Informed Consent Document

Title: Sulforaphane Treatment of Children with Autism Spectrum Disorder (ASD).

NCT: *NCT02561481*

Document Date: *11/28/2016, most recently approved by IRB 07/03/2019*

UNIVERSITY OF MASSACHUSETTS MEDICAL SCHOOL
COMMITTEE FOR THE PROTECTION OF HUMAN SUBJECTS IN RESEARCH

CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Title of research study: Sulforaphane Treatment of Children with Autism Spectrum Disorder (ASD)

Investigator: Andrew W. Zimmerman, MD

Sponsor: United States Department of Defense

Please read this form carefully. It tells you important information about a research study. A member of our research team will also talk to you about taking part in this research study. People who agree to take part in research studies are called "subjects." This term will be used throughout this consent form.

If you have any questions about the research or about this form, please ask us. Taking part in this research study is up to you. If you decide to take part in this research study, you must sign this form to show that you want to take part. We will give you a signed copy of this form to keep.

If you are being asked to give permission for someone else to be in this research study, as you read this consent form, "you" always refers to that person.

Why are you being invited to take part in a research study?

You are being asked to participate because you are between the ages of 3-12 years and have autism.

What should you know about a research study?

Your participation is entirely voluntary.

You do not have to be in this research study. If you join the study, you can stop or leave at any time with no changes in the quality of the health care you receive.

You will be told about any new information or changes in the study that could affect you.

You can ask all the questions you want before deciding if you want to be in this study.

Why are we doing this research?

We are doing this research study to find out if a drug called sulforaphane can help people with autism spectrum disorder (ASD). We also want to find out if sulforaphane is safe to take without causing too many side effects. Sulforaphane is present in extracts of broccoli seeds. The amount of sulforaphane used in this study is however higher than what can be reasonably obtained

through food. We will use an extract of broccoli seeds that is treated in the laboratory to increase the concentration of sulforaphane.

Sulforaphane is an investigational drug. This means that it is not approved by the U.S. Food and Drug Administration (FDA).

How long will the research last?

We expect that you will be in this study for 36 weeks after enrollment. During this time, we will ask that you visit UMass 6 times.

How many people will be studied?

We expect about 50 people will be in this study at UMass Memorial Health Care.

Will I definitely receive the experimental drug?

For the first half of the study you will get either Sulforaphane or a placebo. A placebo is an inactive substance that looks exactly like the experimental drug, but is not expected to have any medical effects. The decision to give you Sulforaphane or placebo will be made by chance, like flipping a coin. Neither you nor the study doctor will choose what you get. You will have an equal chance of being given Sulforaphane or placebo. Neither you nor the study doctor will know what you are getting. In an emergency, a doctor can find out what you are taking by calling (508) 334-1000 and having the operator page the on-call Investigational Pharmacist.

For the second half of the study, all study participants will receive Sulforaphane, including those who received placebo previously.

What happens if I say yes, I want to be in this research?

If you choose to take part in this study, we will ask you to sign this consent form before we do any study procedures. During your participation in the study, we will ask that you visit UMass 6 times. We will draw a total of 5 tablespoons of blood over the entire course of this research study.

Visit 1: Screening/Baseline Visit

The Screening Visit will take about 2.5 hours to complete. During this visit, we will take a history and do an examination to see if you qualify to take part in this research study. The study doctor will review the results of these tests and procedures. If you don't qualify, the study doctor will tell you why.

At this visit, we will:

- Ask about your medical history

- Do a physical exam and check your vital signs (blood pressure, temperature, heart and breathing rates).
- Conduct a play- or social communication-based test, known as the Autism Diagnostic Observation Schedule (or ADOS). During this test we will ask you to complete a series of activities. These activities allow us to assess your social ability. This will consist of simple activities, such as- story-telling, make-believe play, social interaction or imaginative use of materials.
- Draw a blood sample and ask for a urine sample.

You do not have to do the ADOS testing if this test has been performed on you in the past 3 years and the results of the testing are available.

At this visit, we will also:

- Ask parents/guardians questions to determine the IQ, ASD severity, social responses and behaviors.

Taking the study drug:

We will first need to review your blood test reports to ensure that it is safe for you to participate and until we get the lab test results back (which usually takes less than a day).

- If the lab results are normal, we will mail you an 8 week supply of study drug to take home with you. Alternately we could give you a call and you can pick up the study drug from us. We will give you detailed instructions on how to take the drug and how to contact us if you have problems or questions.
- If the lab results are not normal, we will call to inform you that you are not eligible to take part in the study.

