



Part I - Overview Information

Autism Intervention Research Network on Physical Health (AIR-P)

Title: AIR-P Network: Pilot Subcontracts on Treatment Research Affecting Autism

Request For Applications (RFA) Number: ATN-AIR-09-01

Key Dates

Release/Posted Date: **May 2009**

Letters of Intent Receipt Date: **Not applicable**

Application Submission/Receipt Date: **July 15, 2009**

Review Date: **July/August 2009**

Earliest Anticipated Start Date: **September 1, 2009**

Part II - Full Text of Announcement

Section I. Subcontract-Supported Research Opportunity Description

Research Objectives

Purpose

The Autism Treatment Network (ATN), through the support of the AIR-P Network, requests applications for two levels of pilot-supported activities (subcontract research):

- **LEVEL 1** support for small starter pilot opportunities directed mainly to junior investigators;
- **LEVEL 2** support for larger pilot studies to gather preliminary data to support more extensive research programs

Mission, Goals and Objectives

The ATN, an established program of Autism Speaks (AS), is a national network of fifteen leading hospitals and medical centers dedicated to improving the health and well-being of individuals with autism spectrum disorders (ASD) and other developmental disabilities. The ATN's unique strengths include access to an established collaborative network infrastructure across multiple institutions, and considerable collective scientific and clinical experience as a platform for research on evidence-based practices for interventions, policy development and dissemination.

The goal of the ATN is to a) expand the number of high-quality multidisciplinary clinical sites providing comprehensive evaluation and care for children and youth with ASD; b) develop, review, and disseminate common clinical standards and evidence-based guidelines for medical care for children and adolescents with ASD; and c) populate a data registry of children receiving ongoing care in participating sites to compare clinical efforts in a search for best practices for children with ASD.

Under the Combating Autism Act Initiative, the Maternal and Child Health Bureau (MCHB) initiated programs in several critical areas, including the Autism Intervention Research Network Program. This program includes two Autism Intervention Research Networks that focus on intervention research, guideline development and information dissemination—one network focuses on

physical health interventions (AIR-P), and one network focuses on behavioral, mental, social, and/or cognitive health interventions (AIR-B).

The ATN has an existing infrastructure consistent with the goals and mission of the AIR-P Network. Under the support of this AIR-P Network Program, the ATN now actively engages in efforts to:

- Conduct research on evidence-based practices for interventions to improve the physical health and well-being of children and adolescents with ASD and other developmental disabilities,
- Develop evidence-based guidelines and work to validate tools for interventions to improve the health care of children and adolescents with ASD and other developmental disabilities, and
- Disseminate critical information on its research findings, guidelines developments, and validated tools to health professionals and the public, especially families impacted by ASD and other developmental disabilities.

Through this support of the AIR-P Program, the ATN's research activities are conducted across ATN centers (collaborating research entities - CREs). These CREs serve under the leadership of the ATN's Network Coordinating Center to develop screening, treatment and evaluative tools for primary care physicians and subspecialists and to help standardize care across the diverse settings where children with ASD receive services. These centers are actively providing ongoing, comprehensive behavioral and medical treatment to children and adolescents with ASD. The centers have extensive experience in providing care, as well as single and multi-site research, clinical trials, and observational/intervention studies. The CREs currently include:

- Baylor College of Medicine
- Cincinnati Children's Hospital
- Columbia University
- Kaiser Permanente Northern California
- Kennedy-Krieger Institute
- LADDERS/MassGeneral Hospital
- Oregon Health & Science University
- Toronto Autism Network (Bloorview Kids Rehab, Surrey Place Centre and the Hospital for Sick Children)
- University of Arkansas/Arkansas Children's Hospital
- University of Colorado
- Denver/The Children's Hospital
- University of Missouri
- University of Pittsburgh
- University of Rochester
- Seattle Children's/University of Washington
- Vanderbilt University

This RFA builds upon the existing ATN infrastructure and scientific expertise that exists across the network CREs:

