Program Announcement

Department of Defense Congressionally Directed Medical Research Programs

Defense Health Program

Autism Research Program

Clinical Trial Award

Funding Opportunity Number: W81XWH-11-ARP-CTA

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), July 20, 2011
- **Invitation to Submit an Application:** September 21, 2011
- **Application Submission Deadline:** 11:59 p.m. ET, November 30, 2011
- **Scientific Peer Review:** January 2012
- **Programmatic Review:** March 2012

New for fiscal year 2011 (FY11): The formal protocol for the proposed clinical trial should not be submitted as the Clinical Trial Award application. A formal protocol will be requested if the application is recommended for funding.

New for 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 Assistant Secretary of Defense for Health Affairs, Defense Health Program is soliciting applications for the Autism Research Program (ARP). The ARP was established in 2007 to provide support for innovative, high-impact research focused on autism spectrum disorders (ASD). Appropriations for the ARP from FY07 through FY10 totaled $29.9 million (M). The FY11 appropriation is $6.4M.

The ARP's vision is to improve the lives of individuals with ASD *now* by promoting innovative research that advances the understanding of ASD and leads to improved outcomes.

B. FY11 ARP Areas of Interest

The FY11 ARP Areas of Interest are specific for the Clinical Trial Award mechanism *only*. The FY11 ARP encourages applications that address the critical needs of the ASD community in the following areas:

- Pharmacological interventions
- Complementary and alternative medicine
- Behavioral interventions specifically for school-age children, adolescents, or adults
- Treatment of co-morbid conditions in school-age children, adolescents, or adults

C. Award Information

The Clinical Trial Award mechanism was first offered in FY09. Since then, 25 Clinical Trial Award applications have been received, and 3 have been recommended for funding.

The ARP Clinical Trial Award supports research with the potential to have a major impact on the treatment and/or management of ASD. ***Funding from this award mechanism must support a clinical trial and cannot be used for preclinical research studies.*** A clinical trial is defined as a prospective accrual of human subjects where an intervention (e.g., device, drug, biologic, surgical procedure, rehabilitative modality, behavioral intervention or other) is tested on a human subject for a measurable outcome with respect to exploratory information, safety, effectiveness, and/or efficacy. This outcome represents a direct effect on the human subject of that intervention or interaction. Principal Investigators (PIs) seeking funding for a preclinical research project should consider one of the other award mechanisms/funding opportunities being offered. The term "human subjects" is used in this Program Announcement/Funding Opportunity to refer to individuals who will be recruited for, or who will participate in, the proposed clinical trial.

If the study proposed involves the use of a drug that has not been approved by the Food and Drug Administration (FDA) for its investigational use, then an Investigational New Drug (IND) application to the FDA may be required and must be submitted to the FDA prior to the grant submission. If the proposed study involves an Investigational Device that has not been approved or cleared by FDA for its investigational clinical use, the study may be required to comply with the FDA Investigational Device Exemption (IDE) regulations. If applicable, the IDE application

must be submitted prior to the grant submission. The Government reserves the right to withdraw funding if the documented status of the IND or IDE has not been obtained within 6 months of the award date.

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

- The proposed clinical trial is expected to begin no later than 12 months after the award date.
- Include preliminary data that are relevant to the proposed research project.
- The proposed research project should be based on sound scientific rationale that is established through logical reasoning and critical review and analysis of the literature.
- Demonstrate availability of and access to a suitable human subject population that will support a meaningful outcome for the study. Discuss how accrual goals will be achieved and how standards of care may impact the study population.
- Describe appropriate and clearly defined endpoints for the proposed clinical trial.
- Clearly articulate the statistical analysis plan. Include a power analysis reflecting sample size projections that will clearly answer the objectives of the study.
- Discuss the potential impact of the study results for individuals affected by ASD.
- Include a study coordinator(s) who will guide the clinical trial protocol through the local Institutional Review Board (IRB) of record and other regulatory approval processes, coordinate activities from all sites participating in the trial, and coordinate human subject accrual.
- Demonstrate institutional support.