Telephone survey 1: 3 weeks:

In order to safeguard your child's safety, we will conduct a telephone survey at 3 weeks. This will help us ensure that she/she does not experience any unwanted side effects from taking the study drug. This survey will take around 15 minutes to complete. During this phone call we will ask you questions about your child's health since starting the study. We will ask you questions about any side effects that your child may have experienced since starting the study drug.

Visit 2: 7 week follow-up visit

You will return to the clinic 7 weeks after you start taking the study drug. Please bring all of your unused study drug and your study diary with you. This visit should take about 1.5 hours to complete. At this visit we will:

- Do a physical exam and check your vital signs (blood pressure, temperature, heart and breathing rates)
- Ask you about side effects or health problems since your last visit

- Draw a blood sample and ask for a urine sample

At this visit, we will also:

- Ask parents/guardians to complete questionnaires. These questionnaires will ask questions to determine disease severity, social responses and behaviors.

At this visit, we will give you a 7 week supply of study drug to take home with you. You should still have 1 week of drug supply left with you from your last visit. You should finish the study drug from the first lot before starting the second lot. You should keep taking the drug unless we tell you to stop. We will review the results of your blood tests to see if there are any side effects.

If your test results are not normal, we will call you and ask you to stop taking the drug for 2 weeks. We will then ask you to return to UMass for another blood test.

- If at this time the test results are normal, we will ask you to restart the study drug.
- If the test results are still not normal, you will not start taking the study drug again. If this happens, we will ask you to return for a final visit. More information about this visit is included in the "**what happens if I say yes, but I change my mind later"** section of this document.

Visit 3: 15 week follow-up visit

You will again come for a visit 15 weeks after you start the drug. This visit should take about 1.5 hours to complete. During this visit, we will:

- Do a physical exam and check your vital signs (blood pressure, temperature, heart and breathing rates)
- Ask you about side effects or health problems since your last visit
- Draw a blood sample and ask for a urine sample

At this visit, we will also:

- Ask parents/guardians to complete questionnaires. These questionnaires will ask questions to determine disease severity, social responses and behaviors.

After this visit all participants (whether originally in the sulforaphane or placebo group) will be assigned to receive the active study drug, sulforaphane. At this visit therefore we will give you an 8 week supply of sulforaphane to take home with you. You should keep taking the drug unless we tell you to stop. We will review the results of your blood tests to see if you are having any side effects.

If your test results are not normal, we will call you and ask you to stop taking the drug for 2 weeks. We will then ask you to return to UMass for another blood test.

- If at this time the test results are normal, we will ask you to restart the study drug again.
- If the test results are still not normal, you will not start taking the study drug again. If this happens, we will ask you to return for a final visit. More information about this visit is

included in the "**what happens if I say yes, but I change my mind later"** section of this document.

Telephone survey 2: 18 weeks:

In order to safeguard your child's safety, we will conduct a telephone survey at 18 weeks. This will help us ensure that she/she does not experience any unwanted side effects from taking the study drug. This survey will take around 15 minutes to complete. During this phone call we will ask you questions about your child's health since starting the study. We will ask you questions about any side effects that your child may have experienced since starting the study drug.

Visit 4: 22 week follow-up visit

Visit 4 will take about 1.5 hours to complete. At this visit, we will:

- Do a physical exam and check your vital signs (blood pressure, temperature, heart and breathing rates)
- Ask you about side effects or health problems since your last visit
- Draw a blood sample and ask for a urine sample

At this visit, we will also:

- Ask parents/guardians to complete questionnaires. These questionnaires will ask questions to determine disease severity, social responses and behaviors.

At this visit we will give you a 7 week supply of Sulforaphane to take home with you. You should still have 1 week of drug supply left with you from your last visit. You should finish the study drug from previous lot before starting the new lot. You should keep taking the drug unless we tell you to stop. There will be no blood or urine tests at this visit.

Visit 5: 30 week follow-up visit

Visit 5 will take about 1.5 hours to complete. At this visit, we will:

- Do a physical exam and check your vital signs (blood pressure, temperature, heart and breathing rates)
- Ask you about side effects or health problems since your last visit
- Draw a blood sample and ask for a urine sample

At this visit, we will also:

- Ask parents/guardians to complete questionnaires. These questionnaires will ask questions to determine disease severity, social responses and behaviors.

At this visit we will not give you any more study drug to take. Please bring with you and return to us all unused study drug.

Visit 6: 36 week follow-up visit

Visit 6 will take about 1.5 hours to complete. At this visit, we will:

- Do a physical exam and check your vital signs (blood pressure, temperature, heart and breathing rates)
- Ask you about side effects or health problems since your last visit
- Draw a blood sample and ask for a urine sample

At this visit, we will also:

- Ask parents/guardians to complete questionnaires. These questionnaires will ask questions to determine disease severity, social responses and behaviors.

