# INFORMATION AND CONSENT FORM

For Parents/Guardians of New Participants

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| **Sponsor / Study Title:** | **National Institute of Health / "Choline Supplementation As A Neurodevelopmental Intervention in Fetal Alcohol Spectrum Disorders"** |
| **Protocol Number:** | **1R01AA024123** |
| **Principal Investigator:** | **Jeffrey R. Wozniak, PhD** |
| **Telephone:** | **(612) 273-9741**<br>**(612) 273-6212 (24-Hours)** |
| **Address:** | **Psychiatry Department - F282/2A West**<br>**2450 Riverside Ave.**<br>**Minneapolis, MN 55454** |

The study in investigator wants to know if you and your child would like to be part of a research study. If you have any questions about or do not understand something in this form, you should ask the study investigator or study staff. You should also discuss your and your child's participation with anyone you choose in order to better understand this study and your and your child's options. Participating in a research study is not the same as getting regular medical care. The purpose of regular medical care is to improve health. The purpose of a research study is to gather information.

## WHAT IS THIS STUDY ABOUT?

Researchers want to find out more about a nutrient called choline. For purposes of this study, choline is regulated and monitored as an "investigational drug" by the U.S. Food and Drug Administration (FDA) because it is being tested as a potential treatment for Fetal Alcohol Spectrum Disorder (FASD), and is not approved in the United States by the FDA. The main purpose of this study is to see whether choline can help cognitive development (thinking / memory) in children with FASD.

The study will also compare choline with a placebo to see if taking choline is better than taking a placebo. The placebo in this study looks and tastes like choline but has no choline in it. About 60 children with FASD will be in this study. Throughout this form, the term "study drug" refers to choline and placebo.

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**HOW DOES CHOLINE WORK?**

Choline is a nutrient found in many foods that your child eats. Choline is grouped within the vitamin B complex. The Institute of Medicine (IOM, a non-profit division of the National Academies of Sciences, Engineering and Medicine) recommends that children ages 1-3 eat 200 mg. of choline per day while those ages 4-8 eat 250 mg per day. The IOM's recommended upper tolerable intake level is 1000 mg per day for children aged 1-8 years.

Prenatal alcohol exposure can damage the brain during pregnancy, and children with prenatal alcohol exposure can have learning and behavioral problems as a result (including difficulties with attention, memory, problem-solving, and behavioral control). Recent studies in animals suggest that nutrients, like choline, may be helpful to brain development - even after the initial damage from alcohol has occurred. These studies also suggest that choline may contribute to long-term improvements in learning. Because this is one of the first studies of its kind, we do not yet know whether choline will actually help children with FASD.

**IS THERE ANYTHING ELSE MY CHILD CAN DO FOR HIS/HER FASD?**

If you decide not to allow your child to participate in this study, your child's normal clinical care will continue. Alternatives to participating in this study could involve behavioral interventions and/or special education services for your child. There are no specific biological interventions for FASD.

You should discuss your child's alternatives to participating in this research with the study investigator or study staff. In addition, you may discuss your options with your child's regular health care provider.

**WHAT IS MY ALTERNATIVE TO BEING IN THE STUDY?**

Your participation in this study does not involve treatment for any condition. Your alternative is to not participate in the study.

**WHO IS PAYING FOR THIS STUDY?**

The National Institutes of Health (NIH), the sponsor of the study, is paying for this study.

**WILL IT COST ANYTHING TO BE IN THIS STUDY?**

The sponsor will cover all costs associated with this study.

**HOW LONG WILL MY CHILD AND I BE IN THE STUDY?**

If you decide to be in this study and to allow your child to be in the study, and the study investigator says you and your child can be in the study, your and your child's participation will last 10 months (9 months in the study and one follow-up call at 10 months).

- If you decide to be in this study and to allow your child to be in the study, the screening will be completed during the first visit.
- If you and your child continue your participation past the first visit, your child will begin the study drug dosing period, as described in this form. Your child may continue to receive study drug for

up to 9 months unless you and/or the study investigator decide to stop your child's study drug dosing.
- If study drug dosing is stopped, you and your child may continue your study participation by taking part in the study's follow-up period (described in this form).

