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TITLE: Treating Gastrointestinal and Autism Symptoms in Adults with Autism Using Microbiota Transfer Therapy (MTT)

PRINCIPAL INVESTIGATOR: James B. Adams

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5d. PROJECT NUMBER

5e. TASK NUMBER

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7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

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8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

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12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for public release – distribution unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

Purpose: The purpose of this study is to determine the safety and efficacy of Microbiota Transfer Therapy for adults with autism and chronic gastrointestinal problems.
Scope: The scope of the project is a randomized, double-blind, placebo-controlled trial of MTT for 84 adults with autism. The trial also includes an extension, partial cross-over, and long-term follow-up (6, 12, and 18 months). It includes extensive evaluation of autism-related and gastrointestinal symptoms, evaluation of microbiome composition, and blood safety tests. It includes 84 neurotypical controls (half with GI symptoms, half without) for comparison of baseline microbiota (no treatment for the neurotypical group).
Major findings: none to report yet

15. SUBJECT TERMS Autism; gastrointestinal problems; constipation; diarrhea; microbiota transplant; fecal transplant					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON USAMRMC
a. REPORT U	b. ABSTRACT U	c. THIS PAGE U	UU	18	19b. TELEPHONE NUMBER *(include area code)*

Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std. Z39.18

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1. **INTRODUCTION:** Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.

The purpose of this research is to investigate the use of a new treatment, Microbiota Transfer Therapy (MTT) for the treatment of adults with both autism and chronic gastrointestinal problems. The scope of the research involves a Phase 2 clinical trial to determine the safety and efficacy of MTT, and to investigate how to optimize the therapy to maximize benefit while minimizing risk.

2. **KEYWORDS:** Provide a brief list of keywords (limit to 20 words).

Autism; gastrointestinal problems; constipation; diarrhea; microbiota transplant; fecal transplant

3. **ACCOMPLISHMENTS:** The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction.

What were the major goals of the project?
List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

The original specific aims of the project are:
1) Conduct a multi-site, randomized, double-blind, placebo-controlled trial of MTT in 84 adults with ASD who also have gastrointestinal problems. Evaluate the efficacy of MTT in adults with ASD, including gastrointestinal symptoms and autism-related symptoms.
2) Evaluate the effect of MTT on gastrointestinal microbiota and biomarkers of GI health.
3) Compare the GI microbiota of adults with ASD vs. neurotypical controls, matched for age and gender, half of whom have similar GI symptoms
4) Validate the GSRS for adults with autism.

The original milestones and target dates for year 1, and the actual completion dates or % of completion, are shown below:

Milestone	**Original Target Date**	**Actual Completion Date or % Completed**
Subtask 1: Submit study plans to FDA and IRBs for approval	Sept-May	**Sept 2016-Aug 2017**
Submit modification of IND to FDA	Sept	**March 2017**
Respond to FDA	Oct	**March-April 2017**

Milestone Achieved: FDA approval of IND	Dec	**April 2016**
Submit to IRB and USAMRMC ORP HRPO	Jan	**May 2017 (IRB) and Aug 2017 (HRPO)**
Review feedback from IRBs and USAMRMC ORP HRPO	Feb	**May 2017-Aug 2017**
Final submission to IRBs and USAMRMC ORP HRPO	March	**Aug 2017 (IRB); still awaiting HRPO feedback**

What was accomplished under these goals?
For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

1) **Major Activities:** The major activities were writing all of the documents for the IND and IRB, and rewriting them as requested, and work on ACES-ASD, a smart-phone "App" for collecting data from participants and incorporating it into our central database.

2) **Specific Objectives:**
Subtask 1: Submit study plans to FDA and IRBs for approval
Submit modification of IND to FDA
Respond to FDA
FDA approval of IND
Submit to IRB and USAMRMC ORP HRPO
Review feedback from IRBs and USAMRMC ORP HRPO
Final submission to IRBs and USAMRMC ORP HRPO

3) **Significant Results/Key Outcomes**
   a. Permission from the FDA to proceed with our IND protocol (after two rounds of revisions)
   b. Approval of our IRB from NEIRB (after several rounds of revisions)
   c. Initial meeting of our Data Safety Monitoring Board (DSMB), who reviewed and approved the draft charter that we wrote, and reviewed and approved our plans for data and safety monitoring. If the DoD HRPO requests any significant changes to the protocol then they will meet again to review those.
   d. Creation of ACES-ASD, a software application ("App") for smart phones which we have created specifically for this research study in collaboration with ACES. This HIPAA-compliant app will enable participants to enter daily and weekly reports, engage in HIPAA-compliant texting with the study coordinators, and receive reminders about appointments and medications. ACES-ASD will allow study coordinators to monitor each participant's progress on a daily basis. ACES-ASD is coupled with a full database which will allow us to store all the data collected from the study. ACES-ASD is approximately 75% complete as of August 30 2017, and is expected to be completed by October 30 2017. We think that this App will be very convenient for participants, significantly enhance the monitoring by our study coordinators, and improve participant compliance with the study protocol.

