RFA ATN-AIR-19-11

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

Request for Applications (RFA) Number: **ATN-AIR-19-11**
Title: **AIR-P Network: Research Projects**

Key Dates

Release Date: February 5, 2019
Proposal Due Date: April 8, 2019
Review Period: April 2019
Announcement Period: May 2019*
Earliest Start Date: June 1, 2019

* The peer review process may require proposal revisions and additional SRC review before final funding decisions can be made.

SECTION I. RESEARCH OPPORTUNITY DESCRIPTION

OBJECTIVES

Purpose

This opportunity provides support for the development and implementation of a 1-year study, which can be modeled as a pilot intervention, qualitative research, quality improvement project (with an evaluative component), or testing of an existing network toolkit or guideline.

All proposals must reflect the network interest in physical health of children with ASD. Proposals should also include vulnerable and underserved populations, address disparities in care, or address issues of importance to underserved populations[1].

Background

Under the 2014 Autism CARES Act, the Maternal and Child Health Bureau (MCHB) continued to support 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).

Through the AIR-P Program, the Network conducts research activities across AIR-P centers (collaborating research entities - CREs). These AIR-P centers actively provide ongoing, comprehensive behavioral and medical treatment to children and adolescents with ASD, as well as participate in single and multi-site research, clinical trials, and observational/intervention studies. The twelve AIR-P CREs currently include:

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[1] *Underserved populations include diverse ethnic/racial, cultural, linguistic, socioeconomic, and geographic (e.g., rural/urban, tribal) populations for whom there is little evidence regarding the effectiveness of interventions, or for whom access to effective treatments is limited.*

1. Children's Hospital of Los Angeles
2. Children's Hospital of Philadelphia
3. Cincinnati Children's Hospital
4. Lurie Center for Autism/MGH
5. Nationwide Children's Hospital
6. Toronto (Holland Bloorview, Surrey Place Centre, and the Hospital for Sick Children)
7. University of Alberta/Glenrose Rehab Hospital
8. University of California – Irvine
9. University of Missouri
10. University of Pittsburgh
11. University of Rochester
12. Vanderbilt University Medical Center

SECTION II. SUBCONTRACT INFORMATION

1. PROJECT PERIOD & AVAILABLE FUNDS

Collaborating Research Entity (CRE) support:
This funding opportunity targets investigators with innovative projects outlined in the Objectives on page 1 of this guidance. The total subcontract budget period for a proposal submitted in response to this funding opportunity may not exceed 12 months and begin no earlier than June 1, 2019. All funded studies will be completed one year after the start date, including analysis and a draft of the primary manuscript. Sites must actively communicate with the network Data Coordinating Center to assure that there is time for completion of the data analysis.

Subcontract Period: June 1, 2019 – May 31, 2020
Award Amounts: Up to $300,000 total costs (inclusive of IDCs) for project period; funding level requested should be appropriate for the type of project proposed and # of network centers involved.

2. INDIRECT COSTS

Indirect costs are those costs incurred for common 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. Indirect costs will be reported using your institutional **Other Sponsored Program** rate for the identified project period(s). No funding can be used to pay indirect costs for non-US institutions.

Please note that the applicant must submit a copy of the latest negotiated Other Sponsored Program rate agreement.

SECTION III. ELIGIBILITY INFORMATION

1. ELIGIBLE INDIVIDUALS & INSTITUTIONS

- Must be a current network center (CRE) at the time of proposal submission (see 'Collaborating Research Entities – CREs" listed in Part II, Section I of this RFA).
- Individuals from non-network centers (including, but not limited to MCHB LEND trainees and MCHB Developmental-Behavioral Pediatrics Fellows) are also eligible to collaborate with an existing network PI/site. The proposal must be organized, managed and submitted directly through an existing network PI/site. The network site would be the recipient of the AIR-P research subcontract and the external investigator would be reported as a named <u>consultant</u> on the proposal. Any external consultant must be identified in the supporting budget and budget narrative pages (i.e., role on project).

2. PRINCIPAL INVESTIGATORS

- PIs may be a junior or senior researcher at an AIR-P center. PIs will have a demonstrated track record of research with individuals with autism or other neurodevelopmental disorders and/or other clear investigative skills that could apply to ASD research.
- Junior investigators, those with a maximum of 10 years post-doctoral training, are strongly encouraged to apply but are required to document active and ongoing mentoring from an established investigator at an existing network site.

