Children's Hospital of Philadelphia

Informed Consent and HIPAA Authorization Form

Study Title: *RH* genotype matched red cells for patients with sickle cell disease and anti-D

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You, or your child, may be eligible to take part in a research study. This form gives you important information about the study. It describes the purpose of this research study, and the risks and possible benefits of participating.

In the sections that follow, the word "we" means the study doctor and other research staff. If you are a parent or legal guardian who is giving permission for a child, please note that the word "you" refers to your child.

Study Overview

You are being asked to take part in this research study because you have sickle cell disease, need transfusions, and have formed an antibody against the "D" blood marker even though your own blood cells are D+.

The purpose of this study is to find out if we can find blood that is matched to you by your *RH* blood genes and whether it is safe to give you D+ blood again.

*B*lood matched to you by your *RH* genes is a new way to match blood that we think may give better matched blood for patients with sickle cell disease, but is not yet approved by the FDA because it is new.

If you agree to take part, your participation will last for up to two years. The number of visits depends on how many units of blood you need. You will receive *RH* gene matched blood for each of your transfusions. You will receive blood as you normally do, but will get some blood that is D+ that are *RH* gene matched. This D+ blood will have more information about the blood than a usual unit of D+ blood. You will also return to have blood drawn approximately one week after each transfusion. This is the main difference between this study and your usual care.

The main risks of this study are:

- A possible delay up to 7 days to find you gene matched blood. We will try to avoid this by keeping track of your next transfusion visit and ordering blood for you earlier.
- The anti-D antibody coming back that may cause you to destroy transfused blood that is D+. We think this is unlikely because you will be matched with D+ blood by your genes.
- If you destroy transfused blood, you may have pain, yellow skin and eyes, and feel very tired. We will try to avoid this by only giving you one D+ blood unit the first two study transfusion visits. We will add one unit with each visit until all the units you need are D+.

We will look for the anti-D coming back and for blood breakdown with an extra visit for a blood draw approximately one week after each transfusion. If you feel bad or different after your transfusion, we will also ask you to come back for a. blood draw so we can do extra tests.

You may benefit if *RH* gene matched blood is better matched for you. Better matched blood means having less problems after the transfusion such as making an antibody against the transfused blood. The main question we are asking in this study is whether we can find *RH* gene matched blood for patients with sickle cell disease who have made an antibody against "D" even though their own blood is D+.

If there is anything in this form you do not understand, please ask questions. Please take your time. You do not have to take part in this study if you do not want to. If you take part, you can leave the study at any time. If you do not choose to take part in this study, you can discuss treatment options with your doctor.

Please see below for additional details about the study.

How many people will take part?

About 20 individuals will take part in this study.

What is the current standard of treatment for this disease?

Patients whose blood have the "D" marker but have made an antibody against D, usually get blood without "D." This can make it harder to find blood for that person. Blood is usually not matched your blood genes. If you choose not to take part in this study, you will receive blood matched by the usual testing for blood markers.

What are the study procedures?

Tests that are part of your regular, routine medical care will continue to be performed. Additional tests may be performed if you make anti-D and/or have any signs of red cell breakdown. The study involves the following tests and procedures.

Experimental Procedures:

Study Intervention: You will need to be transfused with D+ *RH* genotype matched blood for each of your transfusion visits for between 4 months and two years, depending on how many red cells units you require per transfusion visit.

Routine Clinical Trial Procedures:

Interviews: A team member will take your medical history, along with a listing of any medications you are taking. Throughout the study you will be asked to report if you think that anything bad has happened as a result of the study.

Medical record and laboratory review: A team member will review your medical record and your pre-transfusion laboratory studies that are done as part of clinical care.

Physical exam: A physical exam will be done. The exam will include measurements of weight, height, heart rate, respiratory rate, blood pressure, and listening to your heart sounds and breath sounds.

Blood tests: A blood sample will be collected prior to each transfusion for the research study and stored. We will draw the blood sample at the same time your pre-transfusion laboratory studies are drawn or when you have an IV line placed or when your central line is accessed. Occasionally, if we can not get the sample at those times, we may ask you if we can draw your blood.

We need to draw your blood (2 to 4 teaspoons) 5 to 12 days after the transfusion study intervention to test whether you make anti-D or have signs of red cell break down. These blood tests will be repeated after every transfusion visit while on study. We will try not to stick you more than once.

Genetic Testing:

The study involves some genetic testing. We will look at some genes that are involved in red cells and sickle cell disease but will not perform genome-wide sequencing.

Visit Schedule

The table below provides a brief description of the purpose and duration of each study visit.

