Hydroxyurea for the Prevention of Brain Injury of Sickle Cell Disease
(HU Prevent)

RESEARCH PARTICIPANT INFORMED CONSENT AND PRIVACY AUTHORIZATION FORM

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Patient I.D. Plate

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Protocol Title: Hydroxyurea for the Prevention of Brain Injury of Sickle Cell Disease

Application No.: NA_00041623

Sponsor: National Center for Research Resources
Johns Hopkins Institute for Clinical and Translational Research - Clinical Research Unit (ICTR-CRU)
National Heart, Lung, and Blood Institute

Principal Investigator: James F. Casella, MD
720 Rutland Avenue
Ross 1125
Baltimore, MD 21205
410-955-6132 (office)
410-955-8208 (fax)

1. What you should know about this study:

- You are being asked to allow your child to join a research study.
- This consent form explains the research study and your child's part in the study.
- Please read it carefully and take as much time as you need.
- Please ask questions at any time about anything you do not understand.
- You are a volunteer. If you allow your child join the study, you can change your mind later. You can decide not to allow your child to take part or you can quit at any time. There will be no penalty or loss of benefits if you decide to quit the study.
- During the study, we will tell you if we learn any new information that might affect whether you wish to continue to allow your child to be in the study.
- Ask your study doctor or the study team to explain any words or information in this informed consent that you do not understand.
- For clinical trials: A description of this clinical trial will be available at 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 the Web site at any time.
- If children and adults can join this study, the word "you" in this consent form will refer to both you and your child.
- A statement will be added to your medical record that you are in this research study. Results from any clinical tests you have will be included in your medical record. Doctors outside of Johns Hopkins may not have access to this information. You can ask the research team to send this information to any of your doctors.

- During this study, you will not have access to certain medical information and test results collected for study purposes. If an emergency occurs while you are in the study, medical information needed for your treatment can be made available to your study physician and other physicians who treat you. When the study is completed, all the information in your medical record will be available to you.

2. Why is this research being done?

Sickle cell disease is an inherited disease of the blood. We do not know why some people have more problems related to sickle cell disease than others. Our overall goal of this study is to see if treatment with hydroxyurea will help prevent brain problems like strokes in children with sickle cell disease. Children with sickle cell disease are at high risk for strokes. Strokes can lead to problems with learning, mental development, and school work.
This study has 3 goals. These goals are:

1. To compare hydroxyurea to placebo (a placebo is a substance that looks like the study drug, but does not affect you) for the prevention of brain problems like stroke. This is a small study at two hospitals in preparation for a larger study.

2. To determine the safety of the study medicine and other study procedures for infants and children with sickle cell disease.

3. To collect and store blood for testing at a later date. We plan to study genes and proteins in the blood that may be markers of brain injury or an increased risk of brain injury.

Other things you should know about this study include:

Hydroxyurea is approved by the Food and Drug Administration (FDA) for the treatment of frequent painful crisis in adult patients with sickle cell disease. It is not approved to prevent or treat central nervous system complications such as fast blood flow in the brain and stroke in sickle cell disease therefore the use of hydroxyurea in this study is investigational. The FDA is allowing the use of hydroxyurea in this research study.

Lidocaine is approved by the Food and Drug Administration (FDA) for local anesthesia. It is routinely used intravenously to reduce the pain from infusion of propofol, but it is not specifically approved by the FDA for this use.

Nitrous oxide is approved by the Food and Drug Administration (FDA) for procedural sedation in children.

Propofol is approved by the Food and Drug Administration (FDA) for procedural sedation and anesthesia in children.

Sevoflurane is approved by the Food and Drug Administration for anesthesia in children.

Midazolam is approved by the Food and Drug Administration to reduce anxiety in children before procedures.

Children with sickle cell disease between the ages of 12 to 48 months (1-4 years) may join this study; they may begin screening for this study at age 9 months.

This is a randomized double blind study. There is a 50% chance your child will receive the study drug, hydroxyurea and a 50% chance your child will receive a placebo. A placebo is a substance that looks like the study drug, but does not contain hydroxyurea. Neither you nor the study doctors will know which your child will be getting. This information can be gotten in an emergency.

How many people will be in this study?