SECTION IV. NETWORK INTERESTS & RESOURCES

1. RESEARCH PRIORITIES / AREAS OF INTEREST

Proposals shall address 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. Projects should include vulnerable and underserved populations, address disparities in care, or address issues of particular importance to underserved populations**.** The AIR-P encourages proposals that address the areas listed below. This list includes a sample of priority topics for the network. Other topics will be considered if they address the overall mission of AIR-P.

1. Interventions targeting common co-morbidities
   - Psychopharmacology
   - Psycho-educational (e.g., for sleep & anxiety)
   - Complementary and Alternative Medicine (e.g., probiotics and GI disorder, CBD)
2. Health services
   - Transition to adulthood
   - Co-management with community physicians
   - Referral & Diagnosis
3. Health promotion and well-being among children with ASD
   - Overweight / Obesity
   - Diet & Nutrition
   - GI Disorders
   - Injury / Safety / Awareness
4. Other areas related to the physical health of children with ASD including but not limited to:
   - Puberty
   - Regression
   - Seizures / EEG
   - Neuroinflammation

2. NETWORK RESEARCH SUPPORT

The AIR-P network provides support for several research functions for specific research proposals and projects. These include:

- The network Data Coordinating Center (DCC) – the MGH Biostatistics core – will provide statistical support, including help with development of focused research questions/objectives and analytic design. Investigators are encouraged to speak with the MGH biostatistics team early in the proposal development process (**Robert Parker**, email – rparker4@mgh.harvard.edu).
- In response to this RFA, the MGH Biostatistics team has provided access to 4 online statistics tutorials, listed here by topic. We encourage review of these materials if you plan to prepare and submit a proposal under this RFA. The password for all videos is "*catalyst*".
  - **Hypothesis testing**: https://vimeo.com/62208331
  - **ANOVA and Regression**: https://vimeo.com/62208333
  - **Dichotomous and survival outcomes**: https://vimeo.com/62208332
  - **Sample size and study design**: https://vimeo.com/62208334

3. CLINICAL AND TRANSLATIONAL SCIENCE AWARD PROGRAM (CTSA Program)

Sites are strongly encouraged to collaborate with their Clinical and Translational Science Award Program - (CTSA), if they have one. The CTSA Programs, formerly known as General Clinical Research Centers (GCRCs), support investigators by offering a specialized research environment that provides the infrastructure necessary to conduct patient-oriented research. The CTSA program provides the infrastructure and resources for medical investigators to conduct safe, controlled, state-of-the-art, inpatient and outpatient studies of both children and adults.

If you're not sure whether your institution has a CTSA Program, please follow this link to review the list of funded institutions (*Ctrl + Click to follow link*):

https://www.researchmatch.org/partners/index_participatingctsa.php

4. FAMILY PARTNERS

Family Advisory Partnerships

The purpose of the network Family Advisory Committee (FAC) is to ensure representation of children's and families' perspectives in all AIR-P endeavors. Members of the FAC are engaged in several key areas, including:

- Developing and implementing network procedures, policies, and activities.
- Advising the AIR-P Network on current and future clinical and research priorities.
- Providing family perspective on the activities of the subspecialty committees.

Investigators must provide clear and detailed evidence of involvement of local FAC members and/or other family advisors at participating sites in proposal development, development of study aims, and in completion of the study. **Letters of support from family partners will strengthen the application.**

SECTION V. REVIEW METRICS

1. PEER REVIEW

Proposals will be peer reviewed by internal members of the network's Scientific Review Committee as well as external biostatistical reviewers and ad hoc reviewers with content expertise.

Proposals will be reviewed using criteria in the following core content areas, and the application should address each of these:

- *Significance:* Does the project generate new data that address an important problem or a critical barrier to progress in the field? How will successful completion of the aims change the concepts, methods, technologies, treatments, services, or preventive interventions that drive this field? How does the project

fit the AIR-P priorities? Does the proposal address disparities experienced by underserved, minority, or rural communities? Will the project lead to an expanded trial, additional publications, intervention activities and grant proposals?

