Informed Consent to Participate in Research

[Insert site logo and/or address]

TITLE: A Study to Compare Bone Marrow Transplantation to Standard Care in Adolescents and Young Adults with Severe Sickle Cell Disease

Principal Investigator: [Insert site PI]
Co-Investigators: [Insert site co-I]

Study Coordinators: [Insert site study coordinator/s]

[Insert site department/facility name, address, and phone number]

Source of Support: National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health (the NIH), Bethesda, Maryland

CONSENT FOR AN ADULT TO BE A SUBJECT IN CLINICAL RESEARCH AND AUTHORIZATION TO PERMIT THE USE AND DISCLOSURE OF IDENTIFIABLE MEDICAL INFORMATION (PROTECTED HEALTH INFORMATION) FOR RESEARCH PURPOSES.

This is a clinical trial, which is a research study to answer specific medical questions.

The information from this study may also help future patients. The Study doctor (the person in charge of the research) will explain the study to you. This research study will include only people who choose to take part in the study. Please take your time to make your decision about taking part in the study. You may discuss your decision with family and friends. You should also discuss this with your healthcare team. If you have any questions, you can ask the Study doctor for more explanation.

1. Introduction

You are being invited to be part of a research study at [Insert institution]. The people who take part in research studies are called "participants". This study is called a clinical trial. A clinical trial is a research study involving treatment of a disease in human patients. Before you decide if you would like to participate, we want you to know why we are doing this study. Being in this study is voluntary. You do not have to take part in this study. You have a choice between a standard treatment for sickle cell disease and this clinical trial. Do not join this study unless all of your questions are answered.

After reading and discussing the important information in this consent form you should know:

- Why this research study is being done
- What will happen during the study
- Any possible benefits to you
- The possible risks to you
- How your personal health information will be treated during the study and after the study is over
- Whether being in this study could involve any costs to you
- What to do if you have problems or questions about this study

Please read, or have read to you, this consent form carefully. After you finish, talk with the study doctor and ask questions. You may also want to talk to family, friends, your primary care doctor, or other health care provider about joining this study. If you decide that you would like to take part in the study, you will be asked to sign this form. You will be given a copy of the signed form to keep.

Please ask the study doctor or the study staff to explain any words or information that you do not clearly understand. You may take home an unsigned copy of this consent form to read and discuss with family or friends before making your decision. There are also names and telephone numbers of people you can call to get answers to any questions you may have now or at any time during or after the study. You may change your mind about staying in the study at any time. However, due to the nature of the treatment provided during this study, it might not be safe for you to immediately stop being in the study. If you have any questions about your staying in the study, please talk with the study doctor or study team.

This research study is sponsored by National Heart, Lung, and Blood Institute of the National Institutes of Health (the "Sponsor"). [Insert institution] is being paid by the Sponsor to conduct this study.

If you choose to take part in this study, it is important that you give a true and complete medical history. You must be honest about your past and present use of medications. Information that is untrue or incomplete could have very serious effects on your health and safety during the study.

2. Background

As you know, SCD is an inherited blood disorder. It is caused by a change in the hemoglobin protein that helps red blood cells (RBC) carry oxygen in the body. This change in hemoglobin leads to blockage of blood flow in small blood vessels that can cause severe pain. It also damages body organs, such as the lungs, brain, spleen, and kidneys. The treatment known as hematopoietic cell or bone marrow transplant (HCT/BMT) can replace the defective blood cells with blood cells from a healthy donor who could be a sibling or an unrelated donor with a tissue-type match that is similar to yours. Unrelated adult volunteer donors are persons who list themselves with a donor registry for the purpose of donating their blood or bone marrow cells to patients who may benefit from HCT/BMT but do not have a sibling who is a tissue-type match to the patient and able to donate bone marrow. This treatment (HCT/BMT) may stop the disease and its health problems. HCT/BMT for SCD is successful in children but has not yet been tested in very many adults.

We are conducting this trial to study if adolescents and young adults who are treated with HCT/BMT live longer than those who are not treated with HCT/BMT. The clinical trial is designed to have two groups. In one group are patients who have a donor and expected to be treated with HCT/BMT (donor arm) and in the other group (no donor arm), patients without a donor who will receive standard of care (this is the same treatment you now receive for your SCD).

Neither you or your doctors know whether you have a donor until your doctors confirm you are eligible for the clinical trial. After you have heard about the trial and are interested, your doctor will submit test results and other documents to confirm you are eligible for the trial. Then your blood will be sent for tissue typing along with blood from any available full siblings (brother or sister, from same set of parents) that agree to be typed. If your brother or sister is not a tissue match or if you do not have a brother or sister, your doctor will search the unrelated donor registry for a donor who is tissue matched to you.

- If the tests confirm you have a suitable donor (no longer than 6 months from when you were confirmed eligible), you will be moved to the “donor arm” of the trial.
- If you do not have a donor (no longer than 6 months from when you were confirmed eligible), you will remain in the “no donor arm” for 2 years.

The study will recruit 200 subjects with severe SCD from approximately 40 hospitals in the United States. Approximately a third of subjects (60 subjects) are likely to have a tissue matched donor. These subjects will be assigned to the donor arm and are eligible for transplant (HCT/BMT). The remaining 140 subjects will be assigned to the ‘no donor arm’ and will continue to receive ongoing standard of care treatment for SCD.

This study is open to males and females between 15 - 40 years old with SCD and have one or more serious problems that include:

- stroke or another serious brain complication
- 2 or more episodes of acute chest syndrome in the last 2 years even though treatment such as hydroxyurea to stop acute chest syndrome was given to you

- 6 or more episodes of severe vaso-occlusive pain (pain crises) in the last 2 years
- Receiving regular RBC transfusions (receiving 8 or more blood transfusions per year to prevent sickle related health problems)
- An echocardiographic finding of tricuspid value regurgitant (TRJ) velocity ≥ 2.7 m/sec
- Chronic Pain on a majority of days per month for ≥ 6 months

You cannot be in this study if you:

- Have cirrhosis of the liver (a very serious condition of liver failure)
- Have now or have had a very serious bacterial, viral or fungal infection in the past six weeks
- Have human immunodeficiency virus (HIV) infection
- Have already received a HCT/BMT
- Are currently pregnant or breast feeding

In order for you to qualify to participate in this research study, your medical history and the results of your screening evaluation will be checked to see if the sickle cell disease (SCD) complications that you have had and the results of your screening evaluation make you eligible to take part in this trial. If you are eligible for this trial, we need to first find out if we can identify an individual who can serve as a bone marrow donor for your transplant. This is done by determining your HLA type.

