involved in the vulnerability of tissue to attack, and the success of repair during this phase of disease
- **Secondary progressive MS:** The events that cause relapsing-remitting MS to develop into secondary progressive MS, and identifying ways to stop and reverse disease progression

C. Award Description

The MSRP Metric Development and Validation Award is being offered for the first time in FY09.

The Metric Development and Validation Award is designed to develop and/or validate readily accessible, cost-effective, analytical methods that may be utilized to quantify the disease, monitor disease progress, and/or evaluate the efficacy of disease therapies. Particular emphasis is laid on the development of measurement processes with regard to reproducibility and accuracy and/or the validation of existing and novel measures. Resulting metrics should have broad clinical and/or research applications, as well as the potential for high impact on the MS clinical and/or research community.

Clinical trials are not allowed under this mechanism. Refer to the Application Instructions and General Information, Appendix 6, for additional information on clinical trials.

The overall goal of this award is to accelerate advances in MS research. The following are significant features of this award mechanism:

1. Impact: High-impact measurements, if successful, will significantly improve the sensitivity and/or specificity of current methods, or provide methods specific to novel targets, and thereby will enable improved experiments toward the MSRP vision of preventing the occurrence, reversing or slowing the progression and disability, and lessening the impact of MS.

Proposals should address a central critical problem or question in MS research. Examples include, but are not limited to, the development of:

- Metrics for prognosis and/or progression monitoring within individual patients
- Disease activity or severity metrics for use in longitudinal studies of MS
- Novel methods for integrating and validating existing data sets
- Metrics targeting specific subgroups within the MS population (e.g., ethnicity)
- Quick and inexpensive function-specific measures of physical or cognitive abilities before and after a quantifiable work load

2. Clinical/Research Metrics: It is critical that each proposal address at least one area of MS research in which current measures are inadequate for clinical and/or research needs. Examples of metrics that if systematically validated would be of interest for MS detection and quantification include, but are not limited to:

- **Biometrics:** Biomarkers of central nervous system (CNS) autoimmunity, demyelination, axonal degeneration, synaptic regeneration, microbial exposure, nutritional status, gene expression, epigenetics, genetic susceptibility, etc.
- **Cognitive Disability Metrics:** Memory attention, visual perception, information processing speed, executive function, etc.
- **Imaging Metrics:** Magnetic resonance imaging, optical coherence tomography, positron emission tomography, etc.
- **Multidimensional Metrics:** Algorithms using combinations of multiple metrics
- **Physical Disability Metrics:** Ease of movement, strength, speed, coordination, dexterity, use of assistive devices, etc.
- **Quality of Life Metrics:** Pain, fatigue, sleep disorder, depression, anger, sexual dysfunction, co-morbidities, etc.

3. Preliminary Data: Submission of preliminary data relevant to MS and the proposed project is encouraged but not required. If preliminary data is provided, it must have been generated from the laboratory of the Principal Investigator (PI) or collaborators listed on this award application. Although groundbreaking research often involves a degree of risk due to unforeseen difficulties or results, proposals should be based on a sound scientific rationale

that is established through logical reasoning and/or critical review and analysis of the literature.

D. Eligibility

Investigators at or above the level of Assistant Professor (or equivalent) are eligible to submit applications.

Refer to the Application Instructions and General Information, Appendix 1, for general eligibility information.

E. Funding

- The maximum period of performance for this award mechanism is 1 year.
- The maximum allowable funding for the entire period of performance is **\$100,000** in direct costs.
- The applicant may request the entire maximum direct cost amount for a project that may be less than the maximum 1-year period of performance.
- Regardless of the period of performance proposed, the budget may not exceed the maximum direct cost. In addition to the direct costs, indirect costs may be proposed in accordance with the institution's negotiated rate agreement.

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

- Salary
- Research supplies
- Clinical research costs (Clinical trials will not be supported)
- Travel to scientific/technical meetings
- Travel between collaborating institutions

The CDMRP expects to allot \$1.4M of the \$5M FY09 MSRP appropriation to fund approximately nine Metric Development and Validation Award applications, depending on the quality and number of applications received. Funding of applications received in response to this Program Announcement/Funding Opportunity is contingent on the availability of Federal funds for this program.

F. Award Administration

Changes in PI and institution are discouraged. Such requests will be evaluated on a case-by-case basis and at the discretion of the USAMRMC Contracting Office. Refer to the Application Instructions and General Instructions, Appendix 5, for general award administration information.

II. TIMELINE FOR SUBMISSION AND REVIEW

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

- **Pre-Application Submission Deadline: August 13, 2009, 5:00 p.m. Eastern time**
- **Invitation to Submit an Application: October 1, 2009**
- **Application Submission Deadline: November 24, 2009, 11:59 p.m. Eastern time**
- **Scientific Peer Review: February 2010**
- **Programmatic Review: April 2010**

Awards will be made approximately 4 to 6 months after receiving the funding notification letter, but no later than September 30, 2010.