- ***Investigator(s) & Collaborators:*** Is the PI well suited to the project? Does (s)he have appropriate experience and training? Does the investigator have a successful track record of completing network projects and meeting study goals in accordance with agreed upon timelines?
- ***Mentorship:*** If a co-PI or mentor is listed, does this person have appropriate experience and research productivity? Are there mentorship opportunities for junior investigators involved in the proposal?
- ***Family Advisory Committee Partnership:*** Does the application include collaboration with members of the network Family Advisory Committee and/or other relevant family advisors or parent partners?
- ***Innovation:*** Does the application challenge and seek to shift current research or clinical practice paradigms by utilizing novel theoretical concepts, approaches or methodologies, instrumentation, or interventions? Are the concepts, approaches or methodologies, instrumentation, or interventions novel to one field of research or novel in a broad sense? Is a refinement, improvement, or new application of theoretical concepts, approaches or methodologies, instrumentation, or interventions proposed?
- ***Approach:*** Are the overall strategy, methodology, and analyses well-reasoned and appropriate to accomplish the specific aims of the project? Are potential problems, alternative strategies, and benchmarks for success presented? Are sample and key variables well described and in adequate detail? Can the project be completed in the timeframe?
- ***Environment.*** Will the scientific environment in which the work will be done contribute to the probability of success? Are the institutional support, equipment and other physical resources available to the investigators adequate for the project proposed?
- ***Protections for Human Subjects.*** The committee will evaluate: 1) risk to subjects, 2) adequacy of protection against risks, 3) potential benefits to the subjects and others, 4) importance of the knowledge to be gained, and 5) data and safety monitoring for any proposed clinical trials.
- ***Inclusion of Women, Minorities, and Children.*** The committee will evaluate the proposed plans for inclusion of underserved minority and rural communities and members of both sexes, as well as the inclusion of children.
- ***Budget and Period Support.*** Reviewers will consider whether the budget and the requested period of support are fully justified and reasonable in relation to the proposed research.

2. METRICS FOR SUCCESS

A successful pilot project will be measured by completion of all agreed upon study milestones, including for all projects:

- Meeting all originally funded study aims;
- Completing the agreed upon scope of work within the defined study period;
- Demonstrating responsible fiscal management;
- Ability to enroll subject in a timely fashion;
- Ability to meet minimum 80% of target recruitment goal;
- Collecting complete and clean data for all study measures;
- Collaborating closely with the network Clinical and Data Coordinating Centers;
- Completion of a primary manuscript, which receives formal review by the network Scientific Review Committee and is submitted to a peer-reviewed journal (including results of the study).

SECTION VI. APPLICATION AND SUBMISSION INFORMATION

1. ACCESS TO APPLICATION MATERIALS
This RFA and all supporting application materials/tools will be available on the following network websites by Wednesday, February 6, 2019.
- Network website: www.asatn.org
  - See "CLINICIANS & RESEARCHERS": Details for RFA ATN-AIR-19-11 will be available under "News & Announcements" in the right navigation bar. This page is publicly available and does not require a username or password.
  - http://asatn.org/clinicians
- AIR-P website: www.airpnetwork.org

2. SCHEDULE
Release Date: February 5, 2019
Proposal Due Date: April 8, 2019
Review Period: April 2019
Announcement Period: May 2019*
Earliest Start Date: June 1, 2019

* The peer review process may require proposal revisions and additional SRC review before final funding decisions can be made.

Applicants must send the complete application by email as a single PDF document by 5 pm ET on Monday, April 8, 2019.

The proposal and supporting documents should be emailed as a **single** PDF file to:
> Brian Winklosky
> AIR-P Research Program Manager
> Email: **BWinklosky@mgh.harvard.edu**
> Subject Line of Email: "**RFA ATN-AIR-19-11 Submission**"

SECTION VII. SUBCONTRACT SUPPORT INFORMATION

1. SUBCONTRACT DELIVERABLES & PUBLICATION POLICY
Publication of Data
Prompt and timely presentation and publication in the scientific literature of findings resulting from research undertaken in the network is required. As part of the proposal, investigators should provide a table of likely publications and submission times.

The primary manuscripts should be completed by the end of the grant period and submitted to the scientific review committee for internal review.

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, the awardees agree to follow publication policy as outlined in the network Manual of Procedures. Peer-reviewed publications are the cardinal measure of success of the MCHB Research Program. The number of publications resulting from each funded project contributes to the total number of publications by which the MCHB Research Program is evaluated annually.

2. NETWORK DATA SHARING POLICY

In April 2014, the network released a Data Sharing Policy, which applies to all completed AIR-P research data. The policy states:

All data collected as part of any funded AIR-P research project must be contributed to the AS ATN Registry and related network databases. All AIR-P data will be made available to members of the network following an 18-month hold-back period. This hold-back period is defined as a date no more than 18 months from the final study close-out date (i.e., the final date of the subcontract). This includes all data entered and/or managed through any data management systems, including Advantage EDC, StudyTRAX, the Internet System for Assessing Autistic Children (ISAAC), the Online System for Clinical Research (OSCR), or other research data collected under an AS ATN/AIR-P supported project. Biostatistics and analysis of data can be coordinated for multi-site studies by the MGH Biostatistics team. As with AS ATN Registry data, all research data will become available to external investigators, according to existing data sharing and open-access policies for network data.