4) Goals Not Yet Met

a) We are awaiting feedback from the DoD HRPO, and when we receive that we will make any changes requested and resubmit for final approval.

b) Recruitment: We will be ready to recruit participants after we have approval from the DoD HRPO.

c) IRB approval for the Arkansas site (we have been waiting to submit this for reasons discussed with the program manager Stan Niu).

Explanation of Delay: Our IND submission was delayed from September to March, since our industry collaborator Crestovo (who manufacturers the full-spectrum microbiota for our study) did not receive FDA approval of their product for investigational studies until February 2017. After that late start we have made good progress, and we hope that we can accelerate our recruiting and still finish the full project on-time, or possibly with a no-cost extension.

What opportunities for training and professional development has the project provided?
If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. "Training" activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. "Professional development" activities result in increased knowledge or skill in one's area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.

The Study Coordinator for the ASU site (Devon Coleman) has completed training for The Association of Clinical Research Professionals (ACRP) Clinical Research Coordinator Certification, and will take the exam in late September 2017. This has helped to better prepare her for her role as study coordinator for this study.

How were the results disseminated to communities of interest?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

Nothing to Report yet.

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

We hope to soon receive approval from the DoD HRPO of our study protocol. Once we have that approval we plan to begin recruiting and enrolling participants in our study.
Also, the site headed by Dr. Frye will submit their IRB protocol to NEIRB and HRPO, and also start recruiting and enrolling participants in our study.

4. **IMPACT:** Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:

What was the impact on the development of the principal discipline(s) of the project?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

Nothing to Report Yet

What was the impact on other disciplines?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

Nothing to Report Yet

What was the impact on technology transfer?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:

- *transfer of results to entities in government or industry;*

- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

Nothing to Report Yet

What was the impact on society beyond science and technology?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:
- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

Nothing to Report Yet

5. CHANGES/PROBLEMS: The Project Director/Principal Investigator (PD/PI) is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:

Changes in approach and reasons for change
Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.

1) Change in Study Protocol re. Vancomycin

There is no proposed change to Part 1 of our study, which is the randomized, double-blind, placebo-controlled trial.

However, there is a change to part 2, the partial cross-over. The change is that group B, which received placebo in part 1, will receive only the MoviPrep and Full Spectrum Microbiota in part 2, without the pre-treatment of vancomycin. This change would allow us to compare group B's response in part 2 to the treatment group's response in part 1, and determine if the pre-treatment with vancomycin (antibiotic) is needed or not. The rationale for this change is that, in our discussions with the FDA, they indicated

that they were curious if the pre-treatment was needed, as they would prefer to not include vancomycin if possible, to decrease the risk of complications or over-use of antibiotics.

This change was discussed with the DoD (Stan Niu) in October 2016 and approved by him.

2) **Change in Duration of Follow-Up:**
Our original grant proposal included a follow-up at 6 months after treatment ended. However, we have since learned from our Phase 1 study that the treatment appeared to result in continued improvement over the next 2 years. So, we added brief follow-ups at 12 and 18 months, so that we can better evaluate the full safety and efficacy of this treatment. This does not change the original study, but rather adds to it.

3) **Change in Dosing**
The dosage for the Full-Spectrum Microbiota for the initial dosing was changed from 2.5E12 to 1.2E12. The reason is that the pills were improved with double-encapsulation to better survive the stomach acid, allowing more live bacteria to survive. This also will also improve patient compliance, since fewer pills are needed.

This change was discussed with the DoD (Stan Niu) in March 2017 and approved by him.

