Program Announcement

Department of Defense Congressionally Directed Medical Research Programs

Amyotrophic Lateral Sclerosis Research Program

Therapeutic Idea Award

Funding Opportunity Number: W81XWH-11-ALSRP-TIA
Catalog of Federal Domestic Assistance Number: 12.420

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-application Submission Deadline:** 5:00 p.m. Eastern time (ET)**,** May 25, 2011
- **Invitation to Submit an Application:** June 2011
- **Application Submission Deadline:** 11:59 p.m. ET, August 24, 2011
- **Scientific Peer Review:** November 2011
- **Programmatic Review:** January 2012

New for fiscal year 2011 (FY11): The Grants.gov Research & Related Budget form is a mandatory component of all Grants.gov application packages.

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I. FUNDING OPPORTUNITY DESCRIPTION

A. Program Description

The Amyotrophic Lateral Sclerosis Research Program (ALSRP) was established in 2007 to provide support for research of exceptional scientific merit aimed at preclinical assessment of therapeutics for amyotrophic lateral sclerosis (ALS). Appropriations for the ALSRP from FY07 through FY10 totaled $17.5 million (M). The FY11 appropriation is $8M.

The goal of the ALSRP is to promote the introduction of improved therapies for ALS by encouraging ALS investigators to undertake preclinical studies of novel and existing agents.

B. Award Information

The ALSRP Therapeutic Idea Award mechanism was first offered in FY10. In FY10, 39 Therapeutic Idea Award applications were received, and 6 were recommended for funding**.**

The Therapeutic Idea Award is designed to promote new ideas that are still in the early stages of development with the potential to yield highly impactful data and new avenues of investigation for novel therapeutics for ALS treatment. This mechanism supports conceptually innovative, high-risk/high-reward research that could ultimately lead to critical discoveries or major advancement in ALS therapeutics. Research projects should include a well-formulated, testable hypothesis based on strong scientific rationale.

Presentation of preliminary data is not consistent with the intent of the Therapeutic Idea Award mechanism. While the inclusion of preliminary data is not prohibited, the strength of the application should not rely on preliminary data.

Innovation and Impact are the most important aspects of the Therapeutic Idea Award.

Innovation: Research deemed innovative may introduce a new paradigm, challenge current paradigms, introduce novel concepts or agents, or exhibit other uniquely creative qualities that may lead to potential therapeutics for ALS.

The following list, ***although not all-inclusive***, provides examples of research that is NOT innovative and will not be considered for funding under this mechanism:

- Investigating the next logical step or continuation of a previous research project.
- Proposing work that is an incremental advancement of published data.
- Proposing a project whose scope is primarily small molecule or genomic/proteomic screening.
- Exploring a previously tested hypothesis in a different cell line or in a new population.
- Using a published series of in vitro assays to further characterize a model system.
- Incorporating known biomarkers into in vitro or clinical models of ALS.

Impact: Research that has high potential to significantly impact development of therapeutics for ALS.

Use of human subjects and human anatomical substances: Because these awards are designed for basic preclinical research, projects involving human subjects or human anatomical substances will not be supported unless they are exempt under Title 32, Code of Federal Regulations, Part 219, Section 101(b) (32 CFR 219.101[b]). ***Studies that do not qualify for exempt status during review at any level will be administratively withdrawn and will not be funded.*** For studies using only commercially available or de-identified specimens, a Claim of Exemption Form will be requested if the application is recommended for funding. Additional information regarding exempt status may be found on the US Army Medical Research and Materiel Command (USAMRMC) Human Research Protection Office website (https://mrmc.amedd.army.mil/rodorphrpo.asp) and the General Application Instructions, Appendix 5, for this award mechanism. Clinical trials are not permitted under this Program Announcement/Funding Opportunity.

C. Eligibility Information

- Investigators at all academic levels (or equivalent) are eligible to submit applications.
- Cost sharing/matching is not an eligibility requirement.
- Refer to the General Application Instructions, Appendix 1, for general eligibility information.