3. INVESTIGATOR COMMITMENTS

- The <u>lead</u> principal investigator for any funded AIR-P study is expected to provide a minimum 10% time. It is acceptable to report some uncompensated time to make budgeting more reasonable.
- The AIR-P study investigators are expected to participate regularly in the AIR-P Advances in Autism Research & Care (AARC) webinar series. The monthly 1-hour webinars provide a platform to discuss Network activities, including AIR-P research efforts. This series provides opportunities for mentorship and peer support to Network investigators.
- Investigators are expected to share and present study findings at scientific conferences and internal network meetings. This includes oral and poster presentations, as well as an outline of likely publications and submission times (including targeted journals).
- Investigators are expected to review and abide by the Network review and publication policies found in chapter 12 of the Network Manual of Procedures.

SECTION VIII. NETWORK CONTACTS

Proposal & Budget Development (Clinical Coordinating Center):
    Brian Winklosky – Research Program Manager
    Phone: 617-643-1036
    Email: bwinklosky@mgh.harvard.edu

Statistical Support (Data Coordinating Center):
    Robert Parker – Statistician
    Phone: 617-724-9838
    Email: rparker4@mgh.harvard.edu

SECTION IX. PROPOSAL ASSEMBLY – CONTENT & FORMAT

SECTION	DESCRIPTION / FORMAT
SECTION 1	**AIR-P PROPOSAL COVER PAGE (1-page, TEMPLATE; included in page limit)**: Include PI details as well as the institutional business official responsible for managing/negotiating subcontract agreements. A template is available on the network website. **Please also provide a list of key terms to identify your application.**
SECTION 2	**ABSTRACT (1-page, no template; included in page limit):** Include a concise abstract of the proposed study (250 words or less).
SECTION 3	**STUDY NARRATIVE – RESEARCH QUESTIONS / ANALYTIC PLAN (not to exceed 6 pages, single-sided and single-spaced; included in page limit).** See detailed instructions below.
SECTION 4	**GLOSSARY OF TERMS (no page limit, no template; not included in page limit**): Scientific terms should be highlighted within the text of the application and defined/listed in a summary page at the end of the Research Narrative (SECTION 3). The glossary of key words/terms will assist reviewers in the peer review process.
SECTION 5	**RESEARCH PUBLICATIONS (no page limit, no template; not included in page limit**): Include a summary table of anticipated research publications with targeted submission dates and targeted journal(s). This list should also include plans for abstract/poster submission to scientific meetings at the appropriate time.
SECTION 6	**PROJECT BUDGET PAGE, <u>12 MONTH</u> PERIOD (1-page, TEMPLATE; not included in page limit)**: Funds may be allocated for personnel, consultants, supplies, and miscellaneous expenses. No equipment allocations will be approved. A detailed and well-justified budget must be included with the full application. - You must use the budget template, which is available on the network website. - Indirect costs will be reported using your institutional Other Sponsored Program rate for the identified project period(s). No funding can be used to pay indirect costs for non-US institutions. - Budgets require institutional sign-off by a designated business official (grants and contracts).
SECTION 7	**PROJECT BUDGET JUSTIFICATION (no page limit, no template; not included in page limit)**: Provide detailed and itemized budget by category. You must identify fringe rates for all personnel listed (show calculations). Indirect costs are inclusive of the total award. **Please note that the applicant must submit an updated indirect rate agreement. Your institutional business official/grants office will be able to provide you with this agreement.**
SECTION 8	**BIOSKETCH (not to exceed 2 pages, no template; not included in page limit):** - A biosketch template is also available on the network website. - Include a biosketch for all key research personnel identified on the project, including paid/unpaid consultants. - You are also required to submit a biosketch for any site statistician(s) who will be involved in any part of your data analysis.
SECTION 9	**HUMAN SUBJECTS CERTIFICATION (no page limit, no template; not included in page limit)**: Include proof that all identified personnel have completed appropriate Human Subjects Ethics

training and/or **HIPAA** training. Include copies of completion certificates for all identified key personnel. HIPAA certification can be obtained online through the Collaborative Institutional Training Initiative (CITI) – www.citiprogram.org.

For Canadian site personnel, training through the *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans* (TCPS) is sufficient. Use this link: http://www.pre.ethics.gc.ca/eng/policy-politique/initiatives/tcps2-eptc2/Default/

SECTION 10 **IRB ACKNOWLEDGEMENT (no page limit, no template; not included in page limit):** Include administrative acknowledgement (Institutional Notice or Letter) from the Human Subjects **Institutional Review Board** indicating the IRB's acknowledgement (not approval) of the proposal application. This acknowledgement is intended to demonstrate that the lead PI has carefully considered the timing of the protocol review - to acknowledge a clear understanding of internal submission dates for review, length of typical review period, consideration of amendments/delays, and staff time devoted to IRB development. PIs are not expected to have IRB/REB approvals prior to award <u>notice</u> but will be required to have full IRB/REB approvals before the subcontract can be executed.