4) **Change in GI questionnaire**
In our phase 1 study we used the GSRS to assess GI symptoms. This tool is for general GI symptoms, and is not specific to autism, because there was no GI questionnaire for autism that was validated. Between April 2016 and Sept 2016 Profs. Adams and Frye each received a small grant from Crestovo, and worked with them and RTI (a company that specializes in development of validated questionnaires for clinical trials) on the development of a new GI questionnaire specifically for autism, which we call the Gastrointestinal Stool and Symptom Questionnaire for Autism (GSSQA). This is the first GI questionnaire for autism which has been developed following the FDA guidelines for validated Patient Reported Outcome (PRO) measures. (See Appendix A for details on the development). So, although our original proposal included a plan to validate the GSRS, our current plan is to instead validate the GSSQA, since unlike the GSRS it is specific to autism and has been developed following the FDA's guidelines for PRO measures. The FDA has allowed the use of the GSSQA for the proposed Phase 2 study as an outcome measure, and this study will help validate it in two ways: 1) provide data on sensitivity to change after treatment, and 2) provide a comparison of GSSQA scores between individuals with autism and neurotypical controls.

Actual or anticipated problems or delays and actions or plans to resolve them
Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

The initial submission of our IND was delayed approximately 6 months due to waiting for FDA approval of the manufacturing methods by our industry partner, Crestovo. However, we used that time to improve the IND and IRB documents, so that FDA approval was relatively quick, partly due to very rapid responses from the FDA.

The review of our IRB protocol by New England IRB was delayed about 5 weeks because our primary reviewer at NEIRB left the company, and our submission was lost in their system until we realized the problem and a new reviewer was assigned. Then the review proceeded relatively quickly.

These two delays have set back our timeline somewhat, but we have partially recovered already, and we hope to accelerate recruiting once we have final approval to start.

Changes that had a significant impact on expenditures
Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

The delay in starting recruiting means that we spent significantly less at both sites in year 1 (only about 28% of the year 1 budget) , and will instead spend more in year 2 to accelerate recruiting.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents
Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

Significant changes in use or care of human subjects

No changes to report other than the changes in vancomycin use, longer period for follow-up, and change in FSM dosing reported above.

Significant changes in use or care of vertebrate animals.

Not Applicable.

Significant changes in use of biohazards and/or select agents

No changes to report.

6. **PRODUCTS:** List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."

- **Publications, conference papers, and presentations**
  Report only the major publication(s) resulting from the work under this award.

  Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to Report Yet.

  Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: Author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to Report Yet.

  Other publications, conference papers, and presentations. *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as*

noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.

Nothing to Report Yet.

- **Website(s) or other Internet site(s)**
  List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

Nothing to Report Yet.

- **Technologies or techniques**
  Identify technologies or techniques that resulted from the research activities. In addition to a description of the technologies or techniques, describe how they will be shared.

Nothing to Report Yet.

- **Inventions, patent applications, and/or licenses**
  Identify inventions, patent applications with date, and/or licenses that have resulted from the research. State whether an application is provisional or non-provisional and indicate the application number. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

Nothing to Report Yet.

- **Other Products**

  Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment, and/or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:

  - *data or databases;*
  - *biospecimen collections;*
  - *audio or video products;*
  - *software;*
  - *models;*
  - *educational aids or curricula;*
  - *instruments or equipment;*
  - *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
  - *clinical interventions;*
  - *new business creation; and*
  - *other.*

We are developing ACES-Autism, an "App" for smart phones for data entry by study participants for this study. It is approximately 75% complete.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change."

Name:	**James B. Adams**
Project Role:	**Principal Investigator**
Research Identifier:	
Nearest person month worked:	**3 months**
Contribution to Project:	**Primary author of IND and IRB documents**
Funding Support:	**ASU (2 months) and this DoD grant (3 weeks)**

Name:	**Devon Dale**

Project Role: **Study Coordinator**
Research Identifier:
Nearest person month worked: **3 months**
Contribution to Project: **Assisted with IND and IRB documents**
Funding Support: **this DoD grant**

Name: **Richard Frye**
Project Role: **Co-Principal Investigator**
Research Identifier: **0000-0003-4442-2937**
Nearest person month worked: **1 month**
Contribution to Project: **Assisted with IND and IRB documents**
Funding Support: **this DoD grant**

Name: **Leanna Delhey**
Project Role: **Database Coordinator**
Research Identifier:
Nearest person month worked: **3 months**
Contribution to Project: **Worked with the ACES app**
Funding Support: **this DoD grant**

Name: **John Slattery**
Project Role: **Study Coordinator**
Research Identifier:
Nearest person month worked: **5 months**
Contribution to Project: **Assisted with IND and IRB documents, and ACES app**
Funding Support: **this DoD grant**