III. SUBMISSION PROCESS

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) an application submission through [Grants.gov \(http://www.grants.gov/\)](http://www.grants.gov/). Applications will be invited based on pre-application screening.

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 applications.

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](https://cdmrp.org/) by *5:00 p.m. Eastern time on the pre-application deadline.* In addition to the award-specific information provided below, refer to the Application Instructions and General Information for detailed information.

- **Proposal Information:** Because the invitation to submit an application is based on the contents of the pre-application, investigators should not change the title, research objectives, or FY09 MSRP focus area(s) after the pre-application is submitted.
- **Proposal Contacts**
- **Collaborators and Conflicts of Interest (COI)**
- **Preproposal Narrative:** The Preproposal Narrative has a *one-page limit* inclusive of figures, tables, graphs, photographs, diagrams, chemical structures, pictures, pictorials, cartoons, and other information needed to judge the preproposal. The Preproposal Narrative should address the following:

- Explain the potential impact of the proposed MS research and how it will, if successful, significantly improve the sensitivity and/or specificity of current methods, or provide methods specific to novel targets, and thereby will enable improved experiments toward the MSRP vision of preventing the occurrence, reversing or slowing the progression and disability, and lessening the impact of MS.
- Describe the central critical problem or question in MS research, the metric to be developed and/or validated, and why it will move the field toward preventing the occurrence, reversing or slowing the progression and disability, and lessening the impact of MS.
- Clearly articulate the rationale for the project by presenting the ideas and reasoning behind the proposed research.
- Concisely describe the project's specific aims.
- State which of the FY09 MSRP focus areas this application addresses, if applicable.
- **Pre-Application Supporting Documentation:** The items to be included as supporting documentation for the pre-application are:
 - References Cited (one-page limit).
 - Biographical Sketches: Include biographical sketches for the PI and other key collaborators (four-page limit per Biographical Sketch).

Pre-Application Screening: Pre-applications will be screened by the FY09 MSRP Integration Panel (IP), which is composed of scientists, clinicians, and consumer advocates, based on the following criteria:

- **Adherence to the intent of the award mechanism**
- **Research Idea:** How well the proposed project addresses a central critical problem or question in MS research.
- **Responsiveness to FY09 MSRP Focus Areas:** Whether the proposed research addresses one or more of the FY09 MSRP focus areas.
- **Impact**
 - How well the proposed research will, if successful, significantly improve the sensitivity and/or specificity of current methods, or provide methods specific to novel targets.
 - How well the proposed research will, if successful, enable improved experiments toward the MSRP vision of preventing the occurrence, reversing or slowing the progression and disability, and lessening the impact of MS.

B. Step 2 – Application Components and Submission

Applications will not be accepted unless the PI has received a letter of invitation. Applications must be submitted electronically by the Authorized Organizational Representative through

Grants.gov (www.grants.gov). The PIs and Organizations identified in the application submitted through Grants.gov should be the same as those identified in the pre-application, however, if there is a change in PI or Organization after the submission of the pre-application, the PI must contact the CDMRP eReceipt help desk at help@cdmrp.org or 301-682-5507.

Because the invitation to submit an application is based on the contents of the pre-application, PIs should not change the title, research objectives, or focus area(s).

Each application submission must include the completed Grants.gov application package of forms and attachments identified in [http://www.grants.gov/](http://www.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 and General Information for detailed requirements of each component.

The package includes:

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

2. Attachments Form

- Attachment 1: Project Narrative (four-page limit)

Describe the proposed research in detail using the following outline.

Background: Present the ideas and reasoning behind the proposed research; include relevant literature citations. Describe previous experience most pertinent to this application. Discuss the qualifications of the PI that will enable successful completion the proposed work. The inclusion of preliminary data relevant to MS and the proposed project is encouraged but not required. However, if preliminary data is provided, the data must have been generated from the laboratory of the PI.

Hypothesis and Objective: State the proposed hypothesis and the objective to be reached.

Specific Aims: Concisely explain the project's specific aims to be funded by this application.

Research Strategy: Describe the experimental design, methods, and analyses including appropriate controls and statistical plan in sufficient detail for analysis. Address potential problem areas and present alternative methods and approaches. If human subjects or human biological samples will be used, include a plan for the recruitment of subjects or the acquisition of samples. ***This award may not be used to conduct clinical trials.***

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
- Letters of Collaboration (if applicable)
- Intellectual and Material Property Plan (if applicable)
- Attachment 3: Technical Abstract (one-page limit)
- Attachment 4: Public Abstract (one-page limit)
- Attachment 5: Statement of Work (three-page limit)
- Attachment 6: Detailed Budget and Justification
- Attachment 7: Impact Statement (one-page limit)

State explicitly how the proposed research will, if successful, significantly improve the sensitivity and/or specificity of current methods, or provide methods specific to novel targets. Describe how the results of the proposed project, if successful, will enable improved experiments toward the MSRP vision of preventing the occurrence, reversing or slowing the progression and disability, and lessening the impact of MS.