D. Funding

- The maximum period of performance is **2** years.
- The maximum allowable direct cost for the entire period of performance is $**400,000** plus indirect costs**.**
- All direct and indirect costs of any subaward (subgrant or subcontract) must be included in the total direct costs of the primary award.
- The applicant may request the entire maximum funding amount for a project that may have a period of performance less than the maximum 2 years.
- Regardless of the period of performance proposed, the applicant may not exceed the maximum allowable direct costs. Indirect costs shall be proposed in accordance with the organization's negotiated rate agreement.

Refer to the General Application Instructions, Section II.C., for budget regulations and instructions for the Research & Related Budget form. In addition, for this award mechanism, direct costs:

Must be requested for:

- Travel for the PI to attend one Department of Defense (DOD) military research-related meeting to be determined by the Office of the Congressionally Directed Medical Research Programs (CDMRP) during the award performance period.

May be requested for (not all-inclusive):

- Salary
- Research supplies
- Equipment
- Clinical research costs (research must be exempt under 32 CFR 219.101[b])
- Travel between collaborating organizations
- Travel costs of up to $1,800 per year to attend scientific/technical meetings

The Office of the Congressionally Directed Medical Research Programs (CDMRP) expects to allot approximately $2.56M of the $8M FY11 ALSRP appropriation to fund approximately four Therapeutic Idea 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 upon the availability of Federal funds for this program.

II. SUBMISSION INFORMATION

Submission is a multi-step process requiring both (1) pre-application submission through the CDMRP eReceipt System (https://cdmrp.org/) and (2) application submission through Grants.gov (http://www.grants.gov/).

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

A. Where to Obtain the Application Package

To obtain the complete application package, including all required forms, perform a Grants.gov (http://www.grants.gov/) basic search using the Funding Opportunity Number: W81XWH-11-ALSRP-TIA.

B. Pre-Application Submission Content and Form

All pre-application components must be submitted by the PI through the CDMRP eReceipt System (https://cdmrp.org/). Because the invitation to submit an application is based on the contents of the pre-application, investigators should not change the title or research objectives after the pre-application is submitted.

PIs and organizations identified in the application should be the same as those identified in the pre-application. If a change in PI or organization is necessary after submission of the pre-application, the PI must contact the CDMRP Help Desk at help@cdmrp.org or 301-682-5507.

The pre-application consists of the following components, which are organized in the CDMRP eReceipt System by separate tabs (refer to the General Application Instructions, Section II.B., for additional information on pre-application submission):

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

  Preproposal Narrative (two-page limit): The Preproposal Narrative page limit applies to text and any figures, tables, graphs, photographs, diagrams, chemical structures, pictures, pictorials, and cartoons. The Preproposal Narrative should include the following:

  - **Research Idea:** State the ideas and reasoning on which the proposed work is based.
  - **Research Strategy:** Concisely state the project's objectives and specific aims.
  - **Innovation:** Describe how the project may introduce a new paradigm, challenge current paradigms, introduce novel concepts or agents, or exhibit other uniquely creative qualities that may lead to potential therapeutics for ALS.
  - **Impact:** State explicitly how the proposed work will have an impact on the development of therapeutics for ALS.

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

  - References Cited (one-page limit): List relevant references using a standard reference format that includes the full citation (i.e., author(s), year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate). The inclusion of Internet URLs to references is encouraged.

- **Submit Pre-application – Tab 5**
- **Other Documents Tab**

  No additional documents are required**.**

Pre-Application Screening

- **Pre-Application Screening Criteria**

  To determine the technical merits of the pre-application and the relevance to the mission of the Department of Defense (DOD) and CDMRP, pre-applications will be screened based on the following criteria:

  - **Research Idea:** How the proposed research will advance the development of therapeutics for ALS.
  - **Research Strategy:** How the specific aims are feasible and support the research idea.

- **Innovation:** How the project may introduce a new paradigm, challenge current paradigms, introduce novel concepts or agents, or exhibit other uniquely creative qualities that may lead to potential therapeutics for ALS.
- **Impact:** How the proposed work will have an impact on the development of therapeutics for ALS.