We expect about 20 children at Johns Hopkins Hospital and about 60 children at three other hospitals to take part in the study.

3. What will happen if you join this study?

If you agree to allow your child to be in this study, we will ask you to allow your child to have the following tests.

Visit 1: Screening visit

This visit will last about 4 to 5 hours.

- You will learn about hydroxyurea and the study.
- A hematologist or nurse practitioner will perform a history and physical exam.
- Your child will have a transcranial Doppler ultrasound (TCD). This test measures the speed of the blood flowing through the blood vessels in the neck and brain. Your child will be required to lie on their back while a small microphone is placed on various parts of their head. This test takes approximately 30 minutes and does not cause any discomfort.
- A pediatric neurologist will perform a neurologic history and physical exam.
- Your child will take a series of learning and thinking tests. A trained staff member will give your child a group of standard tests. These tests will measure learning, thinking and memory. We will ask you some questions about your child's behavior and environment. Responses to these questions will be coded so no one will know who you are. You have the right to refuse to answer any question for any reason. The series of tests may take up to 1 hour.
- About one tablespoon of blood will be taken from your child to check their blood counts, amount of Hb F and Hb S, liver and kidney function, and to be stored for testing in the future. This blood will be used for genetic testing and proteomics testing. The blood is used to obtain DNA (the blueprint for a person's identity) and to learn about the genes (the part of the DNA that tells your body how to make proteins) that may be associated with strokes and other factors that change how SCD affects your child. We will modify and store some of the cells so that they can be used as a long term source of DNA. Proteomics is the study of proteins that are found in blood and may be associated with stroke and other complications of SCD.

Visit 2: MRI of the brain with sedation (being put to sleep)

- This study requires four MRI scans of the brain. Your child will have to be sedated (put to sleep) for some or all of the MRI scans. The MRI scan is commonly used in children with sickle cell anemia to take pictures of the brain. The MRI of the brain will show doctors if your child has had a silent stroke. The MRI will take approximately 50 minutes.
- Prior to your child's MRI, you will be asked to complete a standard questionnaire. The purpose of this questionnaire is to make sure that your child is able to safely enter the MRI area. If your child has a history of metal in their head or eyes, they cannot take part in this study.
- To start your child's MRI test, your child will lie on a padded table. A head/neck coil will be placed around your child's head, face, and neck. The coil is necessary to help the MRI machine take pictures. The table on which your child is lying will be moved to the center of an MRI magnet, which looks like a long narrow tube. Even though the tube is open, some people feel confined in small places. If this bothers your child, please notify the MRI staff. You may end your child's

participation in this study at any time by telling the MRI staff. When MRI pictures are taken, radio-signals and magnetic fields are used. When this happens, it is normal for the MRI machine to make loud, banging, and clicking noises. Your child will be asked to wear earplugs or headphones for their comfort during the exam.

- During the exam, the MRI staff is able to see and hear your child.

- ***Sedation evaluation:***
  - Prior to the day of the MRI, you will be asked questions about recent illnesses, and other medical problems including obstructive sleep apnea. This will usually be done by telephone.
  - Due to the increased risk of problems from sedation in children with sickle cell disease, your child must be otherwise well at the time of the sedation and MRI.
  - The MRI will be cancelled if your child has had pain from sickle cell disease in the last two weeks or a cough or other cold symptoms, trouble breathing, or an asthma attack, acute chest syndrome, splenic sequestration or other acute complication (other than pain) of sickle cell disease in the last 4 weeks.
  - The sedation may cause abnormal vital signs or other problems that could lead to hospitalization or a sickle cell crisis. There is also a very small risk for cardiopulmonary arrest, stroke or death. The MRI will be cancelled if you do not consent to the sedation or the MRI. Consent for this will also be done on standard Hospital consent forms.
  - If your child usually can get an intravenous [IV] line, a numbing medicine will be placed on the best site or two. When the skin is numb, the IV will be placed. If your child does not tolerate IV line placement, your child will be placed under general anesthesia first. The IV will then be placed.
  - Midazolam- This medicine may be given by mouth before sedation to help the child relax and to forget being put to sleep.

