Official Title: A Phase 2b, Double-Blind, Three Arm, Randomized, Placebo Controlled Trial With Restricted Response Adaptive Randomization Testing the Efficacy and Safety of High Dose Methylprednisolone or Equine Anti-Thymocyte Globulin as Treatment for Acute Liver Failure in Pediatric Patients

NCT number: NCT04862221

Document Date: Aug 3 2021 (ICF for Randomized Controlled Trial)

# RESEARCH INFORMED CONSENT & HIPAA AUTHORIZATION FORM

| | |
|---|---|
| **Sponsor / Study Title:** | **Ann & Robert H. Lurie Children's Hospital of Chicago / "A Phase 2b, Double-Blind, Three Arm, Randomized, Placebo Controlled Trial with Restricted Response Adaptive Randomization Testing the Efficacy and Safety of High Dose Methylprednisolone or Equine Anti-Thymocyte Globulin as Treatment for Acute Liver Failure in Pediatric Patients"** |
| **Protocol Number:** | **U01DK127995** |
| **Principal Investigator: (Study Doctor)** | **«PiFullName»** |
| **Telephone:** | **«IcfPhoneNumber»** |
| **Address:** | **«PiLocations»** |

*In this consent form, the words "we" and "us"" mean the study doctor and study staff.*

This form is for use in a research study that may involve participants who may or may not have the capacity to consent to take part in the study. When the participant cannot legally consent to take part, pronouns "you" and "your" should be read as referring to the participant rather than the person (legally authorized representative) who is signing and dating this form for the participant. In cases where the participant's representative gives consent, the participant should be informed about the study to the extent possible given his/her understanding. During the course of the study, if the participant regains the capacity to consent, informed consent will be obtained from the participant and the participant offered the ability to leave the study if desired.

| **KEY INFORMATION:**<br>This table includes a short summary of the major components of this study. Detailed information to help you decide whether or not to take part in this study can be found on pages 4-17. | |
|---|---|
| **Why is my child being asked to take part in this research study?** | Because your child has acute liver failure (ALF) |
| **How many children will be in this study?** | 160 |
| **Why is this study being done?** | The purpose of this study is to learn if one study drug is better, the same, or worse for treating children with ALF compared to another study drug or a placebo (fake study drug). |

| | |
|---|---|
| **What happens if I say "Yes, I want my child to be a part of this study?"** | These are the steps in the study:<br>1. Your child will randomly be assigned to one of the three study arms (Placebo, Study Drug #1, or Study Drug #2)<br>2. Your child will be tested for allergies to the assigned study drug. If your child **does** show an allergy, they will not be given the study drug.<br>3. If your child **does NOT** show an allergy to the study drug, the study treatment will begin.<br>**Study Process:**<br>• Begin with daily infusions of study drug for 4 days.<br>• Following completion of study drug infusion, your child will then take an oral steroid or placebo daily for 30 days.<br>• Following daily steroid administration, your child will continue to take the same steroid or placebo every other day for an additional 7 days.<br>4. Your child will take routine tests and exams to check for side effects. Blood samples may be taken up to 6 times to look at liver recovery. |
| **How long will this research study last?** | 12 months total (1.5 months of investigational therapy + 10.5 months follow up observation) |
| **Will my child automatically receive the study drug?** | No. If your child joins this study, they will be randomly assigned to one of three study arms, one of which is the placebo arm. |
| **Are there any risks my child would face by being in this study?** | Your child may be at risk for some side effects (explained further in the Detailed Information section) |
| **Will this study directly benefit my child in any way?** | Your child may not benefit directly from being in this study; however, the results of this study may help doctors learn the best way to treat children with ALF in the future. |
| **Who do I contact if I have questions about this study?** | Contact information for the study doctor can be found on page 1 of this form. |

## What else should I know about the research study?

- Someone will explain this research study to you.
- Whether or not your child takes part is up to you.
- You can choose that your child not take part.
- You can agree that your child take part and later change your mind.

- Your decision will not be held against you.
- You can ask all the questions you want before you decide.
- Your child will receive the regular medical care (care that your child would have received whether or not your child was in the study) for ALF even if your child does not take part in this study.
- There is no cost to you for taking part in the study. All regular medical care charges will be billed in the same way whether or not your child takes part.
- If you consent to take part, you will be asked to sign and date this form.

**Detailed Information**
The rest of this form includes detailed information about this study.

## Tell me more about why this research is being done?

Severe liver damage can result from many different causes, including infections, drugs, and genetic conditions. However, the cause of ALF is known in only half of affected children. Some children with ALF recover on their own, but the majority will require liver transplantation to survive.