Name:
Project Role:
Research Identifier:
Nearest person month worked:
Contribution to Project:
Funding Support:

Name:
Project Role:
Research Identifier:
Nearest person month worked:
Contribution to Project:
Funding Support:

Name:
Project Role:
Research Identifier:
Nearest person month worked:
Contribution to Project:
Funding Support:

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

In October 2016 we received a small grant ($28,000) from Crestovo to conduct a follow-up on the 18 participants in our Phase 1 study of MTT. The data analysis is now mostly complete, and we are writing up the results for publication. This grant has helped us better prepare for this study.

What other organizations were involved as partners?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.
Provide the following information for each partnership:
Organization Name:
Location of Organization: (if foreign location list country)
Partner's contribution to the project (identify one or more)

- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner's facilities for project activities);*
- *Collaboration (e.g., partner's staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); and*
- *Other.*

Organization Name: Crestovo
Location of Organization: Cambridge, MA
Partner's contribution to the project: development of Full Spectrum Microbiota, and supply of it for this project.

Organization Name: ACES Health, Inc.
Location of Organization: Atlanta, GA
Partner's contribution to the project: development of an "App" for smart phones for data entry by participants

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: For collaborative awards, independent reports are required from BOTH the Initiating PI and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to **https://ers.amedd.army.mil** for each unique award.

QUAD CHARTS: If applicable, the Quad Chart (available on https://www.usamraa.army.mil) should be updated and submitted with attachments.

9. APPENDICES: Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.

Appendix 1 – Development of Gastrointestinal Stool and Symptom Questionnaire for Autism (GSSQA)

Our Phase 1 study used two methods for evaluating GI symptoms, a Daily Stool Record (based on the Bristol Stool Form Scale) and the GSRS which was a comprehensive assessment of symptoms, but not specific to autism. Currently, although several GI assessment tools for autism have been developed, none have been validated for individuals with autism. The GSSQA was developed by Research Triangle Institute in collaboration with Prof. Adams at Arizona State University and Prof. Richard Frye at University of Arkansas. The GSSQA was developed to be the first clinical assessment tool for GI symptoms in individuals with ASD that is designed specifically to meet FDA guidelines for a Clinical Outcome Assessment (COA). Due to the communication challenges inherent to individuals with ASD, and since they also often have cognitive and executive function challenges, it was decided that a Patient-Reported Outcome (PRO) was not appropriate, and that instead an Observer-Reported Outcome (ObsRO) measure was needed. The development included the following steps:

1) Review of the literature on GI symptoms in autism, and review of existing GI assessment tools (both for autism and other conditions).
2) A draft conceptual framework was developed for GI symptoms in autism.
2) Concept elicitation interviews (1 hour each) were held with 22 mothers of children with autism ages 4-17 years. In 9 cases their children also participated in the interviews. Parents completed a daily stool record for approximately 7 days prior to the interviews, to become fully aware of their child's stool habits.
3) Based on the interviews, a saturation grid of symptoms and a table of concept endorsement was developed.
4) The conceptual framework was revised, and a list of items for the GSSQA was developed by RTI staff, and Prof. Adams and Prof. Frye.
5) An expanded advisory board including Drs. Adams, Frye, and four other experts reviewed the conceptual framework and item list.
6) A draft GSSQA was evaluated by cognitive debriefing with an additional group of 20 parents of children with ASD, after they had used the GSSQA for approximately 1 week. The cognitive debriefing was done in 3 rounds, and after each round the GSSQA was revised and then evaluated by a different set of parents. At the end of three rounds, the final GSSQA was developed.

The final GSSQA consists of two parts, a Daily Stool Log (DSL) and a Once-Weekly GI Signs Questionnaire (OWGISQ). The DSL includes both evaluation of stool using the Bristol Stool Form Scale, and daily symptoms that are observable, such as soiling, rushing to the toilet, passage of an unusually large stool, and signs of pain or distress. The OWGISQ assesses the frequency of a variety of other GI symptoms.

The GSSQA was developed for children with ASD ages 4-17 years, but based on our clinical and research experience, we believe that adults with ASD have very similar GI problems to children with ASD. Therefore, we propose to use the GSSQA on an experimental basis for this Phase 2 study, and to use the results to try to validate the GSSQA for adults with autism, and determine if it is sensitive to change during the clinical trial.