Purpose	Main Procedures	Duration
Screening visit	Physical exam, medical history	1 hour
Transfusion visit	Blood draw Transfuse D+ *RH* genotyped matched red cells (increase by unit each visit except for second transfusion visit) Review medical record	2-4 hours as per clinical care and transfusion guidelines
Lab visit	Blood draw	1 hour
You will have a transfusion visit, then a lab visit after you get one unit of blood with the D marker. If you do not make anti-D again, you will have another transfusion and lab visit. After the first 2 visits, we will give you one more unit with D marker each time. You will continue to have a transfusion visit and a lab visit until all the blood you get has the D marker. For example, if you get 5 units of blood each time, you would have 1 screening visit, 6 tranfusion visits, and 6 lab visits.		

What will be done with my data and specimens during this study?

During the study, we will collect blood samples from you. By agreeing to participate in the study, you agree to give these samples to CHOP for research purposes.

Will I receive any results from the tests done as part of this study?

Results that could be important for your clinical care will be shared with you. We will not share other results with you.

What are the risks of this study?

Taking part in a research study involves inconveniences and risks. The main risks of taking part in this study are discussed below.

Risks associated with study intervention:

Since you have made an anti-D antibody before, there is a risk of anti-D coming back. Transfused blood may be destroyed when you get D+ blood. We think this is unlikely because you will be matched with D+ red cells by RH genotype. If you do experience signs of destroying blood such as feeling very tired, yellow eyes and skins, or very dark urine, we will treat you with medications and possibly, with another blood transfusion.

Risks of physical exams:

There are no physical risks but you might experience momentary embarrassment or discomfort. The exam is similar to those performed as part of routine medical care.

When blood pressure is taken during physical exams, the blood pressure cuff may cause discomfort or bruising to the upper arm.

Risks of blood tests:

Taking blood may cause some pain, bleeding or bruising at the spot where the needle enters your body. Rarely, taking blood may cause fainting or infection.

Risks of Genetic Studies:

The risks related to genetic analyses can be to individuals or to groups. These harms include stigmatization and insurability. To reduce this risk, only coded samples will be stored and used for future research. Information about this study will not be recorded in your medical record.

The Genetic Information Nondiscrimination Act is a Federal law that makes it illegal for some groups to discriminate against you based on genetic information. This law applies to all health insurance companies, group health plans, and employers with 15 or more employees. This law does not apply to companies that sell life insurance, disability insurance, or long-term care insurance.

Risk of transfusion delay

There is the risk of a delay in your transfusion up to 7 days to find *RH* gene matched red cells for you. This may be inconvenient for you. Sometimes, you may have health problems related to waiting the extra week such as pain, feeling tired, or worsening of the SCD problem that is why you get transfused.

Risks associated with breach of confidentiality:

As with any study involving collection of data, there is the possibility of breach of confidentiality of data. Every precaution will be taken to secure participants' personal information to ensure confidentiality.

At the time of participation, each participant will be assigned a study identification number. This number will be used on data collection forms, blood samples, and in the database instead of names and other private information. A separate list will be maintained that will links each participant's name to the study identification number for future reference and communication.

Are there any benefits to taking part in this study?

- *RH* gene matched blood may be better matched for you.
- Better matched blood means having less problems such as making antibodies.
- This study may help doctors know if there are enough blood donors with *RH* genes that match patients' *RH* genes.
- It will also help doctors know if *RH* gene matched blood with the D marker is safe for patients who had anti-D in the past, even though the person has a D marker.

Do you need to give your consent in order to participate?

If you decide to participate in this study, you must sign this form. A copy will be given to you to keep as a record.

What are your responsibilities?

Please consider the study time commitments and responsibilities as a research subject when making your decision about participating in this study. You will need to follow the study doctor's instructions and keep all study appointments since we are requesting special units of blood for you.

What happens if you decide not to take part in this study?

Participation in this study is voluntary. You do not have to take part in order to receive care at CHOP.

If you decide not to take part or if you change your mind later there will be no penalties or loss of any benefits to which you are otherwise entitled.

Can you stop your participation in the study early?

You can stop being in the study at any time. You do not have to give a reason.

Can the study doctor take you out of the study early?

The study doctor may take you off of the study if:

- The study blood that is *RH* genotyped is no longer available.
- You cannot meet all the requirements of the study.
- New information suggests taking part in the study may not be in your best interests.

What choices do you have other than this study?

There are options for you other than this study including:

- Not participating in this study.
- Continue getting blood that is D- that is matched by current, standard tests

What about privacy, authorization for use of Personal Health Information (PHI) and confidentiality?

As part of this research, health information about you will be collected. This will include information from medical records, procedures, interviews and tests. Information related to your medical care at CHOP will go in your medical record. Laboratory test results will appear in your medical record with the exception of antibody evaluations which are performed only for this research study. This could include physical exams or tests done in the clinical lab. Medical records are available to CHOP staff. Staff will view your records only when required as part of their job. Staff are required to keep your information private. Information that could identify you will not be shared with anyone - unless you provide your written consent, or it is required or allowed by law. We will do our best to keep your personal information private and confidential. However, we cannot

guarantee absolute confidentiality. Your personal information may be disclosed if required by law.