Researchers believe that for some causes of ALF, decreasing inflammation, or swelling, and lowering the body's response to the inflammation will help participants recover. The study doctors want to compare two investigational drugs that help lower inflammation in the body to see if either is better than supportive care alone. Researchers will look at how safe each study drug is, if they cause side effects (adverse events), and which study drug works the best.

The two investigational drugs being tested are (1) equine anti-thymocyte globulin (eATG) (made with blood taken from horses) and (2) high dose methylprednisolone (a form of steroids). There is strong evidence to show that eATG and methylprednisolone slow the body's response to inflammation and improve the recovery of participants with other disorders. This is why researchers believe the study drugs may also help participants with acute liver failure.

Equine anti-thymocyte globulin (eATG) and methylprednisolone are drugs that have been approved by the Food and Drug Administration (FDA) for other disorders but have not been approved to treat patients with ALF. This is why they are considered "investigational."

## Tell me more about the possible benefits for my child from being in the study.

We are testing new treatments that could improve acute liver failure, but we do not know if the treatments in this study will make your child's acute liver failure better. The study results may help doctors learn what works best to treat ALF. This knowledge could help patients with ALF in the future.

## Tell me more about the research procedures for my child.

### ***Pre-study treatment***

If you agree to your child taking part in this study, we will make sure your child meets the study's 'entry criteria' by collecting demographic information, past medical history, family history of illnesses, and list of current treatments and medications. If your child is female and of child-bearing potential, we will collect urine to confirm a negative pregnancy test, and your child must use an effective method of contraception during the study. Please speak with the study doctor regarding the options for appropriate methods of contraception that are accepted for this study. During your child's hospital stay, your child will have routine physical exams and blood tests. We will collect this medical information and the blood test results taken while your child is in the hospital with ALF.

Your child will be assigned to **1** of the following three study treatment groups:

- Study Treatment group 1: Placebo (saline) **or**
- Study Treatment group 2: High dose methylprednisolone **or**
- Study Treatment group 3: eATG

The study treatment group is assigned randomly, or by chance, and is done by a computer. Your child will have an equal chance of being placed into one of the 3 study treatment groups. As the study goes on, each child's chance of being placed in one study treatment group or another will be based on how well the participants enrolled before that child responded. At the time your child receives the study treatment group assignment, if participants in one study treatment group appear to be doing better than another group, then your child will have a better chance of being placed in the group with the participants who may have a better recovery.

You will not be able to choose to which study treatment group your child is assigned. Neither you, your child nor your child's study doctors will know your child's study treatment group assignment. The need for liver transplantation will be determined by your child's regular doctors and will be based on how quickly the liver disease is worsening, regardless of whether your child is in the study or not.

***Infusion Period (up to 4 days)***

A skin test will be done to determine if your child has an allergic reaction to the assigned study treatment. If your child does not show signs of an allergic reaction, the assigned study treatment will proceed. Your child's weight will be taken to let the study doctor know how much of the study drug your child should get. As part of this study, your child will get the study drugs through a vein in his/her arm (also known as intravenously). Intravenous is also called "IV." Your child will receive the assigned study treatment once a day on study Days 1, 2, 3 and 4.

On study Day 1, the series of infusions will last for about 12 hours. Beginning on study Day 2, the series of infusions may last from 5 to 12 hours, depending on whether or not your child has any side effects. If your child does have side effects, then the study doctor may decide if it is better to slow down the infusion or to stop it.

The assigned study treatment will be given as a series of IV infusions once a day as shown in the chart below.

**Assigned Study Treatment Group – Infusion Series**

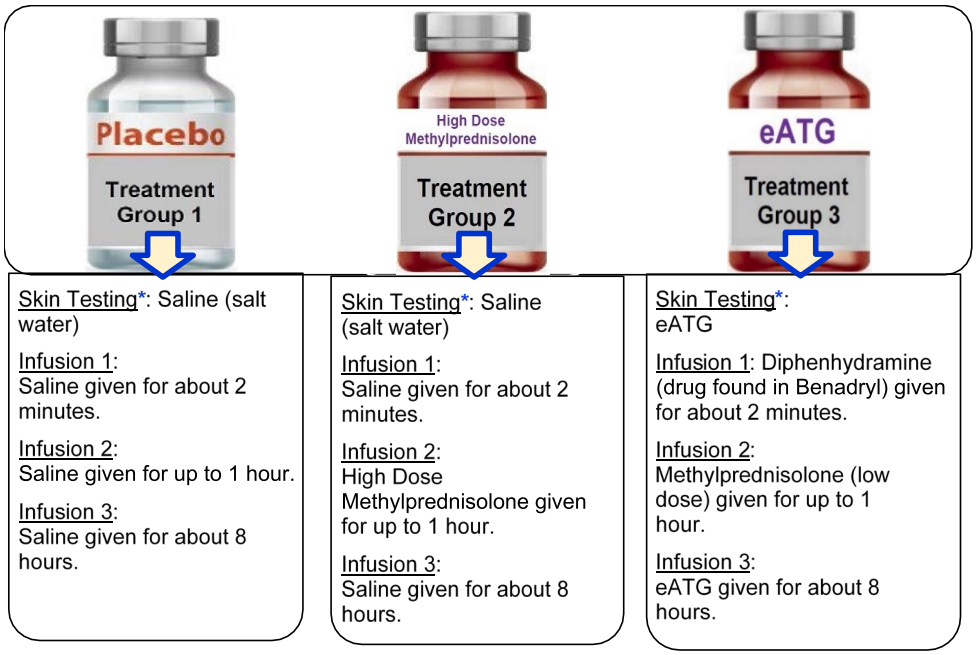
Group 1: Placebo (saline given to look like study treatment groups 2 and 3)