Human Leukocyte Antigen (HLA) typing is done to learn your tissue type. Your immune system uses the HLA genes to tell the difference between your own tissues, which are not attacked, and germs and other foreign cells, which should be attacked. A transplant is most likely to be successful when the donor and recipient share the same HLA type. The person most likely to be HLA matched is a brother or sister from the same parents. It is also possible to search for a volunteer donor who by chance has the same HLA genes as you. In order to receive a HCT/BMT, a suitable HLA-matched donor must be identified and be willing to donate bone marrow.

If you have previously undergone HLA typing and your doctor searched for a donor, you will not be able to take part in this study. We are informing you of all the risks and benefits of participating in this study if you do not have a donor at this time. If you do have a donor, you will be given a second consent form explaining the risks and benefits of HCT/BMT so that you can make a decision as to whether you will be willing to undergo a transplant.

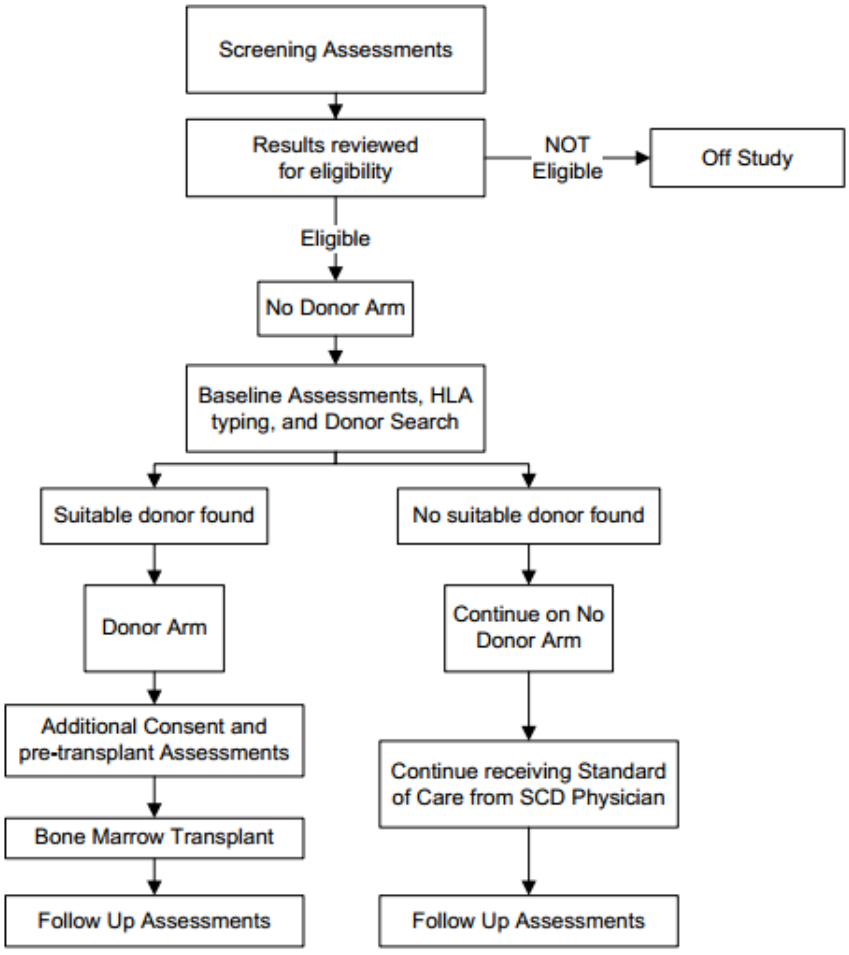
3. Purpose

The purpose of this research study is to compare transplant (HCT/BMT) to standard of care treatment in young adults with SCD.

We recommend that you participate in this study only if you have decided that you wish to take part in a study whose results will help us better understand the best treatment option for severe SCD. This means that if you have a donor, you will be assigned to the donor treatment group and will receive HCT/BMT. If you don't have a donor, you will remain in the no donor

treatment group and will continue to receive the care you are currently receiving. Both treatment groups will be followed for 2 years. There are scheduled tests now and for 2 years after we determine if you have a donor so we can compare how both groups are doing. This comparison allows physicians to compare the two treatment approaches. It is very important that you carefully consider whether assignment to one of two treatment groups is acceptable to you and that you are willing to be followed by 2 years. Between years 3 and 10 from enrollment, we will ask your doctor annually whether you are alive or dead and the date of last contact with your doctor. If you are not alive, we will ask for the date of death and the cause of death. If you doctor has lost contact with you, we will search the National Death Index, maintained by the government to record all deaths that occur in the U.S. Through the National Death Index, we will obtain the date of death and the cause of death.