- To implement a collaborative mechanism to develop innovative research concepts and protocols that will help improve care for children with ASD
- To carry out a series of pilot studies providing preliminary findings and to seek outside funding opportunities to develop full scale implementation and intervention research

For this RFA, the ATN has particular interest in supporting junior investigators in developing their research efforts to improve the medical care of children with autism. Along with this interest in young investigators, the priorities for this RFA also include attention by junior and senior investigators to novel ideas that may face difficulties with funding from other sources, for preliminary data development in critical areas of clinical interest, and/or increased collaboration across research disciplines.

Background

Autistic Spectrum Disorders (ASD) are a set of complex neurodevelopmental disorders defined behaviorally by impaired social interaction, delayed and disordered language, repetitive or stereotypic behavior and a restricted range of interest. Current prevalence studies show that one out of every 150 children in the U.S. is diagnosed with an ASD. Many individuals with ASD have symptoms associated with underlying medical conditions, including seizures, sleep problems, gastrointestinal (GI) disorders, and metabolic conditions, that when left untreated, may compromise not only general health, but also behavioral, developmental, and educational outcomes of individuals with ASD. Unfortunately, children with ASD face many barriers in accessing appropriate healthcare and are less likely than children with mental retardation or other special needs to obtain the specialty medical care that they need.

The barriers to medical care for children with ASD include the lack of primary and specialty health care providers with the training and experience to identify and assess medical conditions appropriately in this population. Even when medical conditions are recognized, physicians are reluctant to treat patients with ASD because there are no standard diagnostic and treatment procedures and minimal medical standards to treat the associated medical conditions or guide their care. This is due, in part, to the fact that physicians and parents have traditionally viewed ASD as a communication and

behavioral disorder. Thus, treatment has tended to focus on these aspects of ASD, while medical conditions in patients have not received adequate attention.

A critical goal of the ATN has been to improve medical treatment for children and youth with ASD by establishing standards of clinical care and evidence-based guidelines. Nonetheless, the evidence supporting clinical care for many conditions associated with ASD is sparse, and there is a pressing need to develop this evidence in systematic ways. This has been a major motivation for the ATN to expand its activities through the AIR-P network. The network's interests extend beyond understanding the associated medical conditions and the implications of these conditions on functioning of individuals and their overall well-being. The ATN seeks to translate data acquired from studies of the conditions affecting ASD to potential treatments directed to improving these conditions and thereby improving functioning.

The goals for the AIR-P Network include forging partnerships with researchers, clinicians, educators, advocates, families, State public health programs and other organizations/agencies critical to improving the health and well-being of individuals with ASD and other developmental disabilities. Establishment of strong partnerships between researchers and practitioners is essential to assure that new interventions, evidence-based guidelines, tools, and systems management approaches are applied in the health care system. Establishment of strong partnerships with the public, families and the advocacy community is also essential to translate vital research findings to assure better access and quality services for individuals with ASD and other developmental disabilities.

The ATN enhances access to a medical home through several mechanisms, including collaboration with community primary care physicians and companion networks, scientific publications, policy development, conferences, trainee mentorships, physician education and parent training. Autism Speaks' nationwide reach enables the ATN to have a significant impact at both State and Federal levels to increase the accessibility of evidence-based treatments. The ATN brings together physicians in the context of a multidisciplinary clinical team, other clinicians, researchers, and families to form a multi-tiered network to ensure rapid dissemination and implementation of treatments, guidelines and tools.

Section II. Subcontract Information

Subcontract-Supported Research & Funds Available

Collaborating Research Entity (CRE) support:

LEVEL 1: Support opportunities targeting junior-level investigators –

To support short-term pilot studies, which can include analyses of existing ATN registry data; proposal leadership should have clear mentoring from senior investigator(s), preferably one at the home institution but can have additional mentoring elsewhere. These studies would likely be conducted in a 12-18 month period.

