THE UNIVERSITY OF CHICAGO
The Division of the Biological Sciences ● The University of Chicago Medical Center

CONSENT/AUTHORIZATION FOR PARTICIPATION IN A RESEARCH PROTOCOL

Protocol Number: 19-0017 Name of Subject: _____
Medical History Number: _____

STUDY TITLE: An Open-Label Study of Glutathione in Children with Autism Spectrum Disorder

Doctors Directing Research: Dr. Karam Radwan
Address: University of Chicago Medical Center Department of Psychiatry
5841 South Maryland Avenue, MC 3077
Chicago, IL 60637
Telephone Number: 773-834-6686

KEY INFORMATION

We are asking you to choose whether or not to volunteer for a research study about using Glutathione supplement in children with Autism Spectrum Disorder. This section is to give you key information to help you decide whether or not to participate. We have included detailed information after this page. Ask the research team questions. If you have questions later, the contact information for the research investigator in charge of the study is above.

WHAT IS THE STUDY ABOUT AND HOW LONG WILL IT LAST?

The purpose of this research is to gather information on the safety and feasibility of using Glutathione as supplement in children with Autism Spectrum Disorder. Glutathione is a US FDA Notified GRAS (Generally recognized as safe) dietary supplement. The supplement is being used in the study for an alternate use than its labeling indications. Labeling indications are listed as detoxification and improving liver function, fitness and lipid metabolism; however, its use in children with Autism Spectrum Disorder has not been tested and is experimental.

You and your child's participation in this research will last about 3.5 months. It will entail a blood draw (two teaspoons) for your child at the beginning and (two teaspoons) at the end of the study to assess their Glutathione level. You will also be giving your child the Glutathione supplement at home (with scheduled dosing recommendations from the study doctors). The study includes, six bi-weekly clinic visits for you to complete research questionnaires related to your child's behavior and to also check your child's vitals and screen for any supplement side effects at each visit.

For children who can not swallow the Glutathione capsules, you will be asked to open the capsules and mix the contents with a non-acidic food item, such as apple sauce or yogurt to help them ingest the Glutathione. Please ensure that they completely ingest the mixed food source during the scheduled administrations. For children and adolescents who are able to swallow capsules whole, they should take the capsules swallowed whole with water.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE TO VOLUNTEER FOR THIS STUDY?

The main potential benefit and reason why you and your child may want to volunteer to participate in this study is that the study supplement (Glutathione) may help to decrease your child's irritability, problem behaviors and reduction in aggression in general, but there is no guarantee that the study supplement will help. For a complete description of benefits, refer to the Detailed Consent.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE NOT TO VOLUNTEER FOR THIS STUDY?

The most common side effects associated with Glutathione include; upset stomach, diarrhea, dizziness, dry mouth or headaches and sometimes, but rarely a skin rash, skin flushing or respiratory distress can be seen. As such, patients with asthma or allergies that have resulted in respiratory distress in the past will not be included in this study to ensure safety. For a complete description of risks, refer to the Detailed Consent.

If you and your child decide not to participate in the study, alternative options are receiving psychotropic medications or other treatments. While no supplement has been approved for the treatment of children and adolescents with problem behaviors related to Autism Spectrum Disorder, treatments without medication or supplements are available, including individual or group psychotherapy and behavioral therapy. Another option is receiving no treatment at all, as it is the choice of you and your child to receive any treatment or not. For a complete description of alternative treatment procedures, refer to the Detailed Consent.

DO YOU HAVE TO TAKE PART IN THE STUDY?

Taking part in this study is voluntary. If you and your child decide to take part in the study, it should be because you and your child really want to volunteer. You and your child will not lose any services, benefits or rights that you and your child would normally have if you choose not to volunteer.

You and your child may choose not to participate at any time during the study. You and your child will not lose any services, benefits or rights you and your child would normally have if you and your child choose to leave the study. The University of Chicago/University of Chicago Medical Center will not condition (withhold or refuse) treating you and your child on whether you sign this Authorization or revoke you and your child's authorization at a later time. If you do not sign this form, you and your child will not receive the research-related intervention(s).

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS OR CONCERNS?