4. Study Treatments and Tests



When you first enroll in the study:

- During this consultation, the BMT physician will review and confirm that you meet the eligibility criteria for the study which is based on your disease (SCD).
- If the BMT physician confirms you meet the eligibility criteria based on your disease and you agree to participate in this study, a series of screening evaluations will be conducted

to determine if your body can tolerate the treatment called transplant (BMT). These **screening assessments** include:

- History, Physical exam, height and weight
- Assessment of your performance status (how well you are able to do your normal activities)
- Urinalysis to check for protein and/or infection in your urine
- Blood Samples (about 3 teaspoons, or 1 tablespoon) will be drawn from one of the veins to conduct routine laboratory blood tests of your …
  - Blood counts (number of each type of blood cell),
  - Blood chemistries (elements and minerals in your blood, as well as elements that show kidney and liver health and check your blood clotting).
  - Hemoglobin S percent (a measure of the different kinds of hemoglobin in the blood such as transfused hemoglobin and sickle hemoglobin)
  - Blood drawn for HLA typing (about 1 tablespoon and tested only when eligibility is confirmed)
- If you are a female who can bear children, a pregnancy test will be performed using a sample of your blood or urine
- Echocardiogram (a test that takes numerous pictures of your heart to make sure the heart is functioning properly)
- Pulmonary function test (a test that measures how well the lungs work)
- 24-hour urine collection (a test to measure the amount of water and chemicals present in the urine) and/or a Radionuclide GFR (a blood test to measure kidney function)

- After you complete your screening assessments, your clinical information and SCD history will be verified to determine whether you are eligible for the study.
  - In the unlikely event you are not eligible for the study, you will not be enrolled on study and you will no longer be asked to provide follow up.
  - If you are confirmed eligible for the study, we will perform tissue typing and search for a donor.
- If you are confirmed eligible, HLA typing (tissue-typing) will be done to determine if you have a suitably matched donor (related or unrelated) who can donate bone marrow cells for HCT/ BMT. If you have full siblings (i.e., from the same parents), we will contact them, and if interested, HLA type them to determine whether you are tissue matched to any of your siblings. If you do not have any full siblings, we will search among unrelated donors to determine if someone is matched to you. We will search for a donor for 180 days. If we are not able to find a donor within 180 days, you will be on the no donor arm for the remainder of the study.
- While we are searching for a donor, we will perform **baseline assessments** so we can have a better idea of your organ function and quality of life. Some of these baseline assessments are done <u>before</u> we know if you have a donor or not. These include:
  - 6 minute walk distance test: a test to measure how far you can walk in 6 minutes
  - Questionnaires about your health and quality of life: surveys to measure health outcomes from the patient perspective. Your doctor and/or the research team will provide the instructions and materials you will need to complete the survey at

each time point it is due Whenever possible, this questionnaire will be completed electronically during your study visits.
    - Pain diary: You will document your pain twice daily for 28 days via an electronic application. Your doctor and/or research team will provide the instructions you will need to complete the pain diary.
- The rest of the baseline assessments are done <u>after</u> we know if you have a donor or not. These include:
    - History, Physical exam, height and weight
    - Assessment of your performance status (how well you are able to do your normal activities)
    - Urinalysis to check for protein and/or infection in your urine
    - 24-hour urine collection (a test to measure the amount of water and chemicals present in the urine) and/or a Radionuclide GFR (a blood test to measure kidney function)
    - Blood Samples (about 3 teaspoons, or 1 tablespoon) will be drawn from one of the veins to conduct routine laboratory blood tests of your …
        - Blood counts (number of each type of blood cell),
        - Blood chemistries (elements and minerals in your blood, as well as elements that show kidney and liver health and check your blood clotting).
        - Hemoglobin S percent (a measure of the different kinds of hemoglobin in the blood such as transfused hemoglobin and sickle hemoglobin)
    - A blood and urine sample for future genetic testing (optional)
    - Echocardiogram (if it was not already done within the last 60 days)
    - Pulmonary function test (if it was not already done within the last 60 days)

If you have a donor:

- If the HLA typing shows that you have a suitably matched donor who is available**,** you will be re-assigned to the donor arm treatment group.
- You will be asked to sign a second consent form explaining the risks and procedures related to HCT/BMT. The detailed information about the risks and benefits of HCT/BMT will be explained by a doctor who performs the HCT/BMT.
- You will undergo **additional assessments in preparation for HCT/BMT** and for monitoring your health after HCT/BMT.
- You will receive the chemotherapy drugs busulfan, fludarabine, and anti-thymocyte globulin. These drugs are given to prepare your body to receive bone marrow from your donor.
- You will have a HCT/BMT
- We will study the side effects of transplant (BMT) including those that are expected and unexpected with additional follow up assessments. You will be followed weekly for the first 100 days after your transplant, and every 3 months thereafter

If you do <u>not</u> have a donor:

- You will remain in the no donor arm

- You will receive standard of care for your SCD (same treatment as you are receiving, or your sickle cell doctor may change that treatment depending on whether there are new medications available)
- You will be followed every 3 months for 2 years after it is determined you do not have a suitable donor

Follow up for all participants:

- You will be asked to come in for a study visit every 3 months for 2 years after we determine if you have a donor or not. We will measure the health of your body organs (lungs, brain, and kidneys) and functional outcomes. These tests will be done at baseline, one, and two years to compare the results between patients who receive standard of care treatment and patients who receive transplant. The following assessments will be performed regardless of whether you have a donor or not:

  Day 100, 180, and 270 Follow up Assessments:
  - History and Physical Exam
  - Review of any SCD events that have occurred since your last visit
  - [only at day 100 and day 180] Blood test to measure your hemoglobin S percent (a measure of the different kinds of hemoglobin in the blood such as transfused hemoglobin and sickle hemoglobin)

  Follow up Assessments at 1 year (Day 365):
  - 6 minute walk distance test: a test to measure how far you can walk in 6 minutes
  - Questionnaires about your health and quality of life: surveys to measure health outcomes from the patient perspective. Your doctor and/or the research team will provide the instructions and materials you will need to complete the survey at each time point it is due Whenever possible, this questionnaire will be completed electronically during your study visits.
  - Pain diary: You will document your pain twice daily for 28 days via an electronic application. Your doctor and/or research team will provide the instructions you will need to complete the pain diary.
  - Echocardiogram
  - Pulmonary function test and oxygen saturation by pulse oximetry

  Day 450, 540, and 630 Follow up Assessments:
  - History and Physical Exam
  - Review of any SCD events that have occurred since your last visit