**OR**

Group 2: High Dose Methylprednisolone (investigational drug)

**OR**

Group 3: eATG (investigational drug)




*Skin testing is done only one time during the study, which is before the Day 1 study treatment starts.

***End of Infusion Period***

After the 4 days of study treatment, your child will be given a daily dose of steroid (Study Treatment groups 2 and 3) or placebo (that looks like the steroid) if your child is assigned to Study Treatment group 1, for the next 30 days. After the 30 days, one dose of steroid or placebo will be given every other day for the next 7 days. The steroid or placebo will be a liquid to take by mouth, if your child is able to take oral drugs. If your child is not able to take drugs by mouth, it will be given through an IV until your child can take oral drugs. If your child leaves the hospital before study Day 42 (Week 6), you will be given the rest of the steroid or placebo doses to take home with you. Your child will stop taking the steroid or placebo on study Day 42 (Week 6). If your child receives a liver transplant during the study, after the transplant they will be switched to the standard medicines used to suppress the immune response in transplant patients, which are similar, but not the same as the drugs in this study.

***Follow-up Period and Procedures***

Follow-up include visits at 1 week (Day 7), 2 weeks (Day 14), and 3 weeks (Day 21) after the day your child started in the study. If your child is discharged from the hospital before study Day 7, the research team will see your child while your child is at the hospital for routine visits with your child's regular doctor. In addition, the research team will contact you by phone or email to schedule each follow-up visit at the hospital for the 6-week, 3-month, 6-month and 12-month study visits.

The chart below shows what your child will do at each of the follow-up visits:

| Follow-up Visits | Study Day | | | | |
|---|---|---|---|---|---|
| | **Days 7, 14 & 21** | **Week 6** | **Month 3** | **Month 6** | **Month 12** |
| Physical Exam | X | X | X | X | X |
| Routine Blood Test | X | X | X | | |
| Questionnaires*<br>*If your child is 5 years of age and older, you and your child will be asked to complete questionnaires about your child's daily activities and mood. If your child is younger than 5 years of age, you will be asked to complete these questionnaires on your child's behalf.<br>If your child is younger than 2 years of age, the questionnaires will not be completed. | | | X | X | |
| General Health Check | X | X | X | X | X |
| Check for Side Effects | X | X | X | X | X |
| Review of Medical Records | X | X | X | X | X |
| Discontinue Study Treatment | | X | | | |

***Research Blood and Tissue Sample Collection and Storage***

All participants with ALF will have frequent blood samples taken (every day during the first week) so study doctors can check how the liver is recovering. We will take additional research blood samples 4 other times during the study so we can learn how your child's immune system is reacting to the liver injury and to the study drug. A small amount of blood (less than 2 teaspoons) will be taken up to 5 times during the entire study. The total amount of blood collected during the study will be about 9 teaspoons (40 ml). This amount of blood should not cause any risk to your child. We will make every effort to take these blood samples when routine blood tests are done.

Also, we are asking your child to provide one additional blood sample to look at your child's genes (DNA), so we can learn more about your child's acute liver failure. The DNA testing is optional. Your child may be in the study whether or not you agree to allow us to take a blood sample for DNA testing.

If your child's regular doctor thinks your child should have a liver biopsy or liver transplant, we would like to take a sample from any liver tissue that is leftover and not needed for medical purposes. Research tissue samples from your child's liver will be taken ***only*** if your child's regular doctor decides that a liver biopsy or transplant is necessary as part your child's regular medical care; neither the biopsy or transplant procedures will be done because your child is in this research study. We will also collect a blood sample if your child has a liver transplant.