Use of Human Subjects and Human Anatomical Substances: All Department of Defense (DOD)-funded research involving new and ongoing research with human subjects and human anatomical substances must be reviewed and approved by the US Army Medical Research and Materiel Command (USAMRMC) Office of Research Protections (ORP), Human Research Protection Office (HRPO), in addition to the local IRB of record. Local IRB approval at the time of submission is NOT required. The HRPO is mandated to comply with specific laws and directives governing all research involving human subjects that is supported by the DOD. These laws and directives are rigorous and detailed, and will require information in addition to that supplied to the local IRB. Allow a minimum of 4 months for regulatory review and approval processes. Information may be found at https://cdmrp.org/Program_Announcements_and_Forms/. Additionally, refer to the General Application Instructions, Appendix 5, for more information.

New for FY11 – Investigators are required to submit their data to the National Database for Autism Research (NDAR), which is a secure bioinformatics platform for data sharing for ASD. It is supported by the National Institutes of Health. For more information, please consult the NDAR at http://ndar.nih.gov/ndarpublicweb.

D. Eligibility Information

- PIs must be at or above the level of Assistant Professor (or equivalent).

- Cost sharing/matching is not an eligibility requirement.
- Refer to the General Application Instructions, Appendix 1, for general eligibility information.

E. Funding

- The maximum period of performance is **4** years.
- The maximum allowable direct costs for the entire period of performance is **$1M** plus indirect costs.
- The applicant may request the entire maximum funding amount for a project that may have a period of performance less than the maximum **4** years.
- All direct and indirect costs of any subaward (subgrant or subcontract) must be included in the total direct costs of the primary award.
- 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:

May be requested for (not all-inclusive):

- Salary
- Research-related subject costs
- Clinical research costs
- Research supplies
- Equipment
- 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 $1.6M of the $6.4M FY11 ARP appropriation to fund approximately one Clinical Trial Award application, 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-ARP-CTA.

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. A change in PI or organization is only permitted for extenuating circumstances and will be decided on a case-by-case basis. 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:** Concisely state the project's objective and specific aims. Briefly describe the proposed project and the population(s) that will be enrolled in the study. Present the reasoning behind the proposed clinical trial, to include relevant literature

citations. Identify the population and the recruitment goals. State how this project meets the intent of the Clinical Trial Award mechanism and the intent of the program.

- **Intervention:** Describe the intervention to be tested and how it is applicable to the study population.
- **Clinical Impact:** Describe the potential impact of this study on the outcomes of individuals with ASD.
- **Personnel:** State how the background, clinical trial experience, and ASD expertise of the clinical team are appropriate to accomplish the proposed trial (e.g., statistical expertise, expertise in ASD research and clinical studies).

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.
- Key Personnel Biographical Sketches (four-page limit per individual)

- **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 DOD and CDMRP, pre-applications will be screened by the ARP Integration Panel (IP) based on the following criteria:

  - **Research Idea:** How the proposed project addresses the intent of the award mechanism and the program. How the rationale and specific aims support the project's objective. How the study population appropriately represents the ASD community and the project's objective.
  - **Intervention:** Whether the intervention is applicable to the study population.
  - **Clinical Impact**: What impact these studies will have on the outcomes of individuals with ASD.
  - **Personnel:** How the personnel's background and expertise are appropriate to accomplish the proposed research (e.g., statistical expertise, expertise in ASD and clinical studies).

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

  Following the pre-application screening, PIs will be notified of 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 Clinical Trial 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**

   New for FY11: The Project Narrative is NOT the formal clinical trial protocol (as in previous years). Instead, all essential elements of the proposed clinical trial necessary for scientific review must be included as directed in Attachment 1 (the Project Narrative) and Attachments 6, 7, and 8 described below. Failure to submit these attachments as part of the application package will result in rejection of the entire application.

   - **Attachment 1: Project Narrative (20-page limit):** Upload as "ProjectNarrative.pdf."

     The Project Narrative page limit applies to text and any figures, tables, graphs, photographs, diagrams, chemical structures, pictures, pictorials, and cartoons.