After You Complete the Study

After you complete the study, we will refer you back to your own doctor for your ongoing medical care. Since Sulforaphane is not approved by the FDA to treat autism, your doctor will not be able to prescribe Sulforaphane for your treatment.

What are the risks of being in this study?

Possible mild side effects from taking sulforaphane include:

- Flatulence (passing bowel gas)
- Gas belching, indigestion
- Soft stool
- Frequent urination
- Weight gain
- Difficulty sleeping

There may be a very slight increased risk of having a seizure. However since patients with ASD have a naturally higher chance of seizures than persons without ASD, we will take your detailed medical history at the outset of the study to ensure that you do not have a past history (within one year) of seizures. There may be other risks of sulforaphane that are currently unknown.

As with any drug, an allergic reaction can occur. Allergic reactions can be mild or more serious, and can even result in death. Common symptoms of an allergic reaction are rash, itching, skin problems, swelling of the face and throat, or trouble breathing. If you think you are having an allergic reaction, call the study doctor right away. If you are having trouble breathing, call 911 immediately.

Risks of Taking Sulforaphane with Other Medications

We do not know of any risks of taking sulforaphane with other medications. For your safety during this study, call your study doctor BEFORE you take any:

- New medications prescribed by your own doctor
- Other medications sold over-the-counter without a prescription
- Dietary or herbal supplements

It is important that you not take any other commercially available supplements while you are participating in this study.

Risks of Blood Draws

The risks of having blood drawn include slight pain when the needle is inserted. If you want, we may apply a little numbing cream at the site of blood draw to reduce the pain associated with the needle. You may develop a harmless black and blue mark, and your arm may be sore. Occasionally, some people feel dizzy or lightheaded when blood is drawn. They may become sweaty, feel cold or tingly, and may faint or throw up. Risks that are possible but unlikely include infection, nerve damage, and puncturing an artery instead of a vein.

There may also be a slight risk of redness or a little swelling at the site where numbing cream is applied. This is usually temporary and will go away on its own.

Risk of Loss of Confidentiality

There is a risk that your personal information could be lost or exposed. This is very unlikely to happen, and we will do everything we can to make sure that your information is protected.

There is also a risk of emotional discomfort and fatigue from completing the study surveys and assessments. We will make all efforts to ensure that you do not have to wait to complete the study assessments.

What are my responsibilities if I take part in this research?

If you take part in the research, it is important for your safety that you:

- Follow the directions of the study doctor and research staff.
- Tell your other health care providers that you are in a research study.
- Tell your study doctor and staff about all medications you are taking (prescription and over the counter) and all of your health issues.
- Call the study doctor or staff at 617-953-1480 if you have any questions.

Will being in this study help me in any way?

You may not benefit from taking part in this research study. It is possible that your ASD symptoms will improve while you are taking sulforaphane. Because sulforaphane is not FDA-approved to treat autism, you should know that your doctor cannot prescribe it after you finish the study.

Others with ASD may benefit in the future from what we learn in this study.

Will being in this study cost me any money?

No. Study funds will pay for the study drug and all of the study procedures.

You or your insurance will be billed for all routine medical and diagnostic costs that are part of the standard of care for treating your condition. This may include the cost of tests, procedures, or medicines to manage any side effects. You will be responsible for any deductibles, co-payments, or co-insurance payments that your coverage normally requires.

What happens to information about me?

We will try to limit access to your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete privacy. The UMMS Institutional Review Board (the committee that reviews, approves, and monitors research on human subjects) and other representatives of UMMS, Quality Associates, Inc. (a company monitoring the study), the US Department of Defense and the Food and Drug Administration may need to review your records. As a result, they may see your name, but they are required not to reveal your identity to others. Your identity will remain confidential in any study results that are made public.

If we learn of any child or elder abuse, or abuse of individuals with disabilities, we are required to break confidentiality and report this to state authorities.

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

Storing Samples for Future Use

We would like to store some of your samples and health information for future research related to autism. We will label all your samples and health information with a code instead of your name and may store them indefinitely in the lab at Johns Hopkins. The key to the code connects your name to your health information and samples. The study doctor will keep the key to the code in a password protected computer/locked file.

Do you agree to let us store your samples for future research related to autism?

Yes ☐ No ☐ Initials_____

Even if you do not agree to allow us to store your samples for future use, you still may participate in the clinical trial. If later you change your mind and want your samples destroyed, contact the study doctor. Please note that if we have already utilized the samples when you request us to destroy the samples, we will be unable to do so.

What happens if I am injured because I took part in this research?

If you are injured while on study, seek treatment and contact the study doctor as soon as you are able.