The chart below shows what and when research blood and liver tissue samples will be taken:

| **Research Blood and Liver Tissue Sample Collection Schedule** | **Day 1** | **Day 7** | **Week 3** | **Month 3** |
|---|---|---|---|---|
| Research Blood Sample | X (Sample will be taken before study treatment begins.) | X | X | X |
| Optional Research Blood Sample for DNA Testing* *Blood for DNA testing will be taken only if you agree. | X** (**Sample can be collected on any study day.) | | | |
| Liver Tissue Sample (Collected only if liver biopsy or transplant is done and tissue is leftover) | X | | | |
| Research Blood Sample at Liver Transplant (if done) | X | | | |

All blood and liver tissue samples will be labeled with only a code number to protect your child's privacy. Only the study staff at your hospital will know the code number that links your child's name to the research blood (including DNA) and tissue samples.

If you agree, blood (including DNA) and liver tissue samples will be sent to the Children's Hospital of Philadelphia for testing and temporary storage. The samples will later be sent to the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) Central Repositories for future research studies on children with ALF and other diseases and will be available to other scientists to study ALF or other diseases. Along with your child's coded samples, other scientists may be given some coded data about your child, such as age, sex, diagnosis, race, and results of the study. This information might be important for research or public health.

Your child may join the study whether or not you allow the research blood (including DNA) and liver tissue samples to be collected and stored with related data at the NIDDK Central Repositories for use in future research.

You can change your mind and withdraw consent to continue participation in this study up until the end of the study. If you decide later that you want to withdraw, send a written request to your study doctor at the address in the section titled "*Whom to contact about this study*" at the end of this consent form. Once your request is received, study doctors will not collect any more data or samples on you for the purpose of this study. Data and samples collected up until the time that you withdraw may be retained and used in order for the study to be scientifically valid. Samples will be stored indefinitely or until they are completely used.

## Tell me more about ways being in this study may be bad for my child.

There are risks and discomforts involved in this study. Your child may have some side effects from the study drugs and/or discomfort while in this research study. The study doctor and study staff will watch your child closely. If your child has any side effects, you should tell the study doctor or study staff as soon as possible.

Side effects can range from mild to severe. Some side effects may last only a short time (hours or days). Others may last longer. Most side effects can be treated effectively. Talk

with your study doctor about possible side effects and ask for more information if you want to read about the drugs used in this study.

This research study may also have risks or side effects that are not known or understood at this time. The side effects we know about are described below and grouped by how likely they are to happen.

Risks related to Equine Anti-Thymocyte Globulin (eATG) - Investigational Drug

The eATG is made using blood taken from horses. Therefore, there is a chance that your child may have an unknown allergy to horses that could cause an allergic reaction. To prevent a possible allergic reaction to eATG, your child will receive skin testing for an eATG allergy, but sometimes participants with a negative skin test have an allergic reaction to the study drug anyway. To lower the risk of an allergic reaction (even if the skin test is negative), your child will be given infusions of a common anti-allergy drug (diphenhydramine) and steroids (methylprednisolone) before each dose of eATG is started. Other risks of eATG are listed below.

Risks related to High-dose Methylprednisolone (Investigational Drug) and Steroids (Low/Regular Dose Methylprednisolone)

The steroids used in this study can affect the hormones your child's body needs to help during stress events like trauma or serious infection. To lessen the effect the steroid has on your child's stress hormones, the dose of the steroid will be slowly lowered over the last weeks before the study treatment ends. **For this reason, it is important that your child does not stop taking the steroid without clear instructions from the study doctor.** Other risks of steroids are listed below.

| Possibility of Risk Occurring | eATG Known Side Effects | Steroids Known Side Effects |
|---|---|---|
| **Likely** ("Likely" means a side effect is expected to occur in 20% of participants or more.) | • Fever<br>• Chills<br>• Low number of blood platelets (which can increase risk of bleeding)<br>• Weak immune system<br>• Skin rash<br>• Joint ache and pain | • Difficulty sleeping<br>• Increased appetite and weight gain in the belly, face, back and shoulders<br>• Stomach (belly) pain<br>• Increase in blood pressure<br>• Increased levels of glucose (sugar) in the blood<br>• Pimples/acne<br>• Mood swings<br>• Upset stomach (heartburn or gastritis) |
| **Less Likely** ("Less likely" means a side effect is expected to occur in 20% of participants or fewer.) | • Headache<br>• Diarrhea<br>• Nausea (feeling sick to your stomach)<br>• Chest pain<br>• Throwing up (vomiting)<br>• Low number of white blood cells<br>• Muscles aches<br>• Infection | • Slow healing of cuts or other wounds<br>• Increased susceptibility to infections<br>• Stretch marks and easy bruising of the skin<br>• Headache<br>• Dizziness<br>• Infections |