You and your child will visit the study center 3 times to have the procedures and tests described in this form. Ask the study investigator or study staff about your and your child's study visit schedule.

**WHAT WILL HAPPEN DURING THIS STUDY?**

The study investigator or study staff will give you a powdered drink mix containing choline or placebo. You will mix it with water and your child will drink it once per day for nine months.

Your child will be assigned by chance (like flipping a coin) to one of the following study groups:

- Group 1: choline bitartrate 19 mg. per kg. (weight based dosing)
- Group 2: placebo (a drink mix that looks and tastes like choline bitartrate but has no choline in it).

Your child has an equal chance of being in either of the study groups. Your child may receive a placebo. Neither you nor the study investigator or study staff will be able to pick which study group your child is in. You will not know and the study investigator and study staff will not know which study group your child is in. The study investigator or study staff can find out if it is necessary to know for your child's health. If this happens and the study investigator decides that it is best to withdraw your child from the study, you will be told which group your child was in. On the other hand, if the study investigator decides that your child can safely continue in the study, you will not be told which group your child is in.

While you and your child are in the study, you must:

- Follow the instructions you are given.
- Come to the study center for all visits with the study investigator or study staff.
- Tell the study investigator or study staff about any changes in your child's health or how they feel.
- Tell the study investigator or study staff if you want to stop being in the study at any time, or if you want your child to stop being in the study at any time.

What happens when we come for study visits?

After you sign this form, the study investigator or study staff will do the things listed below when you and your child come in for study visits. If you would like more information about which tests and procedures will be done at each study visit, ask the study investigator or study staff.

- **Demographic Questions:** Ask you to give personal information, such as your name, your child's name, date of birth, race, telephone numbers, etc.
- **Health and Medication Questions:** Ask you to answer questions about your child's health, medical history, and the medications he or she takes.
- **Behavioral Questionnaires:** Ask you to fill out questionnaires about your child's emotional, behavioral, and cognitive functioning.
- **Dietary Interview:** You will be asked about your child's diet, covering a 24-hour period, on three occasions.

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- **Physical Exam:** Your child will have a brief facial examination including measurements. The study investigator will also look at your child's hands and will ask basic health questions.
- **Photograph and Video:** Your child's face will be photographed to allow for detailed measurements to be taken. Your child will be video-recorded while completing one of the memory tasks to make it easier to score the test afterward. We will not share or release the photograph or the video recording outside of the study. The photograph and video will become part of the study record. You will read more about the photography and video later in this form.
- **Vital Signs:** Check your child's blood pressure by putting a band around the arm (this will squeeze the arm for about a minute).
- **Height, Weight:** Measure how tall your child is and check how much he or she weighs.
- **Blood Testing:** Take some blood to do laboratory tests:
    - Checking levels of certain substances in your child's body to determine how much change occurs with choline supplementation
    - DNA extraction from the same blood sample to look at genetic differences related to how much choline different children's bodies can make on their own. You will read more about this DNA testing later in this form.
- **Cognitive testing:** Your child will have several paper and pencil and interactive assessments including measures of brain function, thinking, memory, and behavior. Your child will be observed in structured play activities and will be asked to perform tasks such as manipulating toys, answering questions, and pointing.
- **Study Diary:** Give you a calendar log sheet for recording days on which your child did and did not take the full amount of the study drug.
- **Study Drug:** Give you a supply of study drug. Ask you to bring back all unused study drug to each visit.

What else will happen during this study?

- **Phone visits:** Between visits at the study center, we will call you approximately once per month to check for potential side effects and see if you need any assistance with the study.
- **Blood samples:** After the blood tests described in this form have been completed, your child's samples will be destroyed.

**WHY WILL MY CHILD BE PHOTOGRAPHED AND VIDEO-RECORDED? HOW WILL THESE BE USED FOR THE STUDY?**

The study investigator or study staff will take a photograph of your child's face. The purpose is to allow for computerized measurement of facial features such as eye width measurement and lip flatness. These facial characteristics can sometimes be affected by prenatal alcohol exposure. The study investigator or study staff will also video-record your child during the performance of one of the memory tasks. This is necessary in order to allow for very detailed scoring of your child's performance afterward. You do not have to let the study investigator or study staff take the photo and video of your child if you don't want to. However, your child cannot be part of the study without the facial photograph and the video recording of the memory task. You can ask the study investigator or study staff questions about it before you decide if you want to let them take the photo and video of your child.