The person in charge of the study is Dr. Karam Radwan of the University of Chicago. If you or your child have questions, suggestions, or concerns regarding this study or you and your child want to withdraw from the study his contact information is:

Dr. Karam Radwan
University of Chicago Medical Center Department of Psychiatry
5841 South Maryland Avenue, MC 3077
Chicago, IL 60637

Telephone Number: 773-834-6686
If you or your child has a research related injury, you should immediately contact Dr. Radwan (the study doctor) immediately at 773-834-6686. Or at 773-834-8037
For questions about you and your child's rights as research subjects, please contact the University of Chicago BSD IRB at 773-702-6505.

DETAILED CONSENT

WHAT IS INVOLVED IN THE STUDY?
About 24 children and 24 parents will take part in this study at the University of Chicago. A total of 48 subjects (children and parents will be included in this study).

If your child is eligible for our study we will ask you to administer daily Glutathione supplements to your child twice a day for a 12-week period. Glutathione is administered in capsule form (a pill). The dosages will be evaluated throughout the study and adjusted as needed. Glutathione is a dietary supplement that is available without a prescription online and in many health food stores. Glutathione is also found naturally in the human body. As a supplement it has been used for many purposes, including detoxification and improving liver function, fitness and lipid metabolism; however, its use in treating problem behaviors in children with Autism Spectrum Disorder is experimental.

In order to determine if your child is eligible to participate in the study, the following will take place:

- The study will be discussed with you and your child and you will be asked to sign this consent form.
- A review of your child's medical history will be completed and a review of the medicines she/he has taken and any past treatments for problem behaviors will be completed.

If your child is eligible for our study we will collect data on your child during 6 scheduled bi-weekly research clinic visits. This study will include 6 study visits to the clinic, and each visit will take between one and two hours. Total duration of the study is 3.5 months.

At the first study visit, we will ask you to fill out two questionnaires regarding your child's recent behavioral problems. We will ask you to fill out these questionnaires at every visit again during the study. We will also draw two teaspoons of blood from your child to determine his/her initial level of Glutathione. We will repeat the blood draw (two teaspoons of blood) at the 5th study visit. A total of 4 teaspoons of blood will be collected for the study.

Also, at the first visit, a urine sample will be tested for drug use, and if the child is a female capable of having a child, the sample will be tested to ensure that she is not pregnant at the time of study entry. The pregnancy test must be negative for the child or adolescent to participate in the study.

Glutathione supplements will begin following baseline screening.
During each study visit, we will perform basic, routine, non-invasive medical tests on your child

that assess their heart rate, blood pressure, temperature, weight and height.

During each study visit, we will ask you to indicate how often you administered the supplement to your child since the last visit and to fill out a checklist of possible side effects that your child may have experienced since the last visit. This information will be used by your study investigators to modify the dosage.

Your child's condition at each visit will also be evaluated by the study doctors using a standardized questionnaire for research purposes.

In the future, identifiers associated with your child's data and/or specimens could be removed from the data and specimens. The de-identified data and specimens could then be used for future research by our research team or other researchers without notifying you or asking your permission for this use.

The research study schedule is as follows:

Consent and Screening:	Today
Visit 1:	Child's next visit in approximately 2 weeks
Visit 2 – Visit 5:	Approximately every 2 weeks
Visit 6:	Final study visit, approximately 14 weeks from today.

Please refer to table on the next page for further clarification of visit details:

SUMMARY OF DATA COLLECTION AND STUDY PROCEDURES BY VISIT							
		Visits (to occur every 2 weeks, ± 2days)					
	Screening	**1**	**2**	**3**	**4**	**5**	**6**
Inclusion/ Exclusion Criteria	X						
Consent Forms:	X						
Medical Procedures on Child							
Blood draw: 2 tsp (Glutathione Levels)	X					X	
Vital Signs	X	X	X	X	X	X	X
Urine Drug Screen/Urine Pregnancy Test	X						
Glutathione Dosing (dispensed at subjects' homes by parent)		X	X	X	X		
Parent Reports on Child							
Aberrant Child Checklist	X	X	X	X	X	X	X
Social responsiveness Scale	X						X
Clinical Global Impression Scale	X						X
Glutathione Side effects checklist		X	X	X	X	X	X
Adverse Event Report		X	X	X	X	X	X

Vineland-3	X						X
Parent Rated Anxiety Scale -ASD	X						X

Clinically relevant research results, including individual research results, can be disclosed to you and your child with a written signed release of information form upon completion and finalization of the study.