- ***Sedation procedure:***
  - Standard American Society of Anesthesiology [ASA] monitoring will be done including heart activity, blood oxygen and pressure, breathing rate, temperature, and exhaled carbon dioxide. <u>An anesthesiologist will remain with your child for the entire procedure.</u>
  - Your child's vital signs will be taken and be documented at least every 5 minutes throughout the procedure.
  - Your child may be given midazolam (a medicine to help people relax) by mouth before the sedation to reduce anxiety and help your child forget about the sedation.
  - Your child will be given oxygen to maintain oxygen saturation above 95% throughout the procedure.
  - If an IV can be easily placed, lidocaine (pain medicine) will be given through the IV followed by propofol (sedation medication). Additional propofol doses will be given by the anesthesiologist until enough sedation is obtained. We will draw a teaspoon of blood to be stored for proteomic testing.
  - If an IV cannot be easily placed, your child will be sedated with a mixture of nitrous oxide (laughing gas), oxygen and sevoflurane (sedation gas) given by a facemask until unconsciousness is achieved. Your child will be monitored continuously during this process. Then the IV is placed and your child will be given oxygen and the propofol (sedation medication) as described above.
  - When the MRI is completed, the propofol will be stopped and your child will be brought to the recovery area.

Visit 3: Randomization visit (this visit will take about 1.5 hours)

- Randomization (like a flip of a coin by a computer) will decide if your child is given hydroxyurea or a placebo. A placebo is a substance that looks like hydroxyurea, but does not affect you. We are using a placebo in this study so that no one, except the pharmacy, will know who is receiving the drug. This way, the results of the study will be fair.
- We will meet with you to provide further education about hydroxyurea and the study. You will be able to ask any questions.
- We will take your child's vital signs and review of any illnesses they may have had. This will take about 1 hour.
- Your child will have 1 teaspoon of blood draw to measure blood counts
- We will collect urine for routine analysis.
- Your child will begin to take the study drug (hydroxyurea or placebo) once a day for 36 months.
- We will watch your child's blood counts closely at each study visit (listed below) and we will make adjustments to your child's dose based on blood counts as necessary. If your child's blood counts become low due to the study drug, we may have your child come in for additional blood draws (1/2 teaspoon) weekly until their blood counts improve. We will ask your child to come in for an additional blood draw (1/2 teaspoon) two weeks after any changes in their study drug.

Follow-up Visits

- *Every 4 weeks (this visit will take about 1.5 hours)*
  - A hematologist or nurse practitioner will perform a history and physical exam.
  - You will be asked questions about your family and medical history and use of medicine by our study staff.
  - Approximately 1/2 teaspoon of blood will be taken from to check your child's blood counts and ½ teaspoon to store for proteomic testing.
  - You will need to bring your child's study medication to clinic so we can measure the amount of remaining in the bottle.
- *In addition, at months 3, 6, and 9, 12, 15, 18, 21, 24, 27, 30, 33, and 36*
  - We will collect 2 teaspoons of blood to measure fetal hemoglobin, kidney and renal function and to save for proteomics.

Once a year visits

These tests will be done over two separate visits:

- A pediatric neurologist will perform a neurologic history and physical exam. This will take about 45 minutes.
- A hematologist or nurse practitioner will perform a history and physical exam. You will be asked questions about your family and medical history and use of medicine by our study staff.
- Your child will have a transcranial Doppler ultrasound (TCD). This test takes approximately 30 minutes and does not cause any discomfort.
- Your child will take a series of learning and thinking tests. A trained staff member will give your child a group of standard tests. These tests will measure learning, thinking and memory. We will also ask you some questions about your child's behavior and environment. Your responses to these questions will be coded so no one will know who you are. These tests will take up to 1 hour.
- Your child will have a sedated MRI of the brain as described above.

Schedule of study tests and visits:

	Screening	Randomization	Every 4 weeks	Annual Visit
Hydroxyurea education	X	X	X	X
MRI of Brain with sedation	X			X
Sedation evaluation	X			X
Neurological exam	X			X
Neurocognitive testing	X			X
History and Physical exam	X	X	X	X
Blood samples	X	X	X	X
Transcranial Doppler (TCD)	X			X
Medication Adherence Questionnaire			X	X

How long will you be in the study?
Your child will be in the study for three years.