  Follow up Assessments at 2 years (Day 730):
  - History and Physical Exam
  - Blood Samples (about 3 teaspoons, or 1 tablespoon) will be drawn from one of the veins to conduct routine laboratory blood tests of your …
    - blood counts (number of each type of blood cell),
    - blood chemistries (elements and minerals in your blood, as well as elements that show kidney and liver health and check your blood clotting).
    - Hemoglobin S percent (a measure of the different kinds of hemoglobin in the blood such as transfused hemoglobin and sickle hemoglobin)
  - Pulmonary function test and oxygen saturation by pulse oximetry
  - 6 minute walk distance test: a test to measure how far you can walk in 6 minutes

- Urine test for protein (albumin) in your urine
- Echocardiogram
- Questionnaires about your health and quality of life: surveys to measure health outcomes from the patient perspective. Your doctor and/or the research team will provide the instructions and materials you will need to complete the survey at each time point it is due. Whenever possible, this questionnaire will be completed electronically during your study visits.
- Pain diary: You will document your pain twice daily for 28 days via an electronic application. Your doctor and/or research team will provide the instructions you will need to complete the pain diary.

- Between years 3 and 10 from enrollment we will ask your doctor annually whether you are alive and the date you last talked with your doctor. If you are not alive, we will ask for the date of death and the cause of death. If you doctor has lost contact with you, we will search the National Death Index, maintained by the government to record all deaths that occur in the U.S. Through the National Death Index, we will obtain the date of death and the cause of death.

5. Risks and Discomforts

All participants will be asked to come in for a study visit every 3 months for 2 years after we determine if you have a donor or not. We will collect information including blood and other tests at follow up visits for 2 years. These tests are associated with no more than minimal risk although you may experience minor discomfort with blood draw. Participating in the health survey will not cause any physical discomfort but you may find some of the questions or topics on the survey upsetting. If this is the case, your doctor will refer you to a psychologist for counseling.

Bone marrow transplant (BMT) and Standard of Care (SOC) are not the same in their chance of causing serious health problems, chance of early death, or chance of curing your sickle cell disease. The Standard of Care (SOC) treatment you receive for supportive care of your sickle cell disease has very low chance of causing health problems, and the chance of early death from your sickle cell disease is very low, but does increase as you get older. The Standard of Care (SOC) treatment you are receiving for your sickle cell disease will not cure the disorder. Bone marrow transplant (BMT) is a procedure that has a higher risk of causing serious health problems and early death. However, BMT may cure your disease.

If you do not have a donor, there are no treatments that are research. Your condition may not get better or may get worse during the course of the study. Your doctor will treat you as before or may offer other treatment options. If your condition gets worse, your doctor will determine the best treatment for care.

All the procedures and potential risks associated with HCT/BMT will be outlined in a separate consent form that will be given to you if you have a donor and are assigned to the donor arm. If you have questions about the procedures, risks, and benefits associated with HCT/BMT you should ask your doctor now.

You will be promptly notified if, during the conduct of this research study, any new information develops which may cause you to change your mind about continuing to participate. If new information is provided to you after you have joined the study, it is possible that you may be asked to sign a new consent form that includes the new information.

6. Possible Benefits

You may or may not receive medical benefit from taking part in this study. If you are assigned to the transplant arm and the transplant is successful, you may benefit by not having further symptoms and complications of severe sickle cell disease.

Allowing us to collect SCD-related information at enrollment and 2 years later would allow us to directly compare the health outcomes for patients who receive HCT/ BMT to those patients who receive standard of care (regular/routine care). This is very important as this is the first time that SCD physicians will be able to do a direct comparison of patients with severe SCD to determine whether HCT/BMT is a better or worse treatment than routine care for severe SCD. In other words, even though you may not benefit directly, you will contribute towards helping treat future patients with severe SCD.

7. Optional Research Samples

This section of the Consent Form is about collection of optional blood and urine research samples from patients who are taking part in the trial. These research samples will be used for future research studies on patients with SCD.

You can choose to give blood and urine samples if you want to. You can still be a part of the main study even if you say "no" to giving optional blood and urine samples for these studies. You and/or your insurance will not have to pay for these samples to be collected or for any of the important research tests to be performed on these samples. Please mark your choice at the end of this section.

We would like to collect two (2) blood and urine samples over the course of the primary study for future research. If you agree, these samples will be collected at two different times during the primary study.

1. Within a few days after your specific primary study therapy is determined, we would collect about 6 teaspoons (31.5 mL) of blood and 10 teaspoons of urine (50 mL). Usually the blood can be drawn from a vein in your arm at the same time as other blood collections.

2. And about 2 years after your primary study therapy was determined, we would once again collect about 6 teaspoons (31.5 mL) of blood and 10 teaspoons of urine (50 mL).

The blood and urine samples collected for future research purposes will be sent to the Children's Healthcare of Atlanta (CHOA) Biorepository. The samples will be labeled with unique codes that do not contain information that could identify you. A link to this code does exist. The link is stored at the Data and Coordinating Center for the Blood and Marrow Transplant Clinical Trials Network (BMT CTN DCC). The staff at the biorepository where your samples are being

stored does not have a link to this code. Your de-identified research samples may also be given to investigators outside of Emory University for approved research studies. However, these laboratory investigators will not be able to trace the sample back to you.

Your research samples will continue to be stored at the (CHOA) Biorepository until they are used up for research. They will be kept unless you happen to change your mind and request to have your samples destroyed by withdrawing from the study or the Sponsor requests use of stored samples to be discontinued. If you stop being in the primary study before it is finished, upon your written request to [Insert site investigator] any remaining research samples you have given will be discarded when you tell us that you want to stop being in the study. Results we get before you stop being in the study will be kept.