     Describe the proposed project in detail using the outline below.

     - **Background:** Describe in detail the rationale for the study and include a literature review, preliminary studies, and/or preclinical data that provide the basis for the proposed clinical trial. The background section should clearly support the choice of study variables and should explain the basis for the study questions and/or study hypotheses. This section should establish the relevance of the study and explain the applicability of the proposed findings.

       If the proposed clinical trial was initiated using other funding prior to this application, explain the history and background of the clinical trial and declare

the source of prior funding. Specifically identify the portions of the study that will be supported with funds from this award.

- **Objectives/Specific Aims/Hypotheses:** Provide a description of the purpose and objectives of the study with detailed specific aims and/or study questions/ hypotheses.
- **Study Design:** Describe the type of study to be performed (e.g., prospective, randomized, controlled) and outline the proposed methodology in sufficient detail to show a clear course of action.
  - Identify the intervention to be tested and describe the projected outcomes.
  - Define the study variables and describe how they will be measured. Include a description of appropriate controls and the endpoints to be tested.
  - Describe the methods that will be used to recruit a sample of human subjects from the accessible population (e.g., convenience, simple random, stratified random).
  - Describe the human subject-to-group assignment process (e.g., randomization, block randomization, stratified randomization, age-matched controls, alternating group, or other procedures), if applicable. Explain the specific actions to accomplish the group assignment (e.g., computer assignment, use of table of random numbers).
  - Describe the reliability and validity of psychometric measures, if applicable.
- **Statistical Plan and Data Analysis:** Include a complete power analysis to demonstrate that the sample size is appropriate to meet the objectives of the study. Specify the approximate number of human subjects that will be enrolled. If multiple study sites are involved, state the approximate number to be enrolled at each site. If a subpopulation of a recruited sample population will be used for analysis, complete a statistical analysis to ensure appropriate power can be achieved within the subpopulation study (e.g., defined subpopulation from a named group such as "baby-sibs"). Describe the data analysis plan in a manner that is consistent with the study objectives.

- **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 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: 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): 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.
- Data and Research Resources Sharing Plan: Describe how data and resources generated during the performance of the project will be shared with the research community. Refer to the General Application Instructions, Appendix 4, for more information about the CDMRP expectations for making data and research resources publically available.
- National Database for Autism Research Submission Plan (two-page limit per plan): Provide a plan for submission of human subject data to NDAR, including information on security of personal information (Health Insurance Portability and Accountability Act – [HIPAA]) and data sharing for the bioinformatics platform. Please consult NDAR at http://ndar.nih.gov/ndarpublicweb.

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

  The technical abstract should be written using the outline below.

  - Background: Present the ideas and reasoning behind the proposed work.
  - Objective/Hypothesis: State the objective/hypothesis to be tested. Provide evidence or rationale that supports the objective/hypothesis.
  - Specific Aims: State the specific aims of the study.
  - Study Design: Briefly describe the study design including appropriate controls.
  - Clinical Impact: Briefly describe how the proposed project will have an impact on ASD research and patient care.

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

  The public abstract should be written using the outline below.

  - Clearly describe, in a manner readily understood by lay persons, the rationale and objective for the proposed work.

- Do not duplicate the technical abstract.

o 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?
- Briefly describe how the proposed project will have an impact on ASD research and patient care.

- **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: Human Subject Recruitment and Safety Procedures (no page limit):** Upload as "HumSubProc.pdf." The Human Subject Recruitment and Safety Procedures attachment should include the components listed below.

a. Study Population: Describe the target population (to whom the study findings will be generalized) and the nature, approximate number, and pertinent demographic characteristics of the accessible population at the study site (population from which the sample will be recruited). Demonstrate that the research team has access to the proposed study population. Furthermore, discuss past efforts in recruiting human subjects from the target population for previous clinical trials (if applicable). Address any potential barriers to accrual and plans for addressing unanticipated delays. Include justification of any age, race, ethnicity, or sex limitations provided.

b. Inclusion/Exclusion Criteria: List the inclusion and exclusion criteria for the proposed clinical trial. Inclusion/exclusion criteria should take into consideration the specific risk profile of the studies to be conducted and the standard of care for that patient population. Provide detailed justification for exclusions.