Future Contact
We would like your permission to contact you about other studies that your child may be eligible for in the future.

Please initial your choice below:
____***Yes***, you may contact me in the future about other studies.
____***No***, I do not want you to contact me about other studies.

Future Use of Blood, Tissue, or Data
Your child's tissue and information (which includes your child's study data and blood samples for protein markers) that goes with it will not have your child's name on it, only a code number. We may share your child's blood and information with other investigators doing research in a similar field. These investigators may be at Johns Hopkins University or at other research centers. To protect your child's privacy, your child's name and any identifying information will always be kept separate from their blood and study information.

You will not hear from us unless we find information that may be important for your child's care.

The blood and data that goes into the repository will be used for this study, and also may be used for future studies.

We will keep your child's blood and any information collected on your child for at least 20 years, unless you request we remove your child's information.

Primary care physician / specialist notification option
You and your child's physician will not get these study results. We will try to contact you if we learn your child has a life-threatening medical disorder that current treatment can stop or lessen. We will make every reasonable effort to do so, but you must make sure that we have an accurate and current address or telephone number to allow us to do this.

Please indicate below whether you want us to notify your child's primary care physician or your child's specialist of any life-threatening medical disorder that current treatment can stop or lessen.

☐ Yes, I want the study doctor to inform my child's primary care physician
☐ No, I do not want the study doctor to inform my child's primary care physician
☐ My child does not have a primary care physician/specialist.
☐ The study doctor is my child's primary care physician/specialist.

PHYSICIAN CONTACT INFORMATION

Name: _____

Phone Number: _____

Address: _____

Incidental Findings

The MRI your child is having as part of this research study will be reviewed by a qualified person, just as it would be if your child were having the MRI or CT as part of their routine medical care.

There is a possibility that while reviewing your MRI we may see an abnormality that we did not expect to see in this study. This is what is called an "incidental finding."

We will let your child's doctor know if we see such an incidental finding. Depending on the type of incidental finding, we may contact you by mail or by phone. In the case of a potential serious emergency, someone may go to your home.

A qualified person (usually a member of the research team) will talk to you if there is an incidental finding. You do not have an option to decline information about an incidental finding.

If you want, we will give information about this incidental finding to your child's primary doctor or we will refer your child to an appropriate doctor for further evaluation.

- An incidental finding may cause you to feel anxious.
- Since an incidental finding will be part of your child's medical record, your child could face greater difficulty in getting health or life insurance.
- The costs for any care that will be needed to diagnose or treat an incidental finding would not be paid for by this research study. These costs would be your responsibility.

4. What are the risks or discomforts of the study?

There are two main risks to this study: sedation (required for the MRI) and hydroxyurea.

Sedation

The Food and Drug Administration (FDA) is conducting an ongoing review of the use of anesthesia and sedatives in infants and children. This review is taking place because several studies in animals show that commonly used anesthetics when given for a long time and at very high doses (much longer time and higher doses than for the sedation planned in this study) may affect the development of the brain. There is no direct evidence that anesthesia or sedation are unsafe for children, or that anesthesia should not be given to children; however, caution is suggested in the use of anesthesia for purely elective procedures in children under the age of 4 years. You should balance these theoretical risks against the benefit of knowing whether your child has suffered or is at risk for brain injury due to sickle cell disease.

If you have any questions about the use of sedation in this study, you should talk to the anesthesiologist who is on the research team for this study.

Less Likely: Inadequate sedation may make it more difficult to get good pictures of the brain. Need for help breathing, including repositioning the head or using a small piece of plastic to help the flow of air or a mask to push air into the lungs. Low levels of oxygen in blood during sedation may also cause delayed problems, including pain or acute chest syndrome (pneumonia-like changes in the lungs from sickle cell disease).
Rare: Severe breathing problems or cardiac arrest (sudden loss of heart function), stroke, brain injury or death.

Hydroxyurea
Likely: Low blood counts including low levels of white blood cells (neutropenia), platelets (thrombocytopenia), or red blood cells, (anemia), low sperm counts (causes decreased ability to have children) in men (which reverses after the medication is stopped).
Less Likely: Darkening of the skin and nails, mild nausea or vomiting, open sores of the skin of the legs (ulcerations), increased numbers or severity of headaches.
Rare: Injury to kidneys or liver, skin necrosis (death of skin cells or tissue).