- Attachment 8: Federal Agency Financial Plan (if applicable)
- Attachments 9-15: Subaward Detailed Budget and Justification (if applicable)

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

- PI Biographical Sketch
- PI Current/Pending Support
- Key Personnel Biographical Sketches
- Key Personnel Current/Pending Support

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

IV. INFORMATION FOR APPLICATION REVIEW

A. Application Review and Selection Overview

All applications are evaluated by scientists, clinicians, and consumer advocates using a two-tier review process. The first tier is a scientific peer review of applications against established criteria for determining scientific merit. The second tier is a programmatic review that compares submissions to each other and recommends proposals for funding based on scientific merit 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>

The peer review and programmatic review processes are conducted confidentially to maintain the integrity of the merit-based selection process. Each tier of review requires panelists to sign a non-disclosure statement attesting that application and evaluation information will not be disclosed outside the panel. Violations of the non-disclosure statement can result in the dissolving of a panel(s) and other correcting actions. Correspondingly, institutional personnel and PIs are prohibited from contacting persons involved in the application review process to gain protected evaluation information or to influence the evaluation process. Violations of these prohibitions will result in the administrative withdrawal of the institution's application. Violations by panelists or PIs that compromise the confidentiality of the peer review 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 applications based on one or more of the required attachments or supporting documentation (e.g., Impact Statement).

B. Review Criteria

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

- **Impact**

- How well the proposed research will, if successful, significantly improve the sensitivity and/or specificity of current methods, or provide methods with specificity to novel targets.
- How well the proposed research will, if successful, enable improved experiments toward the MSRP vision of preventing the occurrence, reversing or slowing the progression and disability, and lessening the impact of MS.

- **Research Strategy and Feasibility**

- How well the scientific rationale supports the project and its feasibility as demonstrated by a critical review and analysis of the literature, MS-relevant preliminary data, and/or logical reasoning.
- How well the objectives, aims, experimental design, methods, and analyses are developed and integrated into the project.

- How well the PIs acknowledge potential problems and address alternative approaches.
- Whether the proposal includes an appropriate statistical plan with power analysis, if applicable.

The following aspects will not be individually scored, but may impact the global score.

- **Personnel**

- Whether the PI meets the eligibility requirements.
- The degree to which the PI possesses the appropriate research experience.
- The degree to which the levels of effort are appropriate for successful conduct of the proposed work.

- **Environment**, the degree to which the:

- Scientific environment is appropriate for the proposed research.
- Research requirements are supported by the availability of and accessibility to facilities and resources.
- Quality and extent of institutional support are appropriate.

- **Budget**

- Whether the budget is appropriate for the proposed research and within the limitations of the award mechanism.

- **Application Presentation**

- How the writing and components of the application influenced the review.

2. Programmatic Review: Criteria used by programmatic reviewers to make funding recommendations that maintain the program's broad portfolio include:

- Adherence to the intent of the award mechanism
- Program portfolio balance
- Programmatic relevance
- Ratings and evaluations of the peer reviewers
- Relative impact
- Responsiveness to FY09 MSRP focus areas

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 Integration Panel members and recommended for funding to the Commanding General, USAMRMC.

V. ADMINISTRATIVE ACTIONS

After CDMRP receives the applications from Grants.gov, they will be administratively reviewed for inclusion of appropriate components in accordance with this program announcement. If components are missing or not appropriate, the following administrative actions may occur:

A. Rejection

The following will result in administrative rejection of the pre-application:

- Preproposal Narrative exceeds page limit.
- Preproposal Narrative is missing.
- Page size is larger than 8.5 inches x 11.0 inches (approximately 21.59 cm x 27.94 cm).

The following will result in administrative rejection of the application:

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

B. Modifications

- Pages exceeding the specified limits will be removed for all documents other than the preproposal narrative or project narrative.
- Documents not requested will be removed.
- **NEW FOR FY09:** Following the application deadline, you may be contacted by CDMRP via email with a request to provide certain missing supporting documents (excluding those listed directly above in Section A, Rejection). The missing documents must be provided by 5:00 p.m. Eastern time on the second full business day following the date and time the email was sent. Otherwise, the application will be reviewed without the missing documents.

C. Withdrawal

The following may result in administrative withdrawal of the application:

- The proposed research project is or contains a clinical trial.
- FY09 IP member(s) is found to be involved in the pre-application or application processes including, but not limited to, concept design, application development, budget preparation, and the development of any supporting document. A list of the FY09 IP members may be found at <http://cdmrp.army.mil/09msrppanel>

- Submission of the same research project to different award mechanisms within the same program or to other CDMRP programs.
- The application does not conform to this funding opportunity description to an extent that precludes appropriate scientific peer and programmatic review.
- Direct costs as shown on the detailed budget form exceed maximum allowed by award mechanism.
- Inclusion of URLs with the exception of links to published references.

D. Withhold

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

IV. CONTACT INFORMATION

1. Program announcement, application 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 the 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

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

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 application 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 through Friday, 7:00 a.m. to 9:00 p.m. Eastern time

Email: 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.