| Possibility of Risk Occurring | eATG Known Side Effects | Steroids Known Side Effects |
|---|---|---|
| **Rare, but Serious** (***These possible side effects have been rarely reported, typically in less than 2% of participants. They may be serious if they occur***.) | • Sweating<br>• Tiredness<br>• Swelling of the face<br>• Stomach (belly) pain<br>• Feeling dizzy<br>• Shortness of breath<br>• Joint Stiffness<br>• Nosebleed<br>• Low red blood cells (anemia)<br>• Higher or lower blood pressure<br>• Abnormal heart rate<br>• Serum sickness-like symptoms (can include skin rash, itching, mouth sores, swollen joints)<br>• Kidney injury (in less than 2% of reported cases)<br>• Blisters<br>• Swollen lymph nodes<br>• Throat inflammation (sore, red, swollen throat) (in less than 1% of reported cases)<br>• Severe Lung Injury (in less than 1% of reported cases) | • Blood clot which may cause swelling, pain, shortness of breath<br>• Increased pressure in the eyes<br>• Joint damage, which can cause pain and loss of motion in that joint<br>• Irritation of the pancreas (pancreatitis)<br>• Irregular heartbeat<br>• Stomach and intestinal bleeding ulcers<br>• HPA Axis Suppression: Methylprednisolone or prednisolone may suppress your adrenal glands from making your own normal amounts of steroids. This may cause little or no symptoms. Even without symptoms, your body may not respond to physical stress such as surgery or severe illness. At these times, you may require additional steroids. |

Risks related to Diphenhydramine

Diphenhydramine is an over-the-counter medication that is commonly used in children to treat allergy symptoms. It will be given to participants receiving eATG to lessen the risk of allergic reaction. It commonly causes drowsiness and dry mouth. Other rare side-effects include dizziness, headache, nervousness, diarrhea, and nausea.

Risks related to other treatments or medicines

Some medicines react with each other, so it is important to tell the study doctor or study staff about any other drugs, treatments or medicines you are taking. This includes non-prescription or over-the-counter medicines, vitamins, and herbal treatments. It is also important that you tell the study staff about any changes to your medicines while you are in the study.

Risk for serious infections

It may take weeks or months for your child's immune system to fully recover. During this time, your child has a higher chance of getting an infection that could be serious. If your child gets an infection, your child may have to stay in the hospital longer or be re-hospitalized. The study doctor and study staff will watch your child closely for early signs of infection so treatment can be quickly started.

Risks related to intravenous (IV) infusion

There may be risks and side effects around the area where the IV is placed. These risks can include bruising, infection, pain, or leakage under the skin.

Risks related to research blood and liver tissue collection and storage

- Blood draw: Drawing blood from an IV may cause temporary pain from the needle stick, bruising or swelling at the place where the blood is drawn, and rarely, infection or fainting.
- Liver tissue collection: Liver tissue samples will be collected only if your child has a liver biopsy or liver transplant as part of their regular care. There are no additional risks related to the collection of these samples for research.
- It is possible that new information resulting from use of your data or samples provided to the NIDDK Central Repository may eventually be used in a research publication. In that event, your child's name or other identifying information will not be included, as this information will not be available to the researchers.
- Sometimes, research results in findings or inventions that have value if they are made or sold. These findings or inventions may be patented or licensed, which could give a company the sole right to make and sell products or offer testing based on the discovery. Some of the profits from this may be paid back to the researchers and the organizations doing this study, but you will not receive any financial benefits.

Risks related to Quality of Life Questionnaires

Some of the questions or topics you and your child will be asked as part of this study may make you and/or your child feel uncomfortable or emotional. You may take a break at any time when the questionnaires are being done. Though it is always better to have fully completed questionnaires, you do not need to answer any questions that make you or your child feel uncomfortable.

Risks related to your child's personal privacy and confidentiality

Research that uses health information and involves genetic testing can affect your child's privacy. Every effort will be made to protect your child's health information, but it is possible that a loss of your child's personal private information (confidentiality) can take place because your child takes part in this study.

Risks related to genetic research (DNA testing)

The results of your child's DNA testing (genetic information) can cause risks to participants who take part in research and their families. These risks may include the loss of personal private information (confidentiality), your child's ability to be insured or employed, and an increase in anxiety or stress for you, your child and/or your family members. There is a small chance that research results may indirectly have a negative effect on either some people or groups of people. Future research studies that use health and genetic information could come to be linked to your racial or ethnic group.

Researchers can look closely at large amounts of your genetic information by sequencing, or "reading", every letter in your DNA (your genome). Reading a person's entire genetic code is called whole genome sequencing. The research might include whole genome sequencing (for example, sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).

## What if my child is injured as a result of being in this study?

If your child suffers an injury, including side effects, as a result of taking part in this research study, you should immediately tell the study doctor or study staff. If your child has been sent home from the hospital and suffers a severe injury, your child should immediately go to the emergency room of the nearest hospital. You should tell the doctor at the hospital or emergency room that your child is taking part in a research study, and they will call your child's study doctor to make plans for treatment.