Inclusion of Women and Minorities in Study. Consistent with the Belmont Report and congressional legislation, special attention is given to inclusion of women and/or minorities in studies funded or supported by the USAMRMC. This policy is intended to promote equity both in assuming the burdens and in receiving the benefits of human subjects research. Include an appropriate justification if women and/or minorities will be excluded from the clinical trial.

c. Description of the Recruitment Process: Explain methods for identification of potential human subjects (e.g., medical record review, obtaining sampling lists, health care provider identification).

- Describe the recruitment process in detail. Address who will identify potential human subjects, who will recruit them, and what methods will be used to recruit them.
- Include a detailed description of and justification for the compensation plan if the human subjects will be compensated for participation in the study.

- Describe the recruitment and advertisement materials. The recruitment materials should not be coercive or offer undue inducements, and should accurately reflect the study.

d. Description of the Informed Consent Process: Specifically describe the plan for obtaining informed consent from human subjects.

- Identify who is responsible for explaining the study, answering questions, and obtaining informed consent.
- Include information regarding the timing and location of the consent process.
- Address issues relevant to the mental capacity of the potential human subject (e.g., altered capacity due to administration of any mind-altering substances such as tranquilizers, conscious sedation or anesthesia, brain injury, stress/life situations, or human subject age), if applicable.
- Address how privacy and time for decision making will be provided and whether or not the potential human subject will be allowed to discuss the study with anyone before making a decision.
- Consider the need for obtaining ongoing consent or for re-assessing capacity over the course of a long-term study and describe any relevant procedures to assure continued consent.
- Describe the plan for the consent of the individual's Legally Authorized Representative (LAR) to be obtained prior to the human subject's participation in the study. State law defines who may act as the LAR. The local IRB of record should be consulted for guidance regarding who can serve as LAR for research at the study site. Note: The PI must describe a clear intent to benefit for human subjects who cannot give their own consent to participate in the proposed clinical trial to be in compliance with Title 10 United States Code Section 980 (10 USC 980) (http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=browse_usc&docid=Cite:+10USC980). If applicable, please refer to the General Application Instructions, Appendix 5, for more information.
- Provide a draft in English of the proposed Informed Consent Form. A plan for ensuring that human subjects' questions will be addressed during the consent process and throughout the trial should be included.
- ***Assent.*** If minors or other populations that cannot provide informed consent are included in the proposed clinical trial, a plan to obtain assent (agreement) from those with capacity to provide it, or a justification for a waiver of assent should be provided. PIs should consult with their local IRB to identify the conditions necessary for obtaining assent.

e. Screening Procedures: List and describe any evaluations (e.g., laboratory procedures, history, testing instruments, or physical examination) that are required to determine eligibility/suitability for study participation and the diagnostic criteria for entry. Please note that some screening procedures may

require a separate consent or a two-stage consent process. Informed consent must be obtained prior to initiation of any procedures for the purpose of determining eligibility.

f. Risks/Benefits Assessment:

- **Foreseeable risks:** Clearly identify study risks. Study risks include any risks that the human subject is subjected to as a result of participation in the clinical trial. Consider psychological, legal, social, and economic risks as well as physical risks. If the risks are unknown, this should be stated. If applicable, any potential risk to the study personnel should be identified.
- **Risk management and emergency response:**
  - Describe all safety measures to minimize and/or eliminate risks to human subjects and study personnel, or to manage unpreventable risks. Include safeguards and planned responses such as dose reduction or stopping criteria based on toxicity grading scales or other predetermined alert values.
  - Discuss the overall plan for provision of emergency care or treatment for an adverse event for study-related injuries, to include who will be responsible for the cost of such care.
  - Address any special precautions to be taken by the human subjects before, during, and after the study (e.g., medication washout periods, dietary restrictions, hydration, fasting, pregnancy prevention).
  - Describe any special care (e.g., wound dressing assistance, transportation due to side effects of study intervention impairing ability to drive) or equipment (e.g., thermometers, telemedicine equipment) needed for human subjects enrolled in the study.
- **Potential benefits:** Describe known and potential benefits of the study to the human subject, a specific community, or society.