- **Notification of Pre-Application Screening Results**

  Following the pre-application screening, PIs will be notified as to whether or not they are invited to submit an application; however, they will not receive feedback (e.g., a critique of strengths and weaknesses) on their pre-application.
  Pre-application notification dates are indicated on the title page of this Program Announcement/Funding Opportunity.

C. Application Submission Content and Form

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

Each application submission must include the completed application package of forms and attachments provided in Grants.gov for this Program Announcement/Funding Opportunity. The application package is submitted by the Authorized Organizational Representative (AOR) through the Grants.gov portal (http://www.grants.gov/).

Grants.gov application package components: For the Therapeutic Idea Award, the Grants.gov application package includes the following components (refer to the General Application Instructions, Section II.C., for additional information on application submission):

1. **SF 424 (R&R) Application for Federal Assistance Form:** Refer to the General Application Instructions, Section II.C., for detailed information.
2. **Attachments Form**
   - **Attachment 1: Project Narrative (eight-page limit):** Upload as "ProjectNarrative.pdf."

     Throughout the Project Narrative, describe how the proposed research is innovative and the potential impact it may have on the development of ALS therapeutics. Presentation of preliminary data is not required. However, PIs must demonstrate logical reasoning and a sound scientific rationale established through a critical review and analysis of the literature for the application to be competitive.

     Describe the proposed project using the following outline:

     - **Background:** Present the ideas and reasoning behind the proposed work. Cite relevant literature.
     - **Hypothesis or Objective:** State the hypothesis to be tested or the objective(s) to be reached.
     - **Specific Aims:** Concisely explain the project's specific aims and their relevance to the study objective(s).

- **Research Strategy:** Describe the experimental design, methods, and analyses including appropriate controls in sufficient detail for analysis. Describe the statistical plan, if appropriate, for the research proposed. Address potential problem areas and present alternative methods and approaches.

- **Attachment 2: Supporting Documentation.** Start each document on a new page. Combine and upload as a single file named "Support.pdf." If documents are scanned to pdf, the lowest resolution (100 to 150 dpi) should be used. ***Each component has no page limit unless otherwise noted.***
  - References Cited: List the references cited (including URLs if available) in the project narrative using a standard reference format that includes the full citation (i.e., author[s], year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).
  - List of Abbreviations, Acronyms, and Symbols: Provide a list of abbreviations, acronyms, and symbols.
  - Facilities, Existing Equipment, and Other Resources: Describe the facilities and equipment available for performance of the proposed project and any additional facilities or equipment proposed for acquisition at no cost to the US Army Medical Research and Materiel Command (USAMRMC). Indicate if Government-owned facilities or equipment are proposed for use. Reference should be made to the original or present contract under which the facilities or equipment items are now accountable. There is no form for this information.
  - Publications and/or Patent Abstracts (five-document limit): Include relevant publication URLs and/or patent abstracts. If publications are not publicly available, then they must be included. Extra items will not be reviewed.
  - Letters of Organizational Support (two-page limit per letter): Provide a letter (or letters if applicable), signed by the Department Chair or appropriate organization official, reflecting the laboratory space, equipment, and other resources available for the project.
  - Letters of Collaboration (if applicable) (two-page limit per letter): Provide a signed letter from each collaborating individual or organization that will demonstrate that the PI has the support or resources necessary for the proposed work.
  - Intellectual and Material Property Plan (if applicable): Provide a plan for resolving intellectual and material property issues among participating organizations.

- **Attachment 3: Technical Abstract (one-page limit):** Upload as "TechAbs.pdf."

  The technical abstract is used by all reviewers; however, programmatic reviewers do not have access to the full application and rely on the technical abstract for appropriate description of the project's key aspects.

  Use the outline below.

  - Background: Present the ideas and reasoning behind the proposed work.

- Objective/Hypothesis: State the objectives/hypothesis to be tested. Provide evidence or rationale that supports the objectives/hypothesis.
- Specific Aims: State the specific aims of the study.
- Study Design: Briefly describe the study design including appropriate controls.
- Impact: Summarize briefly how the proposed project will impact the development of therapeutics for ALS.