Other risks related to study drugs and procedures:
Midazolam
Likely: Short periods of no or slow breathing, sleepiness.
Less Likely: Upset stomach, vomiting, hiccoughs, agitation, or involuntary moments, headache.
Rare: Stopping breathing, low blood pressure.

Propofol
Likely: Decreased blood pressure, short periods of no breathing, pain at the place it is given.
Less Likely: Myoclonic movements (brief twitching of a muscle or muscles), priapism (prolonged erection).
Rare: Dystonia (movement problem with sustained muscle contractions, twisting and repeated movements).

Lidocaine
Likely: Nausea
Less Likely: Drowsiness, mental/mood changes, ringing in ears, dizziness, vision changes, tremors, numbness, headache, backache.
Rare: Fever, unusually fast or slow pulse, trouble breathing, seizures, chest pain.

Sevoflurane
Likely: Nausea, crying, confusion, hiccups, increased saliva.
Less Likely: Vomiting, dry mouth, itching, rash, fever, temporary lazy eye.
Rare: Changes in heart rhythm, agitation, difficulty breathing, decrease in blood pressure, shivering, tiredness.

Nitrous Oxide (laughing gas)
Likely: Headache, dizziness, confusion, low blood pressure.
Less Likely: Upset stomach, vomiting, ear pressure, short periods of no breathing.
Rare: Irritation of the liver, increased pressure inside the skull.

MRI of the brain

The effects of magnetic fields in an MRI scanner have been extensively studied, and there are no known significant risks with an MRI exam. Your child may, however, be bothered by feelings of confinement (claustrophobia), and by the noise made by the magnet during the procedure. Your child will be asked to wear earplugs or earphones while in the magnet. Your child may not participate in this study if they have a pacemaker, an implanted defibrillator or certain other implanted electronic or metallic devices. It is important for you to advise the MRI staff if your child has had brain surgery for a cerebral aneurysm, or if your child has implanted medical or metallic devices, shrapnel, or other metal.

Blood Sampling

Likely: Pain and bruising at the site of the needle puncture.
Less Likely: Lightheadedness or fainting.
Rare: Bleeding or infection of the skin at the puncture site.

Genetic Testing

The Genetic Information Nondiscrimination Act (GINA) generally protects employability and the ability to obtain health insurance. However, in spite of the protections provided by GINA and the best efforts of the research team, there may still be a risk if information about your child were to become known to people outside of this study.

Certain genetic research may reveal that your child is a carrier of a genetic disorder. This could mean that your child or members of your child's extended family may have an increased chance of developing the disorder, or may pass on increased risk to his/her children.

If your child's participation in a genetic study becomes known outside of the research in spite of efforts to keep this information private (for example, if your child's participation and results were to be noted in your child's medical record) your child and your family members may be unable to obtain health, life, or disability insurance. Your child might also be refused a job or be fired from his/her current job. This could happen if you/your child choose to talk about your child's participation with your doctor without asking that the information be kept out of your child's medical record. If genetic (or any other) information is noted in your child's medical record, insurance providers may get access to such information.

The genetic studies that will be done are for research purpose only and will not be reported to you. In the very unlikely event that we discover genetic information about your child through these studies that indicates your child has a life-threatening disorder that current treatment can stop or lessen, we will notify you and your child's physician(s) as we would for any other life-threatening medical disorder as discussed earlier in this consent form under "Primary care physician/specialist notification option". We would ask you to have these studies confirmed in a clinical laboratory that performs this testing and recommend a genetic counselor to you, as medical decisions cannot be based on laboratory research studies that do not have certain certifications. The study would not pay for the additional testing or genetic counselor.

Transcranial Doppler Ultrasound (TCD)

There are no known major risks to TCD testing in children. Some children do not like staying still or become uncomfortable or scared during the test.

Neuropsychological Tests
Children may occasionally experience some mild anxiety during testing. The results of tests may affect school placement, but the results are only released by parental request. A relaxed environment with frequent breaks will minimize anxiety.