The photo and video will show your child's full face. It is possible that people who see the photograph and/or video will recognize your child.

Your child's photograph and video recording will be identified by a number only (not a name) and will be stored on a secure file server and not viewed by anyone who is not authorized to see it or published or

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used at scientific meetings. You will not receive copies of the photograph or video and you will not be paid for the photograph or video.

## HOW WILL MY CHILD'S DNA (GENES) BE USED?

The study investigators will examine your child's DNA (genes) in order to better understand the relationship between individual differences and response to choline supplementation. DNA is in your child's cells, and it is what makes him/her different from anyone else. Some DNA controls things like the color of your child's hair or eyes. DNA might make your child more likely to get certain diseases or affect whether a drug helps your child and/or gives them side effects.

We believe that some children may respond better to choline depending on certain differences in specific genes. These differences are called single nucleotide polymorphisms (SNPs). Your child's DNA will be extracted from the blood sample collected at the first visit. His or her DNA sample will be stored until it can be analyzed in bulk with other samples. This will occur during the course of the current study. Once your child's DNA sample has been analyzed for these SNPs, it will be destroyed. There is no physical risk to the genetic portion of the study - other than the risks associated with the blood draw (described elsewhere in this form). **The genetics study is a required part of the main study.**

You and your child will not receive any results from this genetic test and the test results will not be put in your child's regular medical records. The test will not cost you anything. This DNA analysis will not benefit you or your child, but will help researchers understand choline as a potential treatment in FASD.

The risks to you and your family from genetic research are low. Your child's samples will be identified only with his/her study code number. If you change your mind later about allowing your child to be in the study, and the sample has not yet been analyzed, tell the study investigator or study staff and they will destroy your child's DNA sample.

There are laws to protect privacy and to prohibit the misuse of your child's genetic information. However, it is important to know that there is still a risk someone could get access to the information we have stored about your child, including information about a family member (for example, revealing that your child or a blood relative carry a genetic disease).

## WILL BEING IN THIS STUDY HELP ME OR MY CHILD?

Choline may help your child's symptoms from prenatal alcohol exposure, but there is no guarantee that being in this study will help your child. Your child's FASD might not get better while he/she is in this study. Your child may get placebo, which looks and tastes like choline bitartrate, but has no choline in it. Information from this study might help researchers to better understand FASD or come up with new tests or medications to help others in the future.

## WHAT ARE THE RISKS TO ME AND MY CHILD IF WE ARE IN THIS STUDY?

<u>What are the risks of taking choline?</u>

At very high doses (15 to 30 times higher than the dose we will be using), some people have reported:

- Hypotension or lowered blood pressure
- Gastrointestinal symptoms (upset stomach, stomach pain, loss of appetite)

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- One side effect we did observe in our previous study at a fixed dose of 500 mg. per day was "fishy" body odor (noticeable in urine and in sweat). The dose to be used in this study is generally lower than in the previous study. The dose will be adjusted to your child's weight at the first visit. If your child is randomly assigned to choline, he or she will receive a dose of 19 mg. of choline per kg body weight. For example, if your child has a weight of 15 kg at the first visit, the daily dose will be 285 mg. The maximum daily dose amount to be used in this study (500 mg.) is well within the range that could be achieved by most children through dietary choices and the maximum dosage to be used is half of the "upper tolerable intake level" for children in this age range (1000 mg.).

Please tell the study investigator or study staff right away if your child has any side effects. Please tell them if your child has other problems with health or the way he or she feels during the study, whether or not you think these problems are related to the study drug.

It is possible that choline may change how your child's regular medications, vaccines, vitamins or supplements work. It is important that you tell the study investigator about any medications, vitamins or supplements before you give them to your child during the study, or if your child will receive a vaccine during the study.

Could my child have an allergic reaction?