Genetic Studies
DNA from your stored blood samples might be used in future genetic studies. We would like to test your DNA (or genes) to learn if some genes predict who will have serious complications of sickle cell disease. DNA is inherited information like a blueprint about the structure and functions of human body traits that make up the color of our hair and eyes and may affect the way our bodies respond to things that happen outside the body such as smoking, an illness, or infections. Based on genetic studies of patients with sickle cell disease that have been done already, we believe that common differences in genes that control inflammation (entry of white blood cells into tissue) are important reasons for differences in sickle cell disease symptoms. Thus, we are interested in the possibility that there are genes besides the sickle hemoglobin mutation that also contribute to problems with blood flow in your arteries and veins that cause pain and other sickle cell symptoms. In the course of these studies we may find new genes that are inherited and predict the development of other sickle cell disease symptoms.

Risks of Genetic Testing
In the course of these studies we may find new genes that are inherited and predict the development of sickle cell disease related illnesses. Once we have obtained your DNA (or genes) from the white blood cells, we will put the DNA in tubes. These tubes will be labeled with a code, and will have no markings to link the tube with you specifically. If we learn anything of importance to our research from this testing, we may publish the results in a medical journal. However, you will not be identified in the article as the patient who provided the blood sample for our testing.

In rare instances, it is possible that we could find out information about a specific gene that could affect you or other members of your family in terms of insurability, employability or paternity. We will do everything possible to ensure that your identity and confidentiality will not be breached. As previously mentioned, the code linking your identifying information to the sample will be kept secure by the BMT CTN DCC staff in a password protected file on a secure location.

Genome-Wide Association Studies
DNA from your stored blood samples might be used in genome-wide association (GWA) studies for a future project either done or supported by the National Institutes of Health (NIH). Genome-

wide association studies are a way for scientists to find genes that have a role in human disease or treatment. Each study can look at hundreds of thousands of genetic changes at the same time

If your coded samples are used in such a study, the researcher is required to add your test results and sample information into a shared, public research database. This public database is called the NIH Genotype and Phenotype Database and it is managed by the National Center for Biotechnology Information (NCBI). The NCBI will never have any information that would identify you, or link you to your information or research samples, although the results of genetic studies could theoretically include identifying information about you.

Benefits of Genetic Testing
There will be no direct benefit to you for providing this additional blood sample for genetic testing. We hope that the information learned from the study treatment trial and these genetic research tests will help us understand what genes are important. This may further our understanding of the possible treatments to patients with sickle cell disease.

You will be given an additional choice to indicate whether or not your research samples can be used in these important genetic studies. You may choose not to participate in the genetic testing study and still have your blood and urine samples used for other important research. Once again, your decision does not affect your care and participation in the primary study.

Things to Think About:
The choice to let us have blood and urine samples for future research is up to you. No matter what you decide to do, it will not affect your care.

If you decide now that your blood and urine can be kept for future research, you can change your mind at any time. Just contact your study doctor and let him or her know that you do not want us to use your blood sample. Then any blood that remains will no longer be used for research.

In the future, people who do research on these blood and urine samples may need to know more about your health. While the study doctor or others involved in running this study may give the researchers reports about your health, it will not give them your name, address, phone number, or any other information that will let the researchers know who you are.

Your blood and urine will be used only for research and will not be sold. The research done with your blood and urine may help to develop new products in the future.

Benefits:
The benefits of research using blood and urine include learning more about how your body's immune system recovers after a transplant, as well as to gain knowledge that may help people in the future and make transplants even more successful.

Risks:
There is a small risk of an infection or fainting from the blood draw.

The greatest risk to you is the release of information from your health records. We will do our best to make sure that your personal information will be kept private. The chance that this information will be given to someone else is very small.

Making Your Choice:
Please read each sentence below and think about your choice. After reading each sentence, please indicate your choice below. If you have any questions, please talk to your doctor or nurse, or call our research review board at [Insert institution].

No matter what you decide to do, it will not affect your care.

Statement of Consent
The purpose of storing blood and urine samples, the procedures involved, and the risks and benefits have been explained to me. I have asked all the questions I have at this time and I have been told whom to contact if I have more questions. I have been told that I will be given a signed copy of this consent form to keep.

I understand that I do not have to allow the use of my blood and urine for research. If I decide to not let you store research samples now or in the future, it will not affect my medical care in any way.

I voluntarily agree that blood and urine samples may be collected and that my blood, urine and related health information can be stored indefinitely by the Children's Healthcare of Atlanta (CHOA) Biorepository and used for transplant-related and sickle cell disease research.

- ❑ I do agree to give optional blood samples for future research **which may include DNA genetic studies**.
- ❑ I do not agree to give optional blood samples for future research **which may include DNA genetic studies**.
- ❑ I do agree to give optional urine samples for future research.
- ❑ I do not agree to give optional urine samples for future research.

____________________________________ __________
Signature Date

♦ ♦

8. Other Treatments

You do not have to participate in this study. Your participation is ***voluntary***. If you choose not to participate in the study, you will not be missing out on any standard therapy for sickle cell disease. You will receive the same excellent care from the doctors and nurses whether or not you decide to take part in this study. In addition, other types of transplants are currently available to you. In some cases, the source of the stem cells is different from bone marrow. You may also choose to receive a transplant that uses a different combination of medications or a higher or lower dosage of the same medications. The different transplant treatment plans each will have different risks and benefits. Your doctors can discuss each type of transplant with you in greater detail. If you do not have a suitably matched related or unrelated donor and want to still consider HCT/BMT as an option, you may be eligible for other clinical trials that utilize mismatched related or unrelated donors.

9. Costs and Reimbursements

Most of the care given in this study is standard care; it will be billed to you or your insurer in the usual way. This study is also approved by Centers for Medicare and Medicaid Services (CMS) for reimbursement. Standard costs include those of your hospitalization, doctor's visits, standard laboratory tests, medications, and the cost of the donor's bone marrow. There will be no charge for research tests.

The study will pay for the research-related items or services that are provided only because you are in the study as outlined above. If you get a bill you think is wrong, call the researchers.

You or your health plan will pay for all the things you would have paid for even if you were not in the study, like:

- Health care given during the study as part of your regular care
- Items or services needed to give you study drugs or devices
- Monitoring for side effects or other problems
- Treatment of complications
- Deductibles or co-pays for these items or services.