Number of Subcontracts: 3-5 subcontracts available to support Level 1 activity.

Subcontract Amounts: Up to \$40,000 direct costs for 1 year.

LEVEL 2: Support opportunities targeting both junior and senior-level investigators –

To support larger innovative projects gathering pilot data for more in-depth studies fundable by external sources (Autism Speaks, NIH, etc). These studies would likely be conducted over a 2 year period and include efforts to bring multiple research disciplines together.

Number of Subcontracts: 2-3 subcontracts available to support Level 2 activity.

Subcontract Amounts: Up to \$125,000 direct costs (per year) for up to 2 years.

Indirect Costs:

Indirect costs are those costs incurred for common or joint objectives which cannot be readily identified but are necessary to the operations of the organization, e.g., the cost of operating and maintaining facilities, depreciation, and administrative salaries.

Please note that the applicant must submit a copy of the latest negotiated rate agreement. Approved research projects that will be conducted by the Network can charge a research indirect cost rate for the sole purpose of conducting the research study.

Section III. Eligibility Information

1. Eligible Applicants

1.A. Eligible Institutions

- Must be a currently funded ATN center at the time of proposal submission.

1.B. Eligible Individuals

- Individuals holding full-time tenured or tenure-track faculty appointments or equivalent full-time non-tenure track appointments at an existing ATN center are eligible to apply.
- Postdoctoral fellows at an existing ATN center are eligible and encouraged to apply for **LEVEL 1** support.

1.C. Principal Investigators

- PIs must have an M.D. and/or Ph.D.
- Background Requirements:
 - **LEVEL 1 Support:** Postdoctoral fellows / Junior-level investigators are eligible and encouraged to apply for **LEVEL 1** support.
 - **LEVEL 2 Support:** PIs can be junior or senior-level researchers at the institution and must have a demonstrated track record of research with individuals with autism or other neurodevelopmental disorders. Researchers without ASD experience but with other clear investigative skills that could apply to ASD research are also encouraged to apply for **LEVEL 2** support.
 - Research Experience: a proven track record of external funding and peer-reviewed publications and presentations.

2. Targeted Research Topics/Areas of Interest

The goal of the Autism Treatment Network under the support of the AIR-P Network is to establish and maintain a network infrastructure designed to be the platform from which to conduct research on evidence-based practices for interventions to improve the physical health and well-being of children and adolescents with autism spectrum disorders (ASD) and other developmental disabilities. Physical health may include but is not limited to medical, dental, visual, nutrition and speech/hearing components. The ATN invites and encourages proposals in the following areas:

- **Pediatric Gastroenterology:** Many children with ASD appear to have gastrointestinal problems. Whether these occur through some common neurologic mechanism or reflect disordered eating behaviors or have other causes is unclear. Many issues in nutrition and GI complaints and their treatment among children with ASD lend themselves to careful investigation.
- **Pediatric Psychopharmacology:** Many children with ASD are treated with psychotropic medications, even though only one medication has been specifically approved for treatment of ASD behaviors and irritability. The need for systematic research into psychopharmacology for ASD characteristics is clear, esp., taking into account various phenotypic and genotypic differences in the population.
- **Genetics/Metabolics:** A number of genetic and metabolic conditions have phenotypes similar to or consistent with ASD. These associations lend themselves to studies of etiologies and potential mechanisms of disease and treatment.
- **Pain**
- **Immunology:** A number of studies have indicated abnormalities in the immune response in children with ASD and suggested opportunities for new treatments. Evaluation of immune status and markers for inflammation, and novel interventions for altered immune status are areas of interest.
- **Endocrinology:** How do pubertal changes affect ASD and its manifestations?
- **Occupational Therapy/Speech Therapy**
- **Pediatric Neurology:** While ASDs have a clear neurologic basis, it is unclear what mechanisms are responsible or associated with these disorders and their comorbidities. The scope and specifics of neurologic evaluation, use of pharmacologic agents, and utility of various neuroimaging modalities in routine evaluation and management, and in special situations (sleep problems, self-injurious behavior, etc) is still controversial.

