



Request for Applications **Treatments for Gastrointestinal Dysfunction** **in Children and Adolescents with ASD**

I. Introduction

Autism Spectrum Disorders (ASD) are behaviorally defined by deficits in communication, social reciprocity, and repetitive stereotypic behaviors. Many children with ASD also experience co-morbid medical conditions that may be treatable. Conditions of particular concern include gastrointestinal (GI) dysfunction, sleep disorders, metabolic disorders, seizure disorders, hormonal imbalances, and nutritional/feeding issues including food allergies and limited food preferences. The prevalence of GI dysfunction and related symptoms, in particular, appears to be elevated in ASD compared to that of the general pediatric population, but the evidence base remains inadequate. The goal of this RFA is to stimulate research to systematically evaluate treatments for GI dysfunction among children and adolescents with ASD.

Autism Speaks invites applications for pilot grants to conduct research on treatments for co-morbid GI dysfunction in children and adolescents with autism. These proposals will be reviewed by a committee with expertise in pharmacology, clinical trials research, gastroenterology and clinical science.

Research projects may include studies of:

- Pharmacological treatments including currently available treatments that are not well studied in autism, or promising new compounds
- Biomedical interventions such as nutritional supplements or probiotics

Proposals should seek to accomplish one or more of the following objectives:

- Evaluate the efficacy or therapeutic benefit of pharmacological or biomedical treatments for GI dysfunction in children diagnosed with autism and ASD.
- Evaluate the safety of pharmacological or biomedical treatments for GI dysfunction in children and adolescents diagnosed with autism and ASD.
- Compare different pharmacological interventions for treating GI dysfunction in children diagnosed with autism and ASD.

II. Grant Categories and Funds Available

This RFA provides funding for pilot studies of treatments for co-morbid GI dysfunction in children and adolescents with autism. Study designs should be clearly defined so as to enable replications and/or expansions of the initial studies. Proposals for open label studies are eligible for submission.

Applicants may apply as a single site or as a collaboration between two sites. Autism Speaks will make one multi-site award or two single-site awards as determined by the quality of the applications, the efficient use of the funds requested, and the available financial resources of

Autism Speaks. A lead investigator must be identified for a multi-site award who will apply on behalf of both participating sites.

Number of Awards: 1 to 2

Award Amounts: \$75,000 per site, per year (up to three years)

Indirect Costs: An amount not to exceed 10% of direct costs may be given to the Sponsoring Institution for indirect (overhead) costs in addition to the grant amount.

Award Period: The grant will be awarded for a maximum period of three years in an amount not to exceed the maximum amount allowable per year based on the type of award funded. ***While applicants may request funding for a maximum of three years, proposals and applications will be judged, in part, by the efficient use of the funds requested. Applicants must demonstrate the need for the budgeted amounts in their proposal and application.***

III. Investigator Qualifications

Investigators holding full-time tenured or tenure-track faculty appointments or equivalent full-time non-tenure track appointments at accredited academic, medical or research institutions are eligible to apply. **A clinician who does not have an academic affiliation is required to collaborate with an individual with a track record in research at an academic or research institution.** Applications will NOT be accepted from individuals or proprietary organizations to support the research and development of products for profit.

Postdoctoral fellows and medical residents in their last year of training are eligible to apply, but must provide documented evidence of appointment to a full-time academic faculty position before an award will be made.

IV. Submission Requirements

A. Letter of Intent

- a. There is no preliminary Letter of Intent required.
- b. Applicants should submit a complete proposal according to the guidelines in section IV B and section V.

B. Electronic Proposal Submission: General Guidelines

- a. The applicant **must** submit a proposal through the Autism Speaks Grants Administration website at <http://grants.autismspeaks.org/research/login.asp>. **Only Proposals and Applications electronically submitted will be accepted for review.** Proposals or applications submitted by regular mail or by email will be returned without review. A successful electronic proposal submission will be confirmed by a system generated email notification to the applicant.
- b. Investigators new to the Autism Speaks submission process:
 - i. All new investigators are encouraged to review the layout and format of the grants administration system at least one month prior to the application deadline.