Dr. Radwan may decide, if necessary, to take your child off of the study without your consent if:

- You or your child are unable to meet the requirements of the study;
- Your child's medical condition changes;
- The study supplement is no longer available;
- New information becomes available that indicates that participation in this study is not in your child's best interest; or
- If the study is stopped.

WHAT ARE THE RISKS OF THE STUDY?

All supplements can cause side effects, but are typically safe. Side effects are usually reversible when the supplement is stopped. If your child experiences any side effects, you should contact the study doctors immediately.

The most common side effects associated with Glutathione include (likely, but not serious):

- upset stomach
- diarrhea
- dizziness
- dry mouth
- headaches

Additionally, if your child experiences the following you should let the study doctor or staff know right away (less likely, but can be serious):

- a skin rash
- skin flushing
- **respiratory distress (i.e., problems breathing or chest tightening)**

The risks of blood draws involved in this research include: pain, a bruise at the point entry of the needle, redness and swelling of the vein and infection, and a rare risk of fainting.

Loss of confidentiality is also a potential risk with participation in research. Therefore, confidentiality cannot completely be guaranteed. Confidentiality of data concerns safeguarding information that has been given voluntarily for the purpose of research. Breach of confidentiality may result in psychological harm to some individuals, which can include: stress, embarrassment, social harm, and/or guilt.

An additional incidental finding during the research study may be a depressed mood. The study supplement has not been found to cause depression in the past; however, it is not guaranteed that the study supplement will not affect your child's mood.

There may be other risks that could arise which are not reasonably foreseeable. If new information becomes available which could influence you or your child's willingness to continue, this new information will be discussed with you.

ARE THERE ANY BENEFITS TO TAKING PART IN THE STUDY?

We cannot promise that you and your child will benefit from participating in this study. However, possible benefits are that the study supplement may help to decrease your child's irritability and problem behaviors (i.e. temper tantrums, aggressive behavior toward self and others), but there is no guarantee that the study supplement will help. While taking the study supplement, your child's condition may remain the same or worsen due to no effect of the study supplement. The information learned from this study may or may not benefit other children and adolescents with Autism Spectrum Disorder in the future.

WHAT OTHER OPTIONS ARE THERE?

Instead of being in this study, you have these options:

- Receiving psychotropic prescribed medications. While no supplement has been approved for the treatment of children and adolescents with problem behaviors related to Autism Spectrum, treatments without medication are available, including individual and group psychotherapy and behavioral therapy.
- Receiving no treatment.

The decision whether or not you wish to have your child participate in this study will not affect her/his care at the University of Chicago Medical Center.

WHAT ARE THE COSTS?

Clinical services provided during a clinical trial are either research-related or related to usual medical care. Research-related services are done to complete the research and the costs are not the responsibility of you or your insurance.

The costs that are considered research-related for this study include the following: All Glutathione for the duration of the 12 weeks, two blood draws (2 teaspoons each) for Glutathione levels, physical exams, urine pregnancy tests, urine drug tests, and interviews with the study doctors.

Usual medical care costs include any and all services that are considered medically necessary for your child's disease. The cost of this usual, ongoing medical care will be the responsibility of you or your insurance, and may include deductibles and co-payments. Similarly, this care will be subject to all the same requirements and restrictions of your insurance. Once the study has concluded, the continuation of care from a mental health provider will be the responsibility of you and/or your insurance.

If you have questions about whether specific clinical services are research related or part of your usual medical care, please speak to your physician or research contact person.

WHAT HAPPENS IF I HAVE AN INJURY?
If you have a research related injury, you should immediately contact Dr. Radwan or (the study doctor) immediately at 773-834-6686 or 773-834-8037

If you or your child suffers an unanticipated injury as a direct result of this research and require emergency medical treatment, the University of Chicago Medical Center will provide such treatment at the University of Chicago Medical Center at no cost to you. You must notify Dr. Radwan as promptly as possible after the injury in order to receive this care. An injury is "unanticipated" if it is not one of the known effects of a study supplement, medical device or procedure, and is not the result of your child's disease or condition. The costs of any non-emergency care for such an injury will be billed to you or your insurance in the ordinary manner. If you think that you or your child may have suffered a research related injury, you must let Dr. Radwan right away.