Sometimes people have allergic reactions to drugs or product ingredients. If your child has a very bad allergic reaction, he/she could die. Some things that happen during an allergic reaction that could be a sign or symptom of a life-threatening allergic reaction (anaphylaxis) are:

- a rash
- a fast pulse
- sweating
- a feeling of dread
- swelling around the eyes and mouth
- swelling of the throat
- wheezing
- having a hard time breathing
- a sudden drop in blood pressure (making your child feel dizzy or lightheaded)
- inability to breathe without assistance

You should get medical help and contact the study investigator or study staff if your child has any of these or any other side effects during the study.

What if my child is receiving placebo instead of choline during the study?

Some children in the study will get placebo instead of choline. In this study, the placebo is a drink mix that looks and tastes like choline but has no choline in it. Please ask the study investigator or study staff if you have any questions about placebo.

What are the risks of giving blood for this study?

The study investigator or study staff will take your child's blood by sticking a needle in the arm. Some problems your child might have from this are:

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- pain
- bruising
- dizziness
- infection

What are the other risks?

Filling out the questionnaires and answering the study investigator or study staff's questions could lead you to feel uncomfortable or upset. Please tell the study investigator or study staff if you feel uncomfortable or upset while filling out a questionnaire or answering questions. You have the right to refuse to answer any questions.

There is a risk of loss of confidentiality of your and your child's information. You will read more about the protection of your and your child's information later in this form. Please ask the study investigator or study staff if you would like to know more about how your and your child's information will be protected while you and your child are in this study.

**COULD MY CHILD HAVE ANY OTHER HEALTH PROBLEMS IF HE/SHE IS IN THIS STUDY?**

It is possible that your child could have problems or side effects of choline that nobody knows about yet, which include his/her health getting worse. Ask the study investigator if you have questions about the signs or symptoms of any side effects that you read about in this consent form.

**WILL I RECEIVE ANY NEW INFORMATION DURING THE STUDY?**

If the study investigator or study staff learns any new information that might change your mind about continuing in the study, or allowing your child to continue in the study, the study investigator or study staff will tell you about it.

**WHAT IF MY CHILD GETS HURT OR SICK WHILE IN THIS STUDY?**

In the event that this research activity results in an injury, treatment will be available, including first aid, emergency treatment and follow-up care as needed. Care for such injuries will be billed in the ordinary manner, to you or your child's insurance company. Be aware that your child's health care payer/insurer might not cover the costs of study-related injuries or illnesses. The sponsor has no plans to provide any payment for medical treatment. If you think that your child has suffered a research related injury, let the study investigator or study staff know right away. You do not give up any of your or your child's legal rights by signing this form.

**WILL MY CHILD OR I RECEIVE PAYMENT?**

Payment will be made using a pre-paid debit card called Greenphire ClinCard. It works like a bank debit card. We will give you a debit card; each time you are paid for a visit, money will be added to the card. You may use this card at any store that accepts MasterCard or you can use a bank machine to get cash. However, there may be fees for cash withdrawals (ATM use) and inactivity (no use for 3 months). We will give you the ClinCard Frequently Asked Questions information sheet that answers common questions about the debit card. You will also receive letters with additional information on how you can

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use this card and who to call if you have any questions. Be sure to read these letters, including the cardholder agreement, for details about fees.

The card is administered by an outside company. The company, Greenphire, will be given your name. They will use this information only as part of the payment system. Your information will not be used for any other purposes and will not be given or sold to any other company. Greenphire will not receive any information about your health status or the study in which you are participating. You will have the option to receive updates related to appointment reminders and payment reminders and updates via text message and email message (Standard text messaging rates will apply). You will have the opportunity to opt-in to receive these messages; you are not required to provide your phone number or email to be in the study or use a ClinCard. If you choose to receive messages but later decide that you want to stop the messages, you can opt-out. Any demographic information collected and provided to Greenphire is stored in a secure fashion and will be kept confidential, except as required by law.

____Yes, I would like to receive notifications from Greenphire

Email Address: _____

Phone Number: _____

____No, I do not want to receive notifications from Greenphire

Payment you receive as compensation for research is considered taxable income. If payment to an individual exceeds $600 in any one calendar year, the University of Minnesota is required to report this to the Internal Revenue Service (IRS). Research payments to study participants exceeding $600.00 during any calendar year will result in a FORM 1099 (Miscellaneous Income) being issued to you and a copy sent to the IRS.