- **Attachment 4: Public Abstract (one-page limit):** Upload as "PublicAbs.pdf."

  Do not duplicate the technical abstract. The public abstract is used by consumer peer reviewers along with other components of the application package. Describe the scientific objective and rationale for the proposed project in a manner that will be readily understood by readers without scientific or medical backgrounds.

  Describe the ultimate applicability of the research.

  - What types of patients will it help and how will it help them?
  - What are the potential clinical applications, benefits, and risks?
  - What is the projected time it may take to achieve a patient-related outcome?
  - If the research is too basic for clinical applicability, describe the interim outcomes.
  - What are the likely contributions of this study in advancing the development of therapeutics for ALS?

- **Attachment 5: Statement of Work (SOW) (three-page limit):** Upload as "SOW.pdf." Refer to the General Application Instructions, Section II.C., for detailed information.

- **Attachment 6: Impact Statement (one-page limit):** Upload as "Impact.pdf."

  Describe the ultimate vision for how the proposed work, if successful, will impact the development of therapeutics for ALS.

- **Attachment 7: Innovation Statement (one-page limit):** Upload as "Innovation.pdf." Summarize how the proposed study is innovative. Investigating the next logical step or incremental advancement on published data is not considered innovative. The following examples of ways in which proposed studies may be innovative, ***although not all-inclusive***, are intended to help PIs frame the innovative features of their applications:

  - Study concept: Investigation of a novel idea and/or research question.
  - Research method or technology: Use of novel research methods or new technologies, including technology development, to address a research question.
  - Clinical interventions: Use of a novel method or technology for preventing, detecting, diagnosing, or treatment.

- Existing methods or technologies: Application or adaptation of existing methods or technologies for novel research or clinical purposes, or for research or clinical purposes that differ fundamentally from those originally intended.

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

   - PI Biographical Sketch (four-page limit): Upload as "Biosketch_LastName.pdf."
   - PI Current/Pending Support (no page limit): Upload as "Support_LastName.pdf."
   - Key Personnel Biographical Sketches (four-page limit each): Upload as "Biosketch_LastName.pdf."
   - Key Personnel Current/Pending Support (no page limit): Upload as "Support_LastName.pdf."

4. **Research & Related Budget:** Refer to the General Application Instructions, Section II.C., for detailed information.

   - Budget Justification (no page limit): Upload as "BudgetJustification.pdf."

5. **Project/Performance Site Location(s) Form:** Refer to the General Application Instructions, Section II.C., for detailed information.

6. **R & R Subaward Budget Attachment(s) Form (if applicable):** Refer to the General Application Instructions, Section II.C., for detailed information.

D. Submission Dates and Times

All submission dates and times are indicated on the title page of this Program Announcement/Funding Opportunity. Pre-application and application submissions are required. Failure to meet any one of the deadlines shall result in application rejection.

E. Other Submission Requirements

Refer to the General Application Instructions, Appendix 2, for detailed formatting guidelines.

All applications must be submitted through Grants.gov. Organizations are required to provide a Data Universal Number System (DUNS) number and register with the Central Contractor Registry (CCR) to submit applications through the Grants.gov portal. Refer to the General Application Instructions, Appendix 3, for information on Grants.gov requirements.

III. APPLICATION REVIEW INFORMATION

A. Application Review and Selection Process

All applications are evaluated by scientists, clinicians, and consumer advocates using a two-tier review process. The first tier is a peer review of applications against established criteria for determining technical merit. The second tier is a programmatic review that compares applications to each other and makes recommendations for funding to the Commanding General, US Army Medical Research and Materiel Command (USAMRMC), based on technical merit, the relevance to the mission of the Department of Defense (DOD) and CDMRP, and the specific intent of the award mechanism. The highest scoring applications from the first tier of review are not automatically recommended for funding. Additional information about the two-tier review process used by the CDMRP can be found at http://cdmrp.army.mil/about/fundingprocess.