SECTION 11 **STATEMENT OF INTENT (1-page, TEMPLATE; not included in page limit)**: A complete, signed Statement of Intent to enter into a subcontract agreement must accompany the application. Please report your institutional FWA # in the space provided. A Statement of Intent template is available on the Network website.

DETAILED INSTRUCTIONS FOR PILOT STUDY NARRATIVE

General Format:

Total Page Limit:	6 pages (single-sided, single-spaced). This does not include table of contents, references, or supporting materials such as budgets, budget justifications, or other supporting documents.
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 study's PRIMARY/LEAD Principal Investigator as shown below (top right, justified margin).

Principal Investigator: **LAST, First Middle Initial ATN-AIR-19-11**

Pilot Study Narrative Components (not to exceed 6 pages for sections I – IV below for the initial project):

I. Introduction: Should be a brief discussion of what led to the current study:
- Describe what previous studies have shown that led you to formulate this specific question, indicating the potential for therapeutic benefits;
- Brief review of literature;
- Close with a statement of the question(s) to be addressed in the study and brief comment regarding the study design and its importance to the health and well-being of children with ASD.

II. Specific Aims / Hypothesis: Clearly state the study aims and associated hypothesis:
- Describe well-focused hypotheses and objectives;
- Consider your aims to test your hypotheses;
- Limit your proposal to 3-4 clear and specific aims, at most.

III. Background & Significance / Preliminary Studies: Describe the theoretical framework, initial development, and existing empirical support for the study:
- Background for the study design;

- Expected therapeutic benefit(s) and the likelihood that the benefit(s) will outweigh any negative side effects;
- Selection of the targeted symptom(s);
- How the expected benefit(s) of the treatment will address the needs of underserved minority and rural communities, including specific functional outcomes;
- How strong positive findings could be further evaluated in larger studies;
- Use of any biomarkers.

IV. Research Design & Methods: Include recruitment and sample description, well defined inclusion/exclusion criteria, study measures, analytic plan, plans to address Protections for Human Subjects, and Inclusion of Women, Minorities, and Children, and plans to address disparities experienced by underserved minority and rural communities:

- Sampling strategy, implementation and evaluation methods;
- Describe in detail the specific mechanisms you will use to recruit and enroll subjects, how will you apply personnel to subject recruitment, what incentives will you use to recruit and enroll from vulnerable and underserved populations;
- Describe availability and use of CTSA resources;
- Study measures (i.e., what do they measure, how reliable are they, reference them if used in previous studies; for intervention studies, when applied (i.e., before/after, etc.); should include a description of data form development, including assessment schedule, copyright fees and requirements, data collection timeline, and data management needs;
- The nature and relevance of control groups (including the use of historical control groups);
- Methods to control for confounding factors and bias;
- Feasibility of achieving study objectives within the funding period (including sample availability) / timeline.

V. Other Considerations:

- Statistical considerations, including power considerations or accuracy of estimates for subsequent study planning and basic analysis approach;
- Address any ethical issues implicit in study design;
- Project timeline;
- Protections for human subjects;
- Address inclusion of underserved minority and rural communities;
- Address inclusion of women, minorities, and children;
- Address disparities experienced by underserved minority and rural communities.

VI. References: Literature cited with complete literature citations including titles and all authors (use first three authors and "et al." for papers with more than five authors). Not included in 6-page limit.

VII. Budget Considerations:
Please carefully consider the following costs when developing your study budget(s):

- Leadership and staffing (PI/Co-PI, study coordinator, research staff, administrative support, paid/unpaid consultants, **cannot exceed NIH salary cap $189,600**). For more information regarding the change in salary cap: http://grants.nih.gov/grants/policy/salcap_summary.htm
- Training costs (includes travel/meal/lodging costs related to staff training);
- Biospecimen collection (sample supplies, shipping costs, storage fees, lab fees, assay kits);
- Costs associated with conducting Interviews and focus groups;
- Transcription software / services;
- Pharmacy charges, drug/placebo costs, lab fees, labels, shipping costs;
- Patient incentives and reimbursements;
- Conference call costs;
- Travel to scientific meetings (to present AIR-P study findings). This does NOT include attendance at the annual AIR-P research meeting.

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