- **Attachment 7: Intervention (no page limit):** Upload as "Intervention.pdf." The Intervention attachment should include the components listed below.

a. Description of the Intervention: As applicable, the description of the intervention should include the following components: source, dose, schedule, administration route, washout period, duration of the intervention, and concomitant medications allowed. Description of devices should include detailed operational instructions, and any potential risks to users, and intended benefits. Describe any biobehavioral interventions including the modality of the intervention, duration of the intervention, and measurement of the outcomes such as the identification of assessment instruments. Other types of interventions should be fully described.

b. Study Procedures: Describe the interaction with the human subject to include the study intervention that he/she will experience. Provide sufficient detail in chronological order for a person uninvolved in the study to understand what the

human subject will experience. Provide a schedule (e.g., flowchart or diagram) of study evaluations and follow-up procedures.

- **Attachment 8: Data Management (no page limit):** Upload as "Data_Manage.pdf." The Data Management attachment should include the components listed below.

  a. Data Management: Describe all methods used for data collection to include the following:

  - **Identifiers:** Describe the unique identifiers or specific code system to be used to identify human subjects, if applicable.
  - **Confidentiality:**
    - Explain measures taken to protect the privacy of study human subjects and maintain confidentiality of study data. Strategies to protect the privacy and confidentiality of study records, particularly those containing identifying information, should be addressed.
    - Address who will have access to study records, data, and specimens, including an acknowledgment that representatives of USAMRMC are eligible to review study records.
    - Address what measures will be taken to protect the privacy of the study human subjects if video or audio taping will be used during the intervention study.
    - Address requirements for reporting sensitive information to state or local authorities.
  - **Disposition of data:** Describe where data (both electronic and hard copy) will be stored, who will keep the data, how the data will be stored, and the length of time data will be stored.
  - **Sharing study results:** In cases where the human subject could possibly benefit medically or otherwise from the information, explain whether or not the results of screening and/or study participation will be shared with human subjects or their primary care provider, to include results from any screening or diagnostic tests performed as part of the study.

  b. Laboratory Evaluations:

  - **Specimens to be collected, schedule, and amount.** All specimens that will be collected for study purposes must be clearly stated. The collection schedule and amount of material collected must also be clearly described.
  - **Evaluations to be made.** Describe all evaluations that will be made for study purposes. Explain how the results of laboratory evaluations will be used to meet the objectives of the study (or to monitor safety of human subjects).
  - **Storage.** Describe specimen storage, to include location of storage, how long specimens will be stored, any special conditions required, labeling, and

disposition. Outline the plan to store specimens for future use to include considerations for informed consent and providing human subjects with an opportunity to decline participation in the study.

- **Labs performing evaluations and special precautions.** Identify the laboratory performing each evaluation, as well as any special precautions that should be taken in handling the samples. Special precautions that should be taken by the human subject before, during, or after the laboratory procedure should be clearly defined. If transport of samples is required, describe provisions for ensuring proper storage during transport.

- **Attachment 9: Study Personnel and Organization (no page limit):** Upload as "Personnel.pdf." The Study Personnel and Organization attachment should include the components listed below.

  a. Principal Investigator/Study Staff: Provide an organizational chart identifying key members of the study team including institution/center/ department. Briefly describe their roles on the project. Identify the member(s) of the team to coordinate and execute data submission to NDAR. A medical monitor (external to the study and not reimbursed by the study) and study coordinator(s) should be included.

  b. Study Management Plan: Provide a plan for ensuring the standardization of procedures among staff and across sites (if applicable). If the proposed clinical trial is multi-institutional, plans for communication and data transfer between the collaborating institutions, as well as how data, specimens, and/or imaging products obtained during the study will be handled, should be included. Provide a plan for real-time communication among collaborating institutions (if applicable).