Questionnaires
You may experience emotional discomfort when answering some questions. If a particular question makes you uncomfortable, you can discuss its importance and the need to answer it with us. Completing the questionnaire may be inconvenient because of the time it takes to complete them.

Confidentiality
One potential risk of participating in this study is that confidential information about your child may be accidentally disclosed. We will use our best efforts to keep the information about your child secure, and we think the risk of accidental disclosure is very small**.**

Some side effects stated in this consent document, if severe, may cause death. Your child may experience all or some of the risks listed above. There may also be unknown risks.

Throughout the study the study team will watch very closely for any possible risks. The study coordinators and other providers are experienced in care of children and have medications and equipment available to care for possible problems.

5. Are there benefits to being in the study?
Your child may or may not benefit from being in this study. If your child takes part in this study, they may help others with sickle cell disease in the future.

6. What are your options if you do not want to be in the study?
- You do not have to allow your child join this study. If your child does not take part in the study, your child's care at Johns Hopkins will not be affected.
- Your child could get the MRI, TCD, or other testing outside of this study.

7. Will it cost you anything to be in this study?
You will receive a separate Insurance and Research Participant Financial Responsibility Information Sheet (Sheet).

This Sheet will give you the following information:
- The procedures, tests, drugs or devices that are part of this research and that will be paid for by the study (no cost to you).

- The procedures, tests, drugs or devices that will be billed to you and/or your health insurer. If you have health insurance, you will be responsible for any co-pays or deductibles not covered by your insurance.

8. Will you be paid if you join this study?
You will receive $20 for each study visit and an additional $20 for visits that require extra time (sedated MRI, TCD, and cognitive testing). If your child completes all of the study visits (16 visits in the first year, 15 visits in the second year, and 15 visits in the third year) you will receive a total of $1100 over three years.

9. Can you leave the study early?

- You can agree to allow your child to be in the study now and change your mind later.
- If you wish to stop, please tell us right away.
- Leaving this study early will not stop your child from getting regular medical care.
- If your child leaves the study early, Johns Hopkins may use or give out your child's health information that it already has if the information is needed for this study or any follow-up activities.

10. Why might we take you out of the study early?

Your child may be taken out of the study if:

- Staying in the study would be harmful.
- Your child needs treatment not allowed in the study.
- You or your child fail to follow instructions.
- The study is cancelled.
- There may be other reasons to take your child out of the study that we do not know at this time.

11. How will your child's privacy be protected?

Johns Hopkins has rules to protect information about you. Federal and state laws also protect your privacy.

The research team working on the study will collect information about you. This includes things learned from the procedures described in this consent form. They may also collect other information including your name, address, date of birth, and other details.

Generally, only people on the research team will know your identity and that you are in the research study. However, sometimes other people at Johns Hopkins may see or give out your information. These include people who review research studies, their staff, lawyers, or other Johns Hopkins staff.

People outside of Johns Hopkins may need to see your information for this study. Examples include government groups (such as the Food and Drug Administration), safety monitors, other hospitals in the study and companies that sponsor the study.

We cannot do this study without your permission to use and give out your information. You do not have to give us this permission. If you do not, then you may not join this study.

We will use and disclose your information only as described in this form and in our Notice of Privacy Practices; however, people outside Hopkins who receive your information may not be covered by this promise. We try to make sure that everyone who needs to see your information keeps it confidential – but we cannot guarantee this.

The use and disclosure of your information has no time limit. You may cancel your permission to use and disclose your information at any time by notifying the Principal Investigator of this study by phone or in writing. If you contact the Principal Investigator by phone, you must follow-up with a written request that includes the study number and your contact information. The Principal Investigator's name, address, phone and fax information are on page one of this consent form.

If you do cancel your permission to use and disclose your information, your part in this study will end and no further information about you will be collected. Your cancellation would not affect information already collected in the study.

12. Will the study require any of your other health care providers to share your health information with the researchers of this study?

As a part of this study, the researchers may ask to see your child's health care records from his/her other health care providers. We will ask these other health care providers to give us ALL information about your child's health status or your child's health care.

13. What treatment costs will be paid if you are injured in this study?

Johns Hopkins does not have a program to pay you if your child is hurt or has other bad results from being in the study. However, medical care at Johns Hopkins is open to your child as it is to all sick or injured people.