The University of Massachusetts Medical School does not provide funds for the treatment of research-related injury. If you are injured as a result of your participation in this study, treatment will be provided. You or your insurance carrier will be expected to pay the costs of this treatment. No additional financial compensation for injury or lost wages is available.

You do not give up any of your legal rights by signing this form.

Will I be given any money or other compensation for being in this study?

We will compensate you with a gift card worth $15 for each completed visit, up-to a maximum of $90. We will also provide you with a parking voucher when you park your car at the UMass Medical Center parking lot. You will also be given a small soft toy to keep.

In order for us to pay you, you may need to give us private information like your home address or social security number. If you receive more than $600 in a calendar year from being in research studies at UMass Worcester, UMass Worcester may report this to the IRS and send you a 1099 form for tax purposes.

What are my other options?

You do not have to be in this study. If you decide not to be in the research now or later, it will not affect your usual care and it won't be held against you.

Instead of being in this research, your choices may include treatments or procedures that are available to treat autism, such as:

- antipsychotic, antidepressant, anticonvulsant, antianxiety and stimulant medications
- physical therapy
- behavioral therapy
- speech therapy

There are commercially available supplements of broccoli extract available over the counter in the market; however they are not the same as used in this study. We are using a special preparation that is not available commercially at this time. It contains the natural precursor named glucoraphanin, along with myrosinase, the enzyme that converts it to sulforaphane after it is taken by mouth.

We will tell you about any new information that might change your mind about taking part in this study. We may ask you to sign a new consent form if this occurs.

Talk with the study doctor or your healthcare provider if you have questions about any of these treatments or procedures.

What happens if I say yes, but I change my mind later?

You are free to leave the study at any time. There are no penalties and you do not lose any benefits to which you are otherwise entitled. Data that we have already used will stay in the study database and cannot be removed in order to maintain the integrity of the research. However, you can ask us to destroy any information that identifies you so that no one can tell the data belonged to you. Our contact information is below.

For your safety, if you decide to stop taking part in the study for any reason, we will ask you to make a final study visit to be sure that you stop the study safely. You will need to return all unused study drug and your study diary at this visit. The final study visit will take about 1 hour to complete. At this visit, we will:

- Do a physical exam and check your vital signs (blood pressure, temperature, heart and breathing rates) and ask about any side effects or health problems since your last visit
- Draw a blood sample and ask for a urine sample
- Give you some questionnaires to fill out

If you decide to stop, we may ask you if we can contact you for safety reasons or to follow your health. We may also ask you if we can collect data from your medical records and your routine medical care.

Can I be removed from the research without my OK?

The person in charge of the research study or the sponsor can take you out of the study even if you do not want to leave. This may happen if:

- The study doctor thinks it is best for you to stop taking the study drug
- You can't make the required study visits
- The Sponsor decides to stop the study
- We stop doing the study for other reasons

If this happens, the study doctor will explain why you need to stop taking part in the study. We will ask you to come in for a final study visit as described above.

Who can I talk to?

If you have questions, concerns, or complaints, or think the research has hurt you, you can talk to the research team:

- Andrew Zimmerman, MD is the person in charge of this research study. You can call him at 508-856-3279 Monday to Friday's from 9am – 5pm. You may also reach Dr. Zimmerman 24 hours a day/7 days a week through the UMass Page Operator at 508-334-1000.
- You can also call the study coordinator, Kanwaljit Singh, MD MPH at 617-953-1480 at any time with questions about this research study or with questions about the scheduling of appointments or study visits.

This research has been reviewed and approved by an Institutional Review Board. You may talk to them at (508) 856-4261 or irb@umassmed.edu for any of the following:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research subject.
- You want to get information or provide input about this research.

Signature Block for Children

Your signature documents your permission for the named child to take part in this research.

Printed name of child

Signature of parent or guardian

Date

- ❑ Parent
- ❑ Guardian (See note below)

Printed name of parent or guardian

Note on permission by guardians: An individual may provide permission for a child only if that individual can provide a written document indicating that he or she is legally authorized to consent to the child's general medical care. Attach the documentation to the signed document.

Signature of parent

Date

Printed name of parent

If signature of second parent not obtained, indicate why: (select one)

- ❑ The IRB determined that the permission of one parent is sufficient.
- ❑ Second parent is incompetent
- ❑ Second parent is not reasonably available

- ❑ Second parent is deceased
- ❑ Second parent is unknown
- ❑ Only one parent has legal responsibility for the care and custody of the child

Assent

- ❑ Obtained
- ❑ Not obtained because the capability of the child is so limited that the child cannot reasonably be consulted.

Signature of person obtaining consent and assent

Date

Printed name of person obtaining consent