You will be paid for each study visit you complete. The payment schedule is as follows:

Visits 1 & 11 (In-person): $100 each

Visits 2, 3, 4, 5, 6, 7, 9, 10, 12 (Phone visits): $10 each

Visit 8 (In-person): $75

If you complete all of the study visits you will receive a maximum payment of $365.

If you and your child travel to the study center, you will also be reimbursed up to $0.575 per mile. If you live more than 2 hours from Minneapolis, you may also be eligible for hotel reimbursement. You may also be reimbursed for parking costs at the study center (approximately $5-10 per visit). Please ask the study investigator or study staff if you have questions about any reimbursements you and your child may be eligible for during the study.

**DO MY CHILD OR I HAVE TO BE IN THIS STUDY?**

Your and your child's participation in this study is voluntary. You can decide not to be in the study, and not to allow your child to be in the study, and you can change your mind at any time. There will be no penalty to you or your child, and you and your child won't lose any benefits except for benefits having to do with the study. If you want to stop being in the study, or if you want to take your child out of the study, tell the study investigator or study staff.

The study investigator or study staff or sponsor can remove you or your child from the study at any time, even if you want to stay in the study or you want your child to stay in the study. This could happen if:

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- The study investigator or study staff believes it is best for you or your child to stop being in the study.
- You do not follow directions about the study.
- The sponsor stops the study for any reason.

If you or your child stop being in the study early, the study investigator or study staff may ask you some questions about being in the study. The study investigator or study staff may ask you and your child to participate in some procedures or tests to help you leave the study safely and/or to collect more information for the study. If you or your child leaves the study, the study investigator and study staff will still be able to use your information and your child's information that they have already collected. The study investigator or study staff will try to complete the monthly telephone calls with you through the 10 month point, even if you or your child discontinue earlier.

If you change your mind about allowing your child to be in the study later, tell the study investigator or study staff and they will destroy your child's blood samples if they are still available.

## HOW WILL MY AND MY CHILD'S INFORMATION BE KEPT CONFIDENTIAL?

Your identity and your child's identity will be protected as required by law and according to any policies the study center or sponsor may have. Be aware that your and your child's study records (which include your child's medical records, your signed consent form, and other information) will be shared as needed for the study. For example, the study investigator and the study staff members, the University of Minnesota, University of Minnesota Physicians, Fairview Health Services, the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), the National Institutes of Health, and Advarra IRB may look at your and your child's study and medical records.

Your documents and your child's documents and samples will not be labeled with a name or other directly identifying information. The documents and samples will have a code instead. The list that matches the code with your name and your child's name will be stored separately from your documents and your child's documents and samples.

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.

## WHOM TO CONTACT ABOUT THIS STUDY

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the study investigator at the telephone number listed on the first page of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research participants. If you have any questions about your rights as a research participant, and/or concerns or complaints regarding this research study, contact**:**

- By mail:
  Study Participant Adviser
  Advarra IRB

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6940 Columbia Gateway Drive, Suite 110
Columbia, MD 21046

- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Participant Adviser: ***Pro00038437***.

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**CONSENT**

I am the parent/guardian of the child being asked to participate in this study. I have read this form, and I have been able to ask questions about this study. The study investigator or study staff has talked with me about this study. They have answered all my questions. I voluntarily agree to be in this study and allow my child to be in this study. By signing this form, I do not give up any of my or my child's legal rights. I will get a signed copy of this consent form.

_____

Printed Name of Child Participant

_____

Printed Name of Parent/Guardian Participant

_____ _____

Signature of Parent/Guardian Participant Date

I attest that the individual providing consent had enough time to consider this information, had an opportunity to ask questions, and voluntarily agreed to participation in this study and to the child's participation in this study.

_____

Printed Name of Person Explaining Consent

_____ _____

Signature of Person Explaining Consent Date

I attest that I or my representative discussed this study with the individual providing consent.

_____

Signature of Principal Investigator or Sub-Investigator

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