Section IV. Application and Submission Information

1. Content and Form of Application Submission

Letter of Intent: A letter of intent is not required for this subcontract-supported research opportunity.

Full Application: Information and guidelines for the Full Application can be found at www.atnresearch.org. This information will also be sent directly to all currently funded ATN centers.

2. Submission Dates and Times

Full Application Deadline: **Wednesday, July 15, 2009**

Electronic Submission: Applicants should send the complete application by email as a single PDF document. **Applications and supporting materials must be received in the office by 5 pm ET on Wednesday, July 15, 2009.**

The proposal and supporting documents should be emailed as a single PDF file to:

Brian Winklosky
ATN Research Program Manager
Email: BWinklosky@Partners.org
Subject Line of Email: "REF: ATN-AIR-09-01 Submission"

Hard copy submission: In addition, applicants should send hard copies (1 original (single-sided) + 2 copies, (single-sided) to the ATN Clinical Coordinating Center to **be received by** Wednesday, July 15, 2009.

Hard copies should be sent to:

Brian Winklosky
ATN Research Program Manager
Massachusetts General Hospital
50 Staniford Street, Suite 901
Boston, MA 02114
REF: **ATN-AIR-09-01 Submission**

3. Submission and Review Dates

Application Submission/Receipt Date: **July 15, 2009**

Peer Review Date: **July/August 2009**

4. Anticipated Announcement and Subcontract Dates

Subcontracts Announced: **August 2009**

Earliest Anticipated Start Date: **September 1, 2009**

5. Subcontract Restrictions

Funds may be allocated for personnel, consultants, supplies, travel, patient costs, equipment, and miscellaneous expenses. Equipment allocations cannot be used for large, permanent equipment purchases. A detailed budget must be included with the full application.

Section V. Subcontract-Support Information

1. Subcontract Notices

Individuals that submit full applications will be notified of their application status by email in July/August 2009. Official notices will be sent within a week of the email notification. The earliest a subcontract period may start is September 1, 2009. Subcontract periods officially start on the date subcontracts have received an appropriate IRB-approved protocol (and supporting materials) and have an approved, final budget.

2 A. Sharing Research Data

Data must be contributed to the ATN Registry at the end of the study after a mutually agreeable hold-back period. Data may be entered through the ATN Registry data management systems, AdvantageEDC (for clinical or custom forms) or the Internet System for Assessing Autistic Children (ISAAC) database (for copyrighted standardized assessments) Biostatistics and analysis of data can be coordinated for multi-site studies by the ATN data coordinating center (EMMES Corp). If a project lead chooses to use the ATN Registry database systems for data entry, they must include a budget for the associate costs as part of their grant.

2 B. Sharing Research Resources

Publications resulting from use of registry data from the ATN database must acknowledge the ATN and all sites who contributed data to the publication (according to existing ATN publication policy which is outlined in the ATN Manual of Procedures).

Publication of Data (excerpt from the UA3 AIR-P and AIR-B application guidance, regarding publications, followed by sample language crediting the funding source)

Prompt and timely presentation and publication in the scientific literature of findings resulting from research undertaken in the Network is required. As per HHS guidelines, the Awardee agrees to acknowledge HRSA support in the publications and oral presentations resulting from research and/or activities conducted under this cooperative agreement. Investigators must agree to abide by Network policies concerning all publication of Network studies. Prior to the submission of manuscripts for publication Awardees agree to provide preprint copies to the Network Steering Committee according to policies and procedures the Steering Committee may establish to monitor the presentation and publication of research results. Peer-reviewed publications are the cardinal measure of success of the MCH Research Program. The number of publications resulting from each funded project contributes to the total number of publications by which the MCH Research Program is evaluated annually.