All CDMRP review processes are conducted confidentially to maintain the integrity of the merit-based selection process. Each level of review requires panelists to sign a non-disclosure statement attesting that application and evaluation information will not be disclosed outside the panel. Violations of the non-disclosure statement can result in the dissolving of a panel(s) and other corrective actions. Organizational personnel and PIs are prohibited from contacting persons involved in the review process to gain protected evaluation information or to influence the evaluation process. Violations of these prohibitions will result in the administrative withdrawal of the organization's application. Violations by panelists or PIs that compromise the confidentiality of the review process may also result in suspension or debarment of their employing organizations from Federal awards. Furthermore, it is a crime for Federal officials to disclose confidential information of one party to another third party (Title 18 United States Code 1905).

B. Application Review Criteria

1. **Peer Review:** To determine technical merit, all applications will be evaluated according to the following scored criteria, which are listed in decreasing order of importance:

   - **Innovation**
     - How the research proposes new paradigms or challenges existing paradigms in one or more of the following ways: Concept or question, research methods or technologies, or adaptations of existing methods or technologies that will lead to new therapies for ALS.
     - How the application describes a new research idea and not the next logical step or continuation of a previous research project.
     - How the proposed research represents more than an incremental advance upon published data.
     - How the proposed research introduces a novel concept or agent for treatment of ALS.
   - **Impact**

- How the research, if successful, might make a significant contribution toward the development of therapeutics for ALS.
- How the potential gain warrants the perceived risk.

- **Research Strategy and Feasibility**
  - How the scientific rationale supports the project and its feasibility, as demonstrated by a critical review and analysis of the literature and/or by logical reasoning.
  - How well the hypotheses or objectives, aims, experimental design, methods, and analyses are developed and integrated into the project.
  - How well the PI identifies potential problems and addresses alternative approaches.

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

- **Personnel**
  - How the PI, the research team, and any collaborators' background and expertise are appropriate to accomplish the proposed work.
  - How the levels of effort are appropriate for successful conduct of the proposed work.
- **Environment**
  - How the scientific environment is appropriate for the proposed research.
  - How the research requirements are supported by the availability of and accessibility to facilities and resources.
  - How the quality and extent of organizational support are appropriate for the proposed research.
- **Budget**
  - Whether the budget is appropriate for the proposed research and within the limitations of this Program Announcement/Funding Opportunity.
- **Application Presentation**
  - To what extent the writing, clarity, and presentation of the application components influenced the review.

2. **Programmatic Review:** To determine the application's relevance to the mission of the DOD and CDMRP, as well as to make funding recommendations, the following equally considered criteria are used by programmatic reviewers:
   - Ratings and evaluations of the peer reviewers
   - Programmatic relevance
   - Relative innovation and impact on ALS

- Program portfolio composition
- Adherence to the intent of the award mechanism

C. Recipient Qualification

Refer to the General Application Instructions, Appendix 1, for additional information on organization and Government agency requirements.

D. Application Review Dates

All application review dates and times are indicated on the title page of this Program Announcement/Funding Opportunity.

E. Notification of Application Review Results

Each PI and organization will receive notification of the funding recommendation. PIs will receive a scientific peer review summary statement on the strengths and weaknesses of the application.

IV. ADMINISTRATIVE ACTIONS

After receipt of pre-applications from CDMRP eReceipt or applications from Grants.gov, the following administrative actions may occur:

A. Rejection

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

- Preproposal Narrative exceeds page limit.
- Preproposal Narrative is missing.

The following will result in administrative rejection of the application:

- Project Narrative exceeds page limit.
- Project Narrative is missing.
- Budget is missing.
- Submission of an application for which a letter of invitation was not received.

B. Modification

- Pages exceeding the specified limits will be removed prior to review for all documents other than the Project Narrative and Preproposal Narrative.
- Documents not requested will be removed.
- Following the application deadline, you may be contacted by CDMRP via email with a request to provide certain missing supporting documents (excluding those listed in Section IV.A., Rejection). The missing documents must be provided by 5:00 p.m. ET

on the second full business day following the date the email was sent. Otherwise, the application will be reviewed as submitted.