If your child is injured as a result of being in this study, the cost of your child's treatment will first be billed to your child's insurance company. You will be responsible for any co-payments or deductibles that are required by your child's insurance. If the costs for this treatment are not covered by your child's insurer, you may be responsible for these costs. You may wish to contact your child's insurance company to discuss this further.

By signing and dating this document, you will not lose any of your legal rights or release anyone involved in the research from responsibility for mistakes.

## What happens if my child does not take part in the study?

If you choose that your child will not take part in this study, your child will receive the regular medical treatment that is given to children for acute liver failure. This includes closely watching and treating your child for infection, bleeding, brain swelling, and other common problems related to ALF.

## What if I decide or the study doctor thinks my child should stop taking part in the study?

You can stop your child from taking part in this study at any time without any effect on your child's medical care. The study doctor may stop your child from taking part in this study if your child's safety and welfare are at risk. The researchers might also decide to stop the study at any time.

Some of the reasons for stopping are listed below.

- Your child no longer meets the study requirements. Ask the study doctor if you would like more information about this.
- Your child needs a medical treatment that is not allowed in this study.
- The study doctor decides that continuing in the study would be harmful to your child.
- The study is stopped by the Food and Drug Administration (FDA) or the National Institutes of Health (NIH).

## Will there be any additional costs to me if my child is in the study?

There will be no additional costs to you related to your child being in the study. The study sponsor, the National Institute of Diabetes and Digestive and Kidney Disease, will pay for costs related to the study treatment, research exams and tests and other events that are done only because your child takes part in this study.

While your child is in this study, the cost of your child's regular medical care will continue to be billed to you or your insurance.

## Will my child be paid for being in the study?

Your child will be paid at three different times for taking part in this study. Each payment will be given as a $50 gift card, for a total payment of $150. You will get a $50 gift card when you and your child come to the hospital for the 3-month and 6-month study visits and the questionnaires are completed. The third $50 gift card will be given to you when you and your child come to the hospital for the 12-month study visit, providing the questionnaire has been completed during the 6-month study visit.

## What if new information becomes available?

You will be told if we learn new information (either good or bad) that may affect your child's health, safety or make you change your mind about your child being in this study.

## Will I find out about the results of the study and the study drug my child was given?

A description of this clinical trial will be available on 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.

In this study, study doctors will not tell you what they find out about your child as a result of the research DNA testing. They also will not contact you if a test becomes available to diagnose a condition your child might have or later develop.

## HIPAA Authorization and Protection of Personal Information

"Personal Information" means any information that can be used to identify your child, such as your child's name or initials, date of birth, social security number, address, medical and health-related information and any other information that uniquely identifies your child. All of your child's personal information will be removed from study data, reports of study results, and blood (including DNA) and liver tissue samples. All of the information we collect for the study will be coded with a study-specific ID number rather than your child's personal information. Your child's study records will be kept in a secure location and access limited to the study doctor and study staff.

To further protect your privacy, the researchers have obtained a Certificate of Confidentiality from the Department of Health and Human Services (DHHS). With this certificate, the researchers may not give out your child's information (for example by court order or subpoena) that may identify your child in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. Disclosure will be necessary, however, upon request of DHHS for audit or program evaluation purposes. A Certificate of Confidentiality does not prevent you, your child or your family members from voluntarily releasing information about your child's involvement in this research.

Even with the Certificate of Confidentiality, if the study doctor learns about abuse of a child or elderly person or that you intend to harm yourself or someone else, or about certain communicable diseases, they will report that to the proper authorities. If keeping information private would immediately put you or someone else in danger, the researchers would release information to protect you or another person.

A Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against someone based on their genetic information. This law generally will protect your child in the following ways:

- Health insurance companies and group health plans may **not** request or use your child's genetic information that we get from this research.
- Employers with 15 or more employees may not use your child's genetic information that we get from this research when making a decision to hire, promote, or fire someone or when setting terms of employment.

Employers with 15 or more employees, health insurance companies, and group health plans must follow this law. This new Federal law does not protect your child against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

The study doctor and study staff will protect your personal information to the fullest extent allowed by law. However, we cannot promise that there will not be a loss of confidentiality, even though we take steps to prevent it.

## Authorization to Use and Disclose Records

We may need to share your child's personal information for these reasons:

- If it is required by law.
- If we think you or someone else could be harmed.
- To monitor or audit to check data collected for this study is accurate and the research is done safely and legally.