- ii. Each new applicant/investigator must first register with the grants system at http://grants.autismspeaks.org/research/signup_form.asp. Please be sure to choose the role “Investigator”. Please fill out the form completely.
- c. **Proposals are due no later than November 14, 2008 at 11:59 PM (EST).**
 - i. It is the applicant’s responsibility to ensure that the proposal is in compliance with the policies and procedures prescribed in the RFA.
 - ii. Additional proposal materials, such as updated pilot data, will NOT be accepted after the proposal deadline.
 - iii. Autism Speaks reserves the right to return without review any proposal found to be not in compliance with the policies and procedures prescribed on the RFA at any time during the application and review process.

V. Proposal Requirements

A. Information and Formatting

- a. Outlined below are the components that must be included with a full proposal. **Text should be 11 point Arial, with 1” margins. Applications with any sections that exceed the word or page limits will be returned prior to review.**
- b. Guidance on where to upload each of the required elements is provided in the outline below.

B. Registering Your Project

- a. Click on “Begin New Application”. While no Letter of Intent needs to be uploaded for this RFA, you do need to:
 - i. Enter the title of your project (less than 128 characters, spaces included)
 - ii. Select “Treatments for GI Dysfunction” (dropdown menu for Award Type) and choose the number of years.
 - iii. Choose 2-3 keywords germane to your proposal from the drop down menu (at least 2 keywords are required).
 - iv. To complete this section: Click on “Submit Pertinent Project Information” at the bottom of the page.

C. Institutional Info and Grant Contact

- a. “View” the Responsible Official (RO) to assign this role. The Responsible Official is someone from the applicant’s institution, other than the applicant, who can endorse the proposal.
- b. Look up your RO’s e-mail address. If your RO is not in the database, click on “Save Selected Contact” to add their record.

D. Scientific Abstract (maximum 350 words)

- a. Please state your specific hypothesis, and names and affiliations of all active collaborators. The abstract should state a brief synopsis of the research questions, the methods to be used, as well as the expected outcomes.
- b. This is uploaded in the system under “Keywords and Abstract”.

E. Layperson Abstract (maximum 350 words)

- a. The project summary must (1) be easily intelligible to a knowledgeable lay person or non-expert, (2) describe the project goal(s) and/or hypothesis, and (3) include expected results and their significance/relevance to the treatment of ASD and associated medical conditions.

- b. This is uploaded in the grant system under “Keywords and Abstract”
- F. Autism Speaks Research Priorities (1 page max)
- a. A one-page statement on how the proposed research will address Autism Speaks priorities, as well as how the project will answer a question addressing the treatment of GI dysfunction in children with autism spectrum disorders.
 - b. This is submitted in the grant system under “Relationship to our Priorities”.
- G. Research Plan (10 pages max). This should include:
- a. Background: Describe the theoretical framework, initial development, and existing empirical support for the treatment including:
 - i. The background for the study design;
 - ii. The expected therapeutic benefit(s) and the likelihood that the benefit(s) will outweigh any negative side effects;
 - iii. The selection of the targeted symptom(s)
 - iv. How the expected benefit(s) of the treatment will address the needs of the participating children and families, including specific functional outcomes;
 - v. How strong positive findings could be further evaluated in larger studies;
 - vi. The use of any biomarkers.
 - b. Study Design
 - i. Study participants should be from carefully selected populations and the selection criteria described and justified including: Sampling strategy, implementation and evaluation methods; assessment of therapeutic benefit(s); monitoring and reporting of side effects and toxicity; criteria and decision making process for suspending or terminating the study prior to completion; method for validation of the selected outcomes measures; the nature and relevancy of control groups (including the use of historical control groups); methods to control for confounding factors and bias (particularly for open-label studies); statistical power analysis; data analysis plan; potential limitations;
 - ii. Describe the feasibility of achieving study objectives within the funding period (including sample availability). Address any ethical issues implicit in study design.
 - iii. Other Treatments: Describe potential confounding factors or combined interventions (diet, medication etc.) that parents are using in addition to the primary treatment protocol, and their potential or known impact on the treatment protocol.
 - c. This should be one document, uploaded to “Experimental Plan and Methods” under “Research Plan”.
 - d. Please note that there are additional upload fields for relevant images, figures and graphics below “Experimental Plan”. Images uploaded in those fields will not be counted towards the 10 page maximum limit.
- H. Literature cited with complete literature citations including titles and all authors. This is uploaded under “Literature Cited - Bibliography”.
- I. Detailed budget for each year. **Applicants should ensure that their budget is in accordance with the RFA. Budgets which exceed the maximum amount will not be accepted by the grants system.** The budget may include:
- a. Personnel Costs (to be commensurate with the % effort dedicated to the project)