WILL I BE PAID FOR MY PARTICIPATION?
You and your child will not be paid to participate.

WHAT ABOUT CONFIDENTIALITY?
Study records that identify you or your child will be kept confidential. All records will be kept in a secure office in a locked cabinet of the Child & Adolescent Psychiatry Department at the University of Chicago. Only study staff will have access to study records. The data collected in this study will be used for the purpose described in the form. The results from tests and/or procedures performed as part of this study may become part of your child's medical record. Any research information in your child's medical record will be kept indefinitely.

During this study, Dr. Karam Radwan and his research team will collect protected health information (PHI) about your child for the purposes of this research. The research team includes the individuals listed on this consent form and other personnel involved in this study at the University of Chicago. Protected Health Information (PHI) consists of phone numbers, e-mail addresses, and date of birth and any health information that is collected about your child, which could include medical history and new information collected as a result of this study. This information will also include the following: Child and parent(s) names, parents' contact information, basic demographic information (such as child's age, gender, and race), family and other history, medical records number, medical and medication history, and responses from questionnaires. The research team includes the individuals listed on this consent form and other personnel involved in this study at the University of Chicago.

As part of the study, Dr. Karam Radwan and his research team will share information about your child as well as the results of your child's study-related procedures and tests with a Central Lab for the blood draws. These include your child's medical record number and name. This information is being sent to ensure proper and safety tracking of blood draws to assess glutathione levels in your child at the start of the study (baseline) and at the end of the study.

Your child's records may be reviewed by federal agencies whose responsibility is to protect human subjects in research including the Food and Drug Administration (FDA) and Office of

Human Research Protections (OHRP). In addition, representatives of the University of Chicago, including the Institutional Review Board, a committee that oversees the research at the University of Chicago, may also view the records of the research. If your research record is reviewed by any of these groups, they may also need to review your child's entire medical record.

Once information is shared outside the University of Chicago, please note that your identifiable health information may be shared with someone else. The same laws that the University of Chicago must obey may not protect your health information.

During your child's participation in this study, you will have access to their medical record. Dr. Radwan is not required to release to you research information that is not part of your child's medical record.

This consent form will be kept by the research team for at least six years. The study results will be kept in your child's research record and be used by the research team indefinitely.

At the time of study completion, either the research information not already in your child's medical record will be destroyed or information identifying you or your child will be removed from study results.

Data from this study may be used in medical publications or presentations. You and your child's name and other identifying information will be removed before this data is used. If we wish to use identifying information in publications, we will ask for your approval at that time.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

WHAT ARE MY RIGHTS AS A PARTICIPANT?

If you and your child choose to no longer be in the study and do not want any of their future health information to be used, you must inform Dr. Radwan in writing at the address on the first page. Dr. Radwan and may still use your child's information that was collected prior to your written notice.

We will tell you about significant new information that may affect you and your child's willingness to stay in this study.

You will be given a signed copy of this document. Your authorization to use and disclose your child's health information does not have an expiration date.

CONSENT

SUBJECT
The research project and the procedures associated with it have been explained to me. The experimental procedures have been identified and no guarantee has been given about the possible results. I will receive a signed copy of this consent form for my records.

I agree to participate in this study. My participation is voluntary and I do not have to sign this form if I do not want to be part of this research study.

Signature of Subject: _____

Date: _____ Time: _____ AM/PM (Circle)

PERSON OBTAINING CONSENT
I have explained to _____the nature and purpose of the study and the risks involved. I have answered and will answer all questions to the best of my ability. I will give a signed copy of the consent form to the subject and family.

Signature of Person Obtaining Consent: _____

Date: _____ Time: _____ AM/PM (Circle)

INVESTIGATOR/PHYSICIAN:
Signature of Investigator/Physician _____

Date: _____ Time: _____ AM/PM (Circle)

PARENT/GUARDIAN/ OR LEGALLY AUTHORIZED REPRESENTATIVE:
I give my permission for my child/relative/the person I represent to participate in the above described research project.

Signature of Parent/Guardian/ or Legally Authorized Representative: _____
Date: _____ Time: _____ AM/PM (Circle)