- If you have health insurance: The costs for any treatment or hospital care your child receives as the result of a study-related injury will be billed to your health insurer. Any costs that are not paid for by your health insurer will be billed to you.

- If you do not have health insurance: You will be billed for the costs of any treatment or hospital care your child receives as the result of a study-related injury.

By signing this form you will not give up any rights you have to seek compensation for injury.

14. What other things should you know about this research study?

a. What is the Institutional Review Board (IRB) and how does it protect you?

The Johns Hopkins Medicine IRB is made up of:

- Doctors
- Nurses
- Ethicists
- Non-scientists
- and people from the local community.

The IRB reviews human research studies. It protects the rights and welfare of the people taking part in those studies. You may contact the IRB if you have questions about your rights as a participant or if you think you have not been treated fairly. The IRB office number is 410-955-3008. You may also call this number for other questions, concerns or complaints about the research.

b. What do you do if you have questions about the study?

Call the principal investigator, Dr. Casella at 410-955-6132. If you wish, you may contact the principal investigator by letter or by fax. The address and fax number are on page one of this consent form. If you cannot reach the principal investigator or wish to talk to someone else, call the IRB office at 410-955-3008.

c. What should you do if you are injured or ill as a result of being in this study?

Call the page operator at 410-955-6070 and ask them to page Dr. James Casella if your child has an urgent medical problem related to your child's taking part in this study. If Dr. Casella is not available ask for the pediatric hematologist on-call.

d. What happens to Data, Tissue, Blood and Specimens that are collected in the study?

Scientists at Johns Hopkins work to find the causes and cures of disease. The data, tissue, blood and specimens collected from you during this study are important to both this study and to future research.

If you join this study:

- You will not own the data, or the tissue, blood, or other specimens given by you to the investigators for this research.
- Both Johns Hopkins and any sponsor of this research may study your data and the tissue, blood or other specimens collected from you.
- If data, tissue, blood, or other specimens are in a form that identifies you, Johns Hopkins may use them for future research only with your consent or IRB approval.
- If data, tissue, blood or other specimens are in a form that we believe does not identify you, they may be shared with other academic medical centers, non-profit organizations, corporate sponsors and other commercial companies without your consent or IRB approval.
- You will not own any product or idea created by the researchers working on this study.
- You will not receive any financial benefit from the creation, use or sale of such a product or idea.

e. What are the Organizations that are part of Johns Hopkins?

Johns Hopkins includes the following:

- The Johns Hopkins University
- The Johns Hopkins Hospital
- Johns Hopkins Bayview Medical Center
- Howard County General Hospital
- Johns Hopkins Community Physicians.
- Suburban Hospital
- Sibley Memorial Hospital

15. What does your signature on this consent form mean?

Your signature on this form means that:

- you understand the information given to you in this form
- you accept the provisions in the form
- you agree to join the study

You will not give up any legal rights by signing this consent form.

WE WILL GIVE YOU A COPY OF THIS SIGNED AND DATED CONSENT FORM

_____

Signature of Person Obtaining Consent Date/Time

_____

Signature of Parent/Guardian Date/Time

_____

Signature of Legally Authorized Representative (LAR) for **CHILD RESEARCH PARTICIPANT** Date/Time

_____

Description of LAR's authority under Maryland Law to act as surrogate health care decision-maker for child research participant (for example, Legal Guardian, court-ordered representative) Date/Time

NOTE: **A COPY OF THE SIGNED, DATED CONSENT FORM MUST BE KEPT BY THE PRINCIPAL INVESTIGATOR; A COPY MUST BE GIVEN TO THE PARTICIPANT; AND, IF APPROPRIATE A COPY OF THE CONSENT FORM MUST BE PLACED IN THE PARTICIPANT'S MEDICAL RECORD**

ONLY CONSENT FORMS THAT INCLUDE THE JOHNS HOPKINS MEDICINE LOGO CAN BE USED FOR CONSENTING RESEARCH PARTICIPANTS. IF THIS CONSENT FORM DOES NOT HAVE A JOHNS HOPKINS MEDICINE LOGO, DO NOT USE IT TO CONSENT RESEARCH PARTICIPANTS.