Representatives from government agencies, institutional review boards (IRB), the Sponsor and/or the Sponsor's authorized representatives may need access to your child's original medical records and study records for monitoring and/or auditing. By signing and dating this consent form, you authorize representatives from the following agencies/institutions access to your child's medical records and study records:

- Members of the study team and other authorized staff at your child's hospital;
- U.S. Food and Drug Administration;
- Office for Human Research Protections at the Department of Health & Human Services;
- National Institute of Diabetes and Digestive and Kidney Disease (agency that is sponsoring the research study) and the NIDDK Central Repositories;
- Data Coordination Unit at the Medical University of South Carolina; and
- Advarra IRB, the central Institutional Review Board (the committee that oversees research in humans).

Once your child's health data has been shared with authorized users, it may no longer be protected by federal privacy law and could possibly be used or disclosed in ways other than those listed here.

Your child's coded research information may also be used for additional unplanned medical and/or scientific research projects in the future related to acute liver failure in children, similar diseases, or other health-related research and the development of study drugs.

By signing and dating this form, you agree that you will not be able to access your child's research information until the study is over. This is done to maintain the scientific integrity of the study. After the study is complete, you can obtain access to your child's study information by contacting the study doctor.

## How long may my child's personal health information be used or disclosed as part of this study?

Your permission to use and share the information and data from this study will continue until the research study ends and will not expire. In California and any other state that requires an expiration date, the Authorization will expire 50 years after you sign and date this authorization document. Researchers continue to study data for many years and it is not possible to know when they will be completely done.

## May I change my mind about the use of my child's personal information?

You may change your mind and withdraw permission for the study to continue to collect your child's health information at any time. To withdraw your permission, you must contact your child's study doctor in writing. In

the letter, state that you changed your mind and do not want any more of your child's health information collected. Send the letter to your study doctor at the address on the first page of this consent form.

Once your letter is received by the study doctor, the study doctor or study staff will contact you to check if your child has had any additional side effects or injuries since the last study visit. After that, no new information will be collected, and the link from your child's personal information to the study code number will be destroyed. However, the personal information that has already been collected will keep being used for research.

If you decide not to sign and date this form, your child will not be able to take part in the study.

## STATEMENT OF AUTHORIZATION

I have read this form and its contents were explained. My questions have been answered. I voluntarily agree to allow study staff to collect, use and share my health data as specified in this form. I will receive a signed and dated copy of this form for my records. I am not giving up any of my legal rights by signing and dating this form.

_____

*Print Legal Name of Parent(s) or Legal Guardian(s)*

| _____ | _____ | _____ |
|---|---|---|
| *Signature of Parent(s) or Legal Guardian(s)* | *Date of Signature* | *Time of Signature* |

_____

*Print Legal Name of Research Participant (if participant reaches age of majority)*

| _____ | _____ | _____ |
|---|---|---|
| *Signature of Research Participant* | *Date of Signature* | *Time of Signature* |

_____

*Print Legal Name of Legally Authorized Representative*

| _____ | _____ | _____ |
|---|---|---|
| *Signature of Legally Authorized Representative* | *Date of Signature* | *Time of Signature* |

_____

*Authority of Legally Authorized Representative to act on behalf of Participant*

## Whom to contact about this study

During the study, if your child experiences any medical problems, suffers a research-related injury, or if you or your child have questions, concerns or complaints about the study, please contact the study doctor at the telephone number listed on the first page of this consent document. If you seek emergency care for your child, or hospitalization is required, alert the treating physician that your child is 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 child's rights as a research participant, and/or concerns or complaints regarding this research study, contact:

- By mail:
  Study Subject Adviser
  Advarra IRB
  6100 Merriweather Dr., Suite 600
  Columbia, MD 21044
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00054023.

## CONSENT SIGNATURES

**YOU WILL BE GIVEN A SIGNED AND DATED COPY OF THIS CONSENT FORM TO KEEP.**

Your signature on this form means:

- You have read this consent form.
- All your questions about the study and your child's part in it have been answered.
- You understand, to your satisfaction, the information about your child taking part in the research study.
- You do not give up any of your child's legal rights by signing and dating this consent form.
- The researchers, sponsors, or involved institutions are not relieved from their legal and professional responsibilities because you agree that your child will take part in this study.
- You freely agree to be in the study. (Re-consent required for participants at age of majority.)
- If the person reading this form is a parent/legal guardian, you agree to have your child take part in this research study.