- **Attachment 10: Surveys, Questionnaires, and Other Data Collection Instruments, if applicable (no page limit):** Upload as "Surveys.pdf." The Surveys, Questionnaires, and Other Data Collection Instruments attachment should include a copy of the most recent version of surveys, questionnaires, data collection forms, rating scales, interview guides, or other instruments. For each instrument, describe how the information collected is related to the objectives of the study.

- **Attachment 11: Impact Statement (one-page limit).** Upload as "Impact.pdf."

  - Identify the volunteer population(s) that will participate in the proposed intervention and describe the potential impact of the proposed clinical trial on the outcomes of individuals with ASD.

  - Describe the short-term impact: Detail the anticipated outcomes that will be directly attributed to the results of the proposed clinical trial.

  - Describe the long-term impact: Explain the long-range vision for implementation of the intervention in the clinic or field and describe the anticipated long-term benefits for the targeted population.

- Compare the proposed intervention to pharmacologic agents, devices, early intervention modalities, and/or clinical guidance currently available, if applicable.

- **Attachment 12: Transition Plan (two-page limit).** Upload as "Transition.pdf." Provide information on the methods and strategies proposed to move the intervention/product to the next phase of clinical trials and/or delivery to market after successful completion of the award. The transition plan should include the components listed below.
  - Details of the funding strategy that will be used to bring the outcomes to the next level of clinical trials and/or delivery to market (e.g., specific potential industry partners, specific funding opportunities to be applied for).
  - A description of collaborations and other resources that will be used to provide continuity of development.
  - A brief schedule and milestones for bringing the outcome(s) to the next phase of clinical trials and/or delivery to market.
  - A risk analysis for cost, schedule, manufacturability, and sustainability.

3. **Research & Related Senior/Key Person Profile (Expanded):** 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, USAMRMC, based on technical merit, the relevance to the mission of the 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. ***Note that impact does not compensate for deficiencies in scientific merit.*** A statistician will be included on the scientific review panels.

   Scientific merit is the most important criterion, followed by all other listed criteria, which are of equal importance:

- **Scientific Merit**
  - How well the scientific rationale for testing the intervention is supported by the preliminary data, critical review and analysis of the literature, and/or laboratory and/or preclinical evidence.
  - How well the study aims, hypotheses or objectives, experimental design, methods, data collection procedures, and analyses are designed to clearly answer the clinical objective.
  - How well the inclusion and randomization criteria meet the needs of the proposed clinical trial.
  - How well the exclusion criteria are justified.
- **Statistical Plan**
  - How the statistical plan, including sample size projections and power analysis, is adequate for the study and all proposed correlative studies.
  - Whether the statistical plan compensates for the use of a subpopulation of a recruited sample population to ensure appropriate power can be achieved within the subpopulation study.
- **Clinical Impact**
  - How the results of the proposed clinical trial will affect the magnitude and scope of potential clinical applications (e.g., detection, diagnosis, treatment, management, and/or quality of life).
  - How relevant the anticipated outcomes of the proposed clinical trial are to individuals with ASD.
  - How well the sample population represents the targeted patient population that might benefit from the proposed intervention.
  - How the potential outcomes of the proposed clinical trial will provide/improve the short-term benefits for individuals.
  - How significantly the long-term benefits for implementation of the intervention may impact patient care and/or quality of life.
- **Ethical Considerations**
  - How the level of risk to human subjects is minimized.
  - How well the evidence shows that the procedures are consistent with sound research design and, when appropriate, that these procedures are already in use for diagnostic or treatment purposes.
  - To what degree privacy issues are appropriately considered.
  - To what degree the process for seeking informed consent is appropriate and whether safeguards are in place for vulnerable populations.