If you do not have a health plan or if you think your health plan may not cover these costs during the study, please talk to the research team or call your health plan's medical reviewer.

If you receive a bill, or believe your health insurance has been billed for something that is part of the study, notify a member of the research team or [Insert institution] Patient Billing Services.

You and/or your health insurance will be charged, in the standard manner, for services and procedures provided for your routine care. Any deductibles, co-insurances or co-payments that are a part of your insurance coverage will apply.

10. Compensation of Payment

You will be paid $25 for completing the health related quality of life questionnaires. You will be asked to complete these questionnaires when you first enroll and at 1 and 2 years later. You can earn up to a total of $75 for completing the health related quality of life questionnaire.

You will receive $1.00 for each electronic pain diary entry. If you complete the pain diary twice daily, you will receive $2.00/day. This compensation will be the same for all three of the 28-day reporting periods. The potential compensation for completing the pain diary at all of these time points is $168.

The total amount of money you can earn for being in this trial is $243.

11. Physical Injury as a Result of Participation

[Insert institution] researchers and their associates who provide services at the [Insert institution] recognize the importance of your voluntary participation in their research studies. These individuals and their staff will make reasonable efforts to minimize, control, and treat any injuries that may arise as a result of this research.

If you believe that you are injured as a result of the research procedures being performed, please contact [Insert site PI name] immediately. Emergency medical treatment for injuries solely and directly related to your participation in this research study will be provided to you by the hospitals [Insert institution]. The study sponsor, the National Heart, Lung, and Blood Institute, does not offer financial compensation or payment if you are injured as a result in participating in this research study. However, you are not giving up any legal rights by signing this form.

It is possible that [Insert institution] may bill your insurance provider for the costs of this emergency treatment, but none of these costs will be charged directly to you. If your research-related injury requires medical care beyond this emergency treatment, you will be responsible for the costs of this follow-up care unless otherwise specifically stated below.

12. Rights as a Participant

Your participation in this research study, including the use and disclosure of your identifiable information for the purposes described above, is completely voluntary. (Note, however, that if you do not provide your consent for the use and disclosure of your identifiable information for the purposes described above, you will not be allowed, in general, to participate in the research study.) Whether or not you provide your consent for your participation in this research study will have no effect on your current or future relationship with the [Insert institution]. Whether or not you provide your consent for participation in this research study will have no effect on your current or future medical care at a [Insert institution] hospital or affiliated health care provider or your current or future relationship with a health care insurance provider.

Your physician is involved as an investigator in this research study. As both your physician and a research investigator, s/he is interested both in your medical care and the conduct of this research study. Before agreeing to participate in this research study, or at any time during your

study participation, you may discuss your care with another doctor who is not associated with this research study. You are not under any obligation to participate in any research study offered by your doctor.

If you have questions about your rights as a research participant or if you have questions, concerns or complaints about the research, you may contact the [Insert institution] Institutional Review Board (IRB) at the toll free number [Insert IRB Number].

13. Ending Your Participation

You may withdraw your consent, at any time, for your participation in this research study, to include the use and disclosure of your identifiable information for the purposes described above. Any identifiable research or medical information recorded for, or resulting from, your participation in this research study prior to the date that you formally withdrew your consent may continue to be used and disclosed by the investigators for the purposes described above.

To formally withdraw your consent for your participation in this research study, you should provide a written and dated notice of this decision to the principal investigator of this research study at the address listed on the first page of this form. Your decision to withdraw your consent for your participation in this research study will have no effect on your current or future medical care at [Insert institution] hospital or affiliated health care provider or your current or future relationship with a health care insurance provider.

If you are thinking about withdrawing from this study, talk with one of the research team members and your regular doctor first so they can help you decide what may be best for your medical care once you are off study. If you leave the study before the planned final visit, the study doctor may ask to have some of the end of study procedures done for your safety and well-being.

Your study doctor or NHLBI may decide to take you out of the study if:

- The researcher believes that it is not in your best interest to stay in the study.
- You become ineligible to participate.
- Your condition changes and you need treatment that is not allowed while you are taking part in this study.
- You do not follow instructions from the researchers.
- The study is suspended or canceled.

14. Privacy, Confidentiality, and Use of Information

By signing this consent form, you are giving the researchers your permission to obtain, use, and share information about you for this study. Information about you may be obtained from any hospital, doctor, and other health care provider involved in your care. This may include information about hospital admissions or visits during this study, so that we know about any possible problems or side effects. If health information is needed from your doctors or hospitals from other institutions, you will be asked to give permission for these records to be sent to the researchers.

Any information about you obtained from this research will be kept as confidential (private) as possible. Federal Privacy Regulations protect your privacy, restrict who is allowed to look at your records, and require security to protect your records. All records related to your involvement in this research study will be stored in a locked file cabinet. Your identity on these records will be indicated by a unique study ID number rather than by your name, and the information linking these case numbers with your identity will be kept separate from the research records. You will not be identified by name in any publication of the research results unless you sign a separate consent form giving your permission (release).

Information gathered during this study and your medical records may be inspected and verified by staff of the study sponsor (the National Heart, Lung, and Blood Institute/National Institutes of Health), Office for Human Research Protections, [Insert institution], or the Institutional Review Board (IRB). Except when required by law, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier in study records shared outside of [Insert institution]. For records shared outside of [Insert institution], you will be given a study ID number. The list that can match you to the study ID number will be kept in a locked file cabinet in [Insert location].