C. Withdrawal

The following may result in administrative withdrawal of the pre-application or application:

- FY11 ALSRP Integration Panel (IP) member is found to be involved in the preapplication 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 FY11 ALSRP IP members may be found at http://cdmrp.army.mil/alsrp/panels/panels11.
- Submission of the same research project to different funding opportunities within the same program and fiscal year.
- The application does not conform to this Program Announcement/Funding Opportunity description to an extent that precludes appropriate review.
- Direct costs as shown on the Research and Related Budget form exceed the maximum allowed by this Program Announcement/Funding Opportunity.
- Inclusion of URLs with the exception of links to published references.
- Page size is larger than 8.5 inches x 11.0 inches (approximately 21.59 cm x 27.94 cm).
- The application includes non-exempt clinical research.

D. Withhold

Applications that appear to involve research misconduct will be administratively withheld from further consideration pending institutional investigation. The institution will be required to provide the findings of the investigation to the US Army Medical Research Acquisition Activity (USAMRAA) Contracting/Grants Officer for a determination of the final disposition of the application.

V. AWARD ADMINISTRATION INFORMATION

A. Award Notice

Awards will be made no later than September 30, 2012. Refer to the General Application Instructions, Appendix 4, for additional award administration information.

B. Administrative and National Policy Requirements

Refer to the General Application Instructions, Appendix 4, Section C, for general information regarding administrative and national policy requirements.

C. Reporting

Refer to the General Application Instructions, Appendix 4, Section D, for general information on reporting requirements. Annual technical progress reports will be required.

D. Award Transfers

Refer to the General Application Instructions, Appendix 4, Section E, for general information on organization or PI changes.

VI. AGENCY CONTACTS

A. CDMRP Help Desk

Questions related to Program Announcement/Funding Opportunity content or submission requirements and questions related to the submission of the pre-application through the CDMRP eReceipt System should be directed to the CDMRP Help Desk, which is available Monday through Friday from 8:00 a.m. to 5:00 p.m. ET. Response times may vary depending upon the volume of inquiries.

Phone: 1-301-682-5507

Email: help@cdmrp.org

B. Grants.gov Contact Center

Questions related to application submission through the Grants.gov portal should be directed to the Grants.gov Contact Center, which is available 24 hours a day, 7 days a week (closed on U.S. Federal holidays). Note that the CDMRP Help Desk is unable to provide technical assistance with Grants.gov submission.

Phone: 1-800-518-4726

Email: support@grants.gov

Sign up on Grants.gov for "send me change notification emails" by following the link on the Synopsis page for the Program Announcement/Funding Opportunity. If the application package is updated or changed, the original version of the application package may not be accepted by Grants.gov.

VII. APPLICATION SUBMISSION CHECKLIST

Grants.gov Application Components	Action	Completed
SF-424 (R&R) Application for Federal Assistance Form	Complete form as instructed.	
Attachments Form	Upload Project Narrative (ProjectNarrative.pdf) as Attachment 1.	
	Upload Supporting Documentation (Support.pdf) as Attachment 2.	
	Upload Technical Abstract (TechAbs.pdf) as Attachment 3.	
	Upload Public Abstract (PublicAbs.pdf) as Attachment 4.	
	Upload Statement of Work (SOW.pdf) as Attachment 5.	
	Upload Impact Statement (Impact.pdf) as Attachment 6.	
	Upload Innovation Statement (Innovation.pdf) as Attachment 7.	
Research & Related Senior/Key Person Profile (Expanded)	Attach PI Biographical Sketch (Biosketch_LastName.pdf) to the appropriate field.	
	Attach PI Current & Pending Support (Support_LastName.pdf) to the appropriate field.	
	Attach Biographical Sketch (Biosketch_LastName.pdf) for each senior/key person to the appropriate field.	
	Attach Current & Pending Support (Support_LastName.pdf) for each senior/key person to the appropriate field.	
Research & Related Budget	Complete form as instructed. Attach Budget Justification (BudgetJustification.pdf) to the appropriate field.	
Project/Performance Site Location(s) Form	Complete form as instructed.	
R & R Subaward Budget Attachment(s) Form	Complete form as instructed.	