- **Intervention**
  - Whether there is evidence to support availability of the intervention, if applicable, for the proposed clinical trial.
  - To what degree the intervention addresses the clinical need(s) described.
  - How the intervention advances patient care beyond the currently available interventions.
  - Whether a member of the study team holds the IND/IDE and whether the timeline proposed for IND/IDE application is appropriate (if applicable).
  - For investigator-sponsored INDs, whether there is institutional support to serve as a sponsor and whether they are equipped to assume the monitoring required by the FDA (if applicable).
  - Whether measures are described to ensure the consistency of dosing of active ingredients for nutritional supplements (if applicable).
  - To what degree the data collection instruments (e.g., surveys, questionnaires, etc.), if applicable, are appropriate to the proposed study.
- **Recruitment, Accrual, and Feasibility**
  - How well the PI addresses the availability of human subjects for the clinical trial and the prospect of their participation.
  - Whether the PI has demonstrated access to the proposed human subjects population.
  - How the recruitment, informed consent, screening, and retention processes for human subjects will be conducted to meet the needs of the proposed clinical trial.
  - Identification of possible delays and evidence of an adequate contingency plan to resolve potential delays (e.g., slow accrual, attrition).
  - To what extent the proposed clinical trial affects the daily lives of the individual human subjects participating in the study (e.g., Will human subjects still be able to take their regular medications while participating in the clinical trial? Are human subjects required to stay overnight in a hospital?).
- **Transition Plan**
  - Whether the funding strategy described to bring the outcome(s) to the next level of clinical trials and/or delivery to market is appropriate.
  - Whether appropriate collaborations and other resources for providing continuity of development are established and/or well described.
  - How the schedule and milestones for bringing the outcome(s) to clinical trial and/or delivery to market is appropriate.
  - How well the potential risk analysis for cost, schedule, manufacturability, and sustainability is developed.

In addition, the following unscored criteria will also contribute to the overall evaluation of the application:

- **Personnel and Communication**
  - Whether the composition of the study team (e.g., study coordinator, statistician) is appropriate.
  - To what degree the study team's background and expertise are appropriate to accomplish the proposed work (e.g., statistical expertise, expertise in the disease, and clinical studies).
  - How the levels of effort of the study team members are appropriate for successful conduct of the proposed trial.
  - To what degree the logistical aspects of the proposed clinical trial (e.g., communication plan, data transfer, standardization of procedures) are adequate.
- **Environment**
  - To what degree the scientific environment, clinical setting, and the accessibility of institutional resources support the clinical trial at each participating center or institution (including collaborative arrangements).
  - Whether there is evidence for appropriate institutional commitment from each participating institution.
  - If applicable, how the intellectual and material property plan that is agreed upon by each participating institution is appropriate for the proposed clinical trial.
- **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:
   - Adherence to the intent of the award mechanism
   - Programmatic relevance
   - Program portfolio composition
   - Ratings and evaluations of the peer reviewers
   - Relative impact

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.
- Human Subject Recruitment and Safety Procedures attachment (Attachment 6) is missing.
- Intervention attachment (Attachment 7) is missing.
- Data Management attachment (Attachment 8) 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 ARP IP member 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 FY11 ARP IP members may be found at http://cdmrp.army.mil/arp/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 proposed research is not a clinical trial.
- IDE/IND has not been submitted and/or FDA cleared.
- The PI does not meet the eligibility criteria.

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.

Quarterly 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.

A change in PI or organization is only permitted in extraordinary situations and will be decided upon on a case-by-case basis and will be at the discretion of the USAMRAA Contracting/Grants Officer. 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 USAMRAA Contracting/Grants Officer.

E. Pre-Award Meeting

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

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 Human Subject Recruitment and Safety Procedures (HumSubProc.pdf) as Attachment 6.	
	Upload Intervention (Intervention.pdf) as Attachment 7.	
	Upload Data Management (Data_Manage.pdf) as Attachment 8.	
	Upload Study Personnel and Organization (Personnel.pdf) as Attachment 9.	
	Upload Surveys, Questionnaires, and Other Data Collection Instruments (Surveys.pdf), if applicable, as Attachment 10.	
	Upload Impact Statement (Impact.pdf) as Attachment 11.	
	Upload Transition Plan (Transition.pdf) as Attachment 12.	
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.	