All studies funded by these subcontracts should credit the funding source: "This study was supported by cooperative agreement UA3 MC 11054, Autism Intervention Research Network on Physical Health (AIR-P Network) from the Maternal and Child Health Bureau (Combating Autism Act of 2006), Health Resources and Services Administration, Department of Health and Human Services."

3. Reporting

At the end of each year, subcontracts are required to submit a written progress report and an updated budget. A written final report is required at the end of the subcontract period. Release of funds for each additional period is contingent upon receipt of the progress report and the updated budget.

Section VI. Contacts

Proposal Development and Subcontract Budgets:

MGH Network Coordinating Center
Brian Winklosky - Research Program Manager
Phone: 617-643-1036
Email: bwinklosky@partners.org

Administrative Support:

MGH Network Coordinating Center
Jessie Figueroa - Staff Assistant
Phone: 617-643-6772
Email: jfigueroa8@partners.org

Section VII. Content and Form of Application Submission

This RFA and all application materials/forms will also be available to you on the ATN website by Friday, May 15, 2009.

Link: <https://secure.emmes.com/atnweb>

1. The application **Cover Sheet**. Include PI details as well as the institutional business official responsible for managing/negotiating subcontract agreements.
2. An **Abstract** of the Proposal (250 words or less) is required.
3. Administrative Acknowledgement Notice or Letter from the Human Subjects **Institutional Review Board** indicating the IRB's acknowledgement of the grant application.
4. Proof that all identified personnel have completed appropriate Humans Subjects Ethics training and **HIPPA** training. Include copies of completion certificates for all identified key personnel.
5. **Biographical Sketches** (standard PHS 398 pages) for all identified key research personnel should be provided using the NIH format only and should not exceed 4 pages per individual. A copy of the NIH biographical sketch form can be found on the following webpage (<http://grants.nih.gov/grants/funding/phs398/phs398.html>).
6. **Budget Request**: You must use the standard PHS 398 Budget Forms pages 4 & 5 found here: (<http://grants.nih.gov/grants/funding/phs398/phs398.html>).
7. A detailed **Budget Justification**, itemized by category is required. The budget justification is not considered part of your 12-page proposal. Funds may be allocated for personnel, consultants, supplies, travel, patient costs, equipment, and miscellaneous expenses. Equipment allocations cannot be used for large, permanent equipment purchases. Indirect costs are not inclusive of the total award. **Please note that the applicant must submit a copy of the latest negotiated rate agreement.**

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To support larger innovative projects gathering pilot data for more in-depth studies fundable by external sources (Autism Speaks, NIH, etc). These studies would likely be conducted over a 2 year period and include efforts to bring multiple research disciplines together. Funding for year-02 is contingent upon a satisfactory progress report and submission of an updated budget.

Number of Subcontracts: 2-3 subcontracts available to support Level 2 activity.

Subcontract Amounts: Up to \$125,000 direct costs (per year) for up to 2 years.

8. **Proposal**

Total Page Limit: 12 pages (single-sided). This does not include table of contents, references or supporting materials such as budgets, budget justifications, or other supporting documents.

Font: Arial, Times New Roman, or Palatino Linotype typeface and a font size of 12 points. A smaller font size may be used for figures, graphs, diagrams, charts, tables, figure legends, and footnotes, but this type must follow the font typeface requirement and be readily legible.

Margins: 1" on all sides.

Paper: 8 ½ X 11" (no A4)

Numbering: All pages in this proposal should be numbered sequentially in the bottom right corner.

Headers: The RFA number should appear with the full name of the Principal Investigator as shown below (top right, justified margin).

Principal Investigator: **LAST, First Middle Initial**
ATN-AIR-09-01



Autism Intervention Research Network on Physical Health (AIR-P)

This AIR-P Network RFA release was funded by cooperative agreement UA3 MC 11054 through the U.S. Department of Health and Human Services, Health Resources and Services Administration, Maternal and Child Health Research Program.