- i. Principal Investigator (up to 10% salary support)
 - ii. Technical research assistant salary and benefits
 - iii. Graduate Research Assistant or Postdoctoral Fellow stipend, benefits
 - b. Research supplies, services and related expenses
 - c. Essential equipment not to exceed \$5,000. If equipment should exceed the maximum of \$5,000, the investigator must justify the expense.
 - d. Consultants
 - e. Travel to professional meetings
 - f. Patient- or participant-related costs or reimbursements
 - g. Publication and data analysis costs
 - h. Overhead: An amount not to exceed 10% of direct costs may be given to the Sponsoring Institution for indirect (overhead) costs in addition to the grant amount.
 - i. Collaborations: If you are collaborating with a second site, put their total amount in "Other" and upload their line-item budget under "Budget Subcontract". Total indirect costs for both sites cannot exceed the maximum allowed.
 - j. Note: All budget fields must be filled in. If a line item does not apply, please write "0" in the amount, and "N/A" in the description field.
- J. Budget Justification (4 pages max)
 - a. The budget justification should address each category requested for each year.
 - b. The budget justification is uploaded in the "Budget" section.
- K. Resources and research environment (1 page max)
 - a. Describe the resources and environment that will support the successful completion of the project.
 - b. If the project will be utilizing existing samples and/or collecting samples, it should be specified how and when they will be used and shared with the autism community following the end of the project.
 - c. This should be uploaded under "Facilities & Resources".
- L. Letters of Collaboration, if needed. These are uploaded under "Collaborative Arrangements", under the "Other Attachments" section.
- M. Biographical Sketches of the Principal Investigator and named Co-Investigators in NIH format (4 pages max each)
 - a. Indicate education, complete citations (including title) of publications relevant to the proposed research and briefly describe currently funded research projects (especially clinical and research experience with pharmacological or other treatment in mental health disorders)
 - b. Submit these under the "Biographical Sketches" section of "Other Attachments"
- N. Current and pending grant support.
 - a. Indicate funding source, total award amount, award duration (inclusive dates) and project title; clearly explain any overlap with the proposed research including the extent to which the projects are redundant or complementary
 - b. Submit in "Current and Pending Support" under "Other Attachments".

O. Appendices

- a. Publications or other supporting files that are relevant to the application must be referenced in the research plan and may be uploaded to “Other Attachments” under the “Exhibits” section.
- b. A maximum of 3 peer reviewed research publications (including manuscripts under review or accepted for publication) will be accepted; however, manuscripts not yet accepted for review, review articles, book chapters, popular press articles and meeting abstracts will NOT be accepted.
- c. Appendix publications are provided as a courtesy to the reviewers who are under no obligation to read or consult them in evaluating a proposal.

P. Endorsing & Submitting the Proposal

Before the proposal can be submitted online, it needs to be endorsed by your institution.