In addition to the investigators listed on the first page of this authorization (consent) form and their research staff, the following individuals will or may have access to identifiable information (which may include your identifiable medical information) related to your participation in this research study:

> Authorized representatives of the sponsor of this research study, the National Institutes of Health, or the Office for Human Research Protections or the Blood and Marrow Transplant Clinical Trials Network will review and/or obtain identifiable information (which may include your identifiable medical information) related to your participation in this research study for the purpose of monitoring the accuracy and completeness of the research data and for performing required scientific analyses of the research data.
>
> In unusual cases, the investigators may be required to release identifiable information (which may include your identifiable medical information) related to your participation in this research study in response to an order from a court of law.
>
> While the study sponsor understands the importance of maintaining the confidentiality of your identifiable research and medical information, the [Insert institution] cannot guarantee the confidentiality of this information after it has been obtained by the study sponsor. The investigators involved in the conduct of this research study may receive funding from the sponsor to perform the research procedures and to provide the sponsor with identifiable research and medical information related to your participation in the study.
>
> Authorized representatives of the [Insert institution] or other affiliated health care providers may have access to identifiable information (which may include your identifiable medical information) related to your participation in this research study for

the purpose of: (1) fulfilling orders, made by the investigators, for hospital and health care services (e.g., laboratory tests, diagnostic procedures) associated with research study participation; (2) addressing correct payment for tests and procedures ordered by the investigators; and/or (3) for internal hospital operations (i.e., quality assurance).

Data Warehouse Consultants (DWC) which is an agent of Emory University that will manage the pain diary. DWC will have access to your phone number, email address, IP Address and data that is entered in the pain diary application.

At the end of the study, the study sponsor, the National Heart, Lung, and Blood Institute (NHLBI) will be given data from the study, without personal identifying information such as your name, address, Social Security number, or Medicare number. The data and/or materials may be shared with other scientists who meet NHLBI requirements. These requirements include treating the data or materials as medically confidential, obtaining approval from their Human Subjects review boards, and agreeing not to share the data or materials with other parties.

The investigators may continue to use and disclose, for the purposes described above, identifiable information (which may include your identifiable medical information) related to your participation in this research study for ten years from enrollment on to study. Beyond the finding period (5-years), the dataset will be transferred to the Center for International Blood and Marrow Transplant Research at the Medical College of Wisconsin for extended follow up. Data regarding your clinical situation, including follow-up after 2 years, may be obtained from the CIBMTR, which captures information on all US transplants.

Extended follow up: Between years 3 and 10 from enrollment, we will ask your doctor annually whether you are alive or dead and the date of last contact with your doctor. If you are not alive, we will ask for the date of death and the cause of death. If you doctor has lost contact with you, we will search the National Death Index annually using your Social Security number. The National Death Index is maintained by the government to record all deaths that occur in the U.S. Through the National Death Index, we will obtain the date of death and the cause of death. This follow up will apply to all subjects regardless of assigned treatment arm.

In accordance with the [Insert institution] Notices of Privacy Practices document that you have been provided, you are permitted access to information (including information resulting from your participation in this research study) contained within your medical records filed with your health care provider.

Your privacy is very important to us. The study doctors will make every effort to protect it. The study doctors have a privacy permit to help protect your records if there is a court case. However, some of your medical information may be given out if required by law. If this should happen, the study doctors will do their best to make sure that any information that goes out to others will not identify who you are.

15. Health Insurance Portability and Accountability Act (HIPAA)

HIPAA authorization to use and disclose individual health information for research purposes:

a. Purpose: As a research participant, I authorize the Principal Investigator and the researcher's staff to use and disclose my individual health information for the purpose of conducting the research study entitled *Bone Marrow Transplantation for Adolescents and Young Adults with Severe Sickle Cell.*

b. Individual Health Information to be Used or Disclosed: My individual health information that may be used or disclosed to conduct this research includes: demographic information (e.g., age, date of birth, sex, weight), medical history (e.g., diagnosis, complications with prior treatment), physical examination findings, and laboratory test results obtained at the time of work up and after transplantation (e.g., blood tests, biopsy results). The identities of individuals such as names and addresses will not be shared or de-identified to make sure information cannot be linked to you.

c. Parties Who May Disclose My Individual Health Information: The researcher and the researcher's staff may obtain my individual health information from: *(list: hospitals, clinics or providers from which health care information can be requested)*

_____

_____

_____

d. Parties Who May Receive or Use My Individual Health Information: The individual health information disclosed by parties listed in item c and information disclosed by me during the course of the research may be received and used by the following parties:

Members of the BMT CTN Data and Coordinating Center and BMT CTN #1503 Protocol Team

National Heart, Lung, and Blood Institute (NHLBI) and the National Cancer Institute (NCI), both of the National Institutes of Health (NIH), study sponsors

The National Marrow Donor Program and the Center for International Blood and Marrow Transplant Research

The Blood Center of Wisconsin (BCW), which is a central lab that will do specialized testing on blood samples required during the study

Data Warehouse Consultants (DWC) which is an agent of Emory University that will manage the pain diary. DWC will have access to your phone number, email address, IP Address and data that is entered in the pain diary application.

U.S. government agencies that are responsible for overseeing research such as the Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP)

U.S. government agencies that are responsible for overseeing public health concerns such as the Centers for Disease Control (CDC) and federal, state and local health departments

e. Right to Refuse to Sign this Authorization: I do not have to sign this Authorization. If I decide not to sign the Authorization, I will not be allowed to participate in this study or receive any research-related treatment that is provided through the study. However, my decision not to sign this authorization will not affect any other treatment, payment, or enrollment in health plans or eligibility for benefits.

f. Right to Revoke: I can change my mind and withdraw this authorization at any time by sending a written notice to the Principal Investigator to inform the researcher of the decision. If I withdraw this authorization, the researcher may only use and disclose the protected health information already collected for this research study. No further health information about me will be collected by or disclosed to the researcher for this study.

g. Potential for Re-disclosure: My individual health information disclosed under this authorization may be subject to re-disclosure outside the research study and no longer protected. Examples include potential disclosures for law enforcement purposes, mandated reporting or abuse or neglect, judicial proceedings, health oversight activities and public health measures.

h. This authorization does not have an expiration date. However, you can elect at any time to withdraw your authorization to participate in the study.

16. For More Information

If you'd like more information about this study, or if you have any problems while you're participating in this study, you can contact the study doctor or staff. They may be contacted at the telephone numbers listed here:

[Insert name and contact details]

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.