## Consent for Biological Sample Collection & Storage

This section is related to your permission to use some of your child's blood for DNA testing.

| **Consent to DNA Testing (Genetic Research)**<br>Please initial next to **YES to give permission** or **NO to not give permission** to allow a research blood sample to be used for DNA testing. | |
|---|---|
| **Parent or Legal Guardian** | |
| **YES,** I give permission for my child's blood to be used for DNA testing.<br>Initials: _____<br>Date: _____ | **NO,** I do NOT give permission for my child's blood to be used for DNA testing.<br>Initials: _____<br>Date: _____ |
| **Research Participant (or Legally Authorized Representative)**<br>*(required for re-consenting participants at age of majority)* | |
| **YES**, I give permission for my blood to be used for DNA testing.<br>Initials: _____<br>Date: _____ | **NO**, I do NOT give permission for my blood to be used for DNA testing.<br>Initials: _____<br>Date: _____ |

| **Consent to the Storage of Genetic Information**<br>Please initial next to **YES to give permission** or **NO to not give permission** to allow the DNA sample to be stored at the Children's Hospital of Philadelphia and NIDDK Central Repositories. | |
|---|---|
| **Parent or Legal Guardian** | |
| **YES**, I give permission for my child's DNA blood sample to be stored and my child's information/data results shared for other future research that is not currently planned.<br>Initials: _____<br>Date: _____ | **NO**, I do NOT give permission for my child's DNA blood sample to be stored and my child's information/data results shared for other future research that is not currently planned.<br>Initials: _____<br>Date: _____ |
| **Research Participant (or Legally Authorized Representative)**<br>*(required for re-consenting participants at age of majority)* | |
| **YES**, I give permission for my DNA sample to be stored and my information/data results shared for other future research that is not currently planned.<br>Initials: _____<br>Date: _____ | **NO**, I do NOT give permission for my DNA sample to be stored and my information/data results shared for other future research that is not currently planned.<br>Initials: _____<br>Date: _____ |

This section is related to your permission to use and store your blood and tissue samples.

| **Consent to the Storage of Blood Samples (Non-Genetic Research)**<br>Please initial next to **YES to give permission** or **NO to not give permission** to allow the Children's Hospital of Philadelphia and NIDDK Central Repositories to store your blood samples and share data for future research. | |
|---|---|
| **Parent or Legal Guardian** | |
| **YES**, I give permission for my child's blood samples to be stored and my child's information/data shared for other future research that is not currently planned.<br>Initials:_____<br>Date: _____ | **NO**, I do NOT give permission for my child's blood samples to be stored and my child's information/data shared for other future research that is not currently planned.<br>Initials: _____<br>Date: _____ |
| **Research Participant (or Legally Authorized Representative)**<br>*(required for re-consenting participants at age of majority)* | |
| **YES**, I give permission for my blood samples to be stored and my information/data shared for other future research that is not currently planned.<br>Initials: _____<br>Date: _____ | **NO**, I do NOT give permission for my blood samples to be stored and my information/data shared for other future research that is not currently planned.<br>Initials: _____<br>Date: _____ |

| **Consent to the Storage of Liver Tissue Samples (Non-Genetic Research)**<br>Please initial next to **YES to give permission** or **NO to not give permission** to allow the Children's Hospital of Philadelphia and NIDDK Central Repositories to store your liver tissue samples and share data for future research. | |
|---|---|
| **Parent or Legal Guardian** | |
| **YES**, I give permission for my child's liver tissue samples to be stored and my child's information/data shared for other future research that is not currently planned.<br>Initials:_____<br>Date: _____ | **NO**, I do NOT give permission for my child's liver tissue samples to be stored and my child's information/data shared for other future research that is not currently planned.<br>Initials: _____<br>Date: _____ |
| **Research Participant (or Legally Authorized Representative)**<br>*(required for re-consenting participants at age of majority)* | |
| **YES**, I give permission for my liver samples to be stored and my information/data shared for other future research that is not currently planned.<br>Initials:_____<br>Date: _____ | **NO**, I do NOT give permission for my liver tissue samples to be stored and my information/data shared for other future research that is not currently planned.<br>Initials: _____<br>Date: _____ |

## Parent or Legal Guardian Signature

*Print Legal Name of Parent or Legal Guardian*

*Signature of Parent or Legal Guardian* | *Date of Signature* | *Time of Signature*

## Research Participant's (or Legally Authorized Representative's) Signature

*(required for re-consenting participants at age of majority)*

*Print Legal Name of Research Participant*

*Signature of Research Participant* | *Date of Signature* | *Time of Signature*

*Print Legal Name of Legally Authorized Representative*

*Signature of Legally Authorized Representative* | *Date of Signature* | *Time of Signature*

*Authority of Legally Authorized Representative to act on behalf of Participant*

## Study Doctor (or Designee) Signature

I have given this research participant or his/her parent/legal guardian (if applicable) information about this study that I believe is accurate and complete. The participant or their parent/legal guardian have indicated that they understand the nature of the study and the risks and benefits of participating.

*Print Legal Name of Consenting Study Team Member* | *Role in Study*

*Signature of Consenting Study Team Member* | *Date* | *Time*