- a. Enter a Responsible Official in “Institutional Info & Contacts”. A Responsible Official (RO) is someone at the applicant organization, other than the applicant/PI, who can endorse the proposal. On the RO line, click “View”. Enter in the contact’s email address and click “Look Up E-mail”. If they are not already in the system, click on Save Selected Contact and fill out their information.
- b. Once you have finished uploading files for your proposal, click on “E-Mail Responsible Official” in “Approvals & Status”. The RO will receive an email notification with instructions on endorsing your proposal. It is recommended you call or email this person to ensure they received this notification.
- c. The RO will be instructed to review the budget and proposal, and endorse in “Approvals & Status”. You will receive an email that endorsement is complete.
- d. You can now go into “Preview and Submit Proposal” to complete your submission.

VI. Review Process and Evaluation Criteria

Autism Speaks is committed to rapid review and funding of meritorious proposals.

Proposals will be evaluated using the following criteria:

A. Significance and Relevance

Does the proposal address an important autism-specific problem? Will the proposed research and expected results contribute new or important knowledge or methods to advance the goal(s) of understanding the treatment of associated GI dysfunction in autism? If the focus is on a novel treatment, does the proposed research emphasize the impact that such a project will make on knowledge of treatments and provide a replicable method?

B. Innovation or Expansion

Does the proposal develop innovative ideas or methods of research? Does the proposal challenge an existing paradigm, will it validate or replicate previous findings reported elsewhere or will it build on or leverage existing resources? How will the research project improve upon, or repeat, what has been reported elsewhere?

C. Approach

Is the experimental approach hypothesis-based or exploratory? If exploratory, will the approach result in testable hypotheses? Will the experimental design, methods and analyses achieve the stated aims of the proposal? Are the sample description, recruitment and diagnostic measures described? Is the treatment described in detail? Are the outcome measures described in detail? Was a power analysis conducted? Are potential problems and alternative approaches adequately addressed?

D. Investigators' Qualifications

Do the investigators have the appropriate training and experience to conduct the proposed research? Have they demonstrated satisfactory productivity and demonstrated abilities to conduct the research in which they are proposing to engage? Have necessary collaborations been established and documented with letters of agreement? If an investigator does not have the appropriate academic affiliation, has he or she collaborated with an individual with a track record in research at an academic or research institution?

E. Institutional Support

Does the applicant's institution provide an environment conducive to the research and experiment proposed? Do the investigators have access to necessary research resources (e.g. equipment, supplies, pharmacy services) either on site or off site? Has access to necessary special research equipment or facilities been appropriately documented with letters of agreement?

F. Appropriateness for the GI Treatment RFA

How will this project make an important contribution to developing appropriate treatments for co-morbid GI dysfunction in children with ASD? Is the budget described appropriate, given the type of study proposed?

G. Unique Ability to Answer the Questions Posed

Will the study design adequately address the specific aims as listed in the research grant? Does the proposed study leverage other Autism Speaks or federally funded initiatives, and what unique questions will this project answer?

VII. Review, Notification and Payment of Award (Subject to Change)

Funding selections and notification of awardees will be made in December 2008, with an expected award start date in January 2009.

Human Subjects Certifications must be documented with a copy of an official letter of approval (or equivalent for non-US applicants), which identifies the Principal Investigator, project title and date of approval, and is signed by the Review Committee Chair or equivalent responsible institutional/government official. Prior certification for another project cannot be substituted, but can be officially amended to include the proposed project (identified by project title).

IMPORTANT: IRB (or equivalent ethical) certification is NOT required to submit an application; however, IRB (or equivalent ethical) certification must be submitted as soon as possible following official notification of an award. Autism Speaks will NOT issue the first funding increment of a grant until this certification is received.

The first payment will be contingent upon receipt of the countersigned grant agreement letter and certification of ethics approval, if applicable. Subsequent payments on multiyear grants will be paid annually and will be contingent upon receipt and approval of interim progress and financial reporting. Interim reports are due 10 months after the start of the grant.

VIII. Contacts:

Please address questions about proposal submission using the web-based Grants Administration System to Joan New, Grants Assistant, jnew@autismspeaks.org or 609-228-7313. All other questions should be directed to Nancy Jones, Ph.D., Program Director, Autism Treatment Network/Clinical Trials Network at njones@autismspeaks.org or by telephone at 323-297-4754.