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VOLUNTARY CONSENT

All of the above has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions about any aspect of this research study during the course of this study, and that such future questions will be answered by the researchers listed on the first page of this form.

I understand that I may contact the Human Subjects Protection Advocate of the IRB Office, [Insert institution and number] to discuss problems, concerns, and answer any questions I have about my rights as a research participant, to obtain information; offer input; or discuss situations in the event that the research team is unavailable.

By signing this form, I agree to participate in this research study. A copy of this consent form will be given to me.

_____	_____	_____
Signature of Participant	Participant's Printed Name	Date

CERTIFICATION of INFORMED CONSENT

I certify that I have explained the nature and purpose of this research study to the above-named individual(s), and I have discussed the potential benefits and possible risks of study participation. Any questions the individual(s) have about this study have been answered, and we will always be available to address future questions as they arise. I further certify that no research component of this protocol was begun until after this consent form was signed.

_____	_____
Printed Name of Person Obtaining Consent	Role in Research Study
_____	_____
Signature of Person Obtaining Consent	Date

Assent to Participate in Research

[Insert site logo and/or address]

TITLE: A Study to Compare Bone Marrow Transplantation to Standard Care in Adolescents and Young Adults with Severe Sickle Cell Disease

Principal Investigator: [Insert site PI]
Co-Investigators: [Insert site co-I]

Study Coordinators: [Insert site study coordinator/s]

[Insert site department/facility name, address, and phone number]

Source of Support: National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health (the NIH), Bethesda, Maryland

CONSENT FOR A MINOR TO BE A SUBJECT IN CLINICAL RESEARCH AND AUTHORIZATION TO PERMIT THE USE AND DISCLOSURE OF IDENTIFIABLE MEDICAL INFORMATION (PROTECTED HEALTH INFORMATION) FOR RESEARCH PURPOSES.

This is a clinical trial, which is a research study to answer specific medical questions.

The information from this study may also help future patients. The Study doctor (the person in charge of the research) will explain the study to you. This research study will include only people who choose to take part in the study. Please take your time to make your decision about taking part in the study. You may discuss your decision with family and friends. You should also discuss this with your healthcare team. If you have any questions, you can ask the Study doctor for more explanation.

A. Why am I here?

We are inviting you to join our study because you have severe sickle cell disease. You are now receiving blood transfusions, hydroxyurea and/or pain medicines. There is another treatment called bone marrow transplant. A transplant uses blood-making cells from another person (donor) to replace your cells that are not healthy (the sickle red blood cell). A donor is the name for a person who gives some of their blood-making cells for a transplant and their tissue has to match your tissue. Only 3 out of 10 persons will have a tissue-matched donor, so most people do not have a donor. In this study, if you have a donor, you will receive the treatment called bone marrow transplant. If you don't have a donor, you will continue receiving blood transfusion, hydroxyurea, and/or pain medications.

B. Why are you doing this study?

We know transplant works to cure your disease, but we don't know if this is a better treatment than blood transfusions, hydroxyurea, and/or pain medicines.

C. What will happen to me if I receive a transplant?

Before your transplant, you will have check-ups with the study doctors and find out if you have a donor. If you have a donor, you will get a small tube put in your chest in the operating room (you will be asleep for this). The small tube makes it easier for you to get your medicines. It will also make it easier for drawing blood for tests because you will not be poked.

We will give you medicines that will help make the cells from your donor grow in your body. These medicines might make you feel sick. You might throw up, lose your hair, or get sores in your mouth.

After you're done taking the medicines, you will get cells from your donor. This is your transplant. Your donor can be your sister or brother (related) or someone you don't know (unrelated). Your new cells will come from your donor's bone marrow. The cells will make new and healthy cells in your body.

Sometimes the donor cells can cause a problem called graft versus host disease (GVHD). GVHD happens when the donor cells attack your body.. It can give you diarrhea, a skin rash, make you feel sick and throw up, or make you not feel hungry. Your doctors will give you medicines to try to make sure you don't get GVHD.

You will stay in the hospital for several days before your transplant and for about 4 weeks after your transplant. After you go home, you will need to go back to see your doctor often.

It is possible that your disease will come back. If this happens, your doctor will find another way to treat you.

You will be followed for two years with tests for follow up scheduled weekly for the first 100 days and then every 3 months.

D. What will happen to me if I do not receive a transplant?

If you don't have a donor, you will continue receiving blood transfusion, hydroxyurea, and/or pain medications.

You will be followed for two years with tests for follow up scheduled every 3 months.

E. Will it hurt?

For your transplant, we will put a small tube in your chest. It might hurt a little and you might bleed a little. Your doctor and nurses will make sure you feel as little pain as possible.

F. Will the study help me?

We know bone marrow transplant can cure sickle cell disease. What we don't know is whether some of the problems from transplant like GVHD can cause more harm than if you did not have a transplant and continued to receive the care you are receiving now.

G. What if I have questions?

You can ask any questions that you have about the study. If you forget to ask a question and think of it later, you can call me [*insert office number*]. You can also ask your question the next time you see me.

You can call the study office at any time to ask questions about the study.

H. Do I have to be in this study?

You don't have to be in this study. Your doctor and nurses will not be mad at you if you don't want to join. If you decide you don't want to be in this study, you should talk to your doctor, nurses and parents about other ways to treat your disease.

You can say yes now and change your mind later.

Be sure to talk this over with your parents before you decide if you want be in the study. We will also ask your parents to give their permission for you to join this study.

Writing your name on this page means that you agree to be in the study and know what will happen to you. If you decide to quit the study, all you have to do is tell your doctor.

You and your parent or guardian will get a copy of this form after you sign it.

_____	_____
Printed Name of Child	Date
_____	_____
Signature of Child	Age of Child

Certification of Counseling Healthcare Professional: I certify that the nature and purpose, the potential benefits, and possible risks associated with participation in this study have been explained to the above individual and that any questions about this information have been answered.

_____	_____
Printed Name of Person Obtaining Assent	Role in Research Study
_____	_____
Signature of Person Obtaining Assent	Date