The results of this study may be shown at meetings and published in journals to inform other doctors and health professionals. We will keep your identity private in any publication or presentation.

Several people and organizations may review or receive your identifiable information. They will need this information to conduct the research, to assure the quality of the data, or to analyze the data or samples. These groups include:

- Members of the research team and other authorized staff at CHOP;
- People from agencies and organizations that perform independent accreditation and/or oversight of research; such as the Department of Health and Human Services, Office for Human Research Protections;
- New York Blood Center staff, who is testing your blood sample(s) and identifying the *RH* genotyped red cell units that are matched for you. Private information such as your name, birth date or medical record number will be shared with them to order your *RH* genotyped red cell units;
- The National Institutes of Health who is sponsoring this research;
- The Food and Drug Administration who oversees all blood products;

By law, CHOP is required to protect your health information. The research staff will only allow access to your health information to the groups listed above. By signing this document, you are authorizing CHOP to use and/or release your health information for this research. Some of the organizations listed above may not be required to protect your information under Federal privacy laws. If permitted by law, they may be allowed to share it with others without your permission.

There is no set time for destroying the information that will be collected for this study.

Your permission to use and share the information and data from this study will continue until the research study ends and will not expire. Researchers continue to analyze data for many years and it is not possible to know when they will be completely done.

Certificate of Confidentiality (CoC)

A Certificate of Confidentiality (CoC) covers this research. A CoC helps protect your identifiable information and biological samples.

A CoC protects your private information from all legal proceedings. Unless you consent, information from this research study that identifies you will not be shared outside this research.

- No one can be forced to share your identifiable information or biological samples for a lawsuit.
- Your information can't be used as evidence even if there is a court subpoena.

If you consent, your data or biological samples could be shared for:

- other scientific research
- your medical treatment

The CoC does not prevent some disclosures.

- The researchers can't refuse requests for information from those funding this research. The National Institutes of Health may need information to assess this project.
- The US Food and Drug Administration (FDA) may need information information because they oversee all blood products..
- You can still share information about yourself. You can also freely discuss your involvement in this research.
- The researchers must disclose things required by law. This includes suspected child abuse and neglect, harm to self or others, or communicable diseases.

Can you change your mind about the use of personal information?

You may change your mind and withdraw your permission to use and disclose your health information at any time. To take back your permission, it is preferred that you inform the investigator in writing.

Dr. Stella Chou
The Children's Hospital of PhiladelphiaDivision of Hematology
34th Street and Civic Center Blvd.
Philadelphia, PA 19104

In the letter, state that you changed your mind and do not want any more of your health information collected. The personal information that has been collected already will be used if necessary for the research. No new information will be collected. If you withdraw your permission to use your personal health information, you will be withdrawn from the study.

Financial information

While you are in this study, the cost of your usual medical care – procedures, medications and doctor visits – will continue to be billed to you or your insurance.

Will there be any additional costs?

There will be no additional costs to you by taking part in this study.

The National Institutes of Health (NIH) is providing financial support and material for all experimental procedures, as listed above, for this study. The following research procedures, study interventions and study visits will be paid by the NIH:

- Cost of *RH* genotyping the blood to match for you
- Blood tests for new antibody formation and evaluation for red cell breakdown

You or your insurance will be billed for the routine costs of receiving your regular transfusions, which include exams, tests or procedures that are necessary to administer the transfusion.

We can help you understand your financial responsibilities.

- If your insurance does not pay for all the costs, you will be responsible for the remaining costs, including any co-payments and deductibles as required by your insurance.
- If you do not have insurance, you will be responsible for the costs of taking part in this study.

CHOP has programs to help uninsured and underinsured families see if financial assistance is available. If you need financial assistance, you can talk with a financial coordinator.

Will you be paid for taking part in this study?

- Children/participants will be paid $50 for their time and effort in returning for the laboratory visit 5 to 12 days after the transfusion.
- Children/participants will also be reimbursed for travel to the return laboratory visit 5 to 12 days after the transfusion if this poses an economic hardship. Upon submission of receipts, reimbursement will be issued.

You will receive payment or travel reimbursement using a debit card, so the bank will have access to identifiable information. The bank will not have access to any medical information.

We may share your specimens and data with third parties (other researchers/institutions or for profit companies). Your specimens and data may be used for commercial profit. You will not receive any financial benefit from the use of your specimens or data.

Who is funding this research study?

The National Institutes of Health is providing funding for this study.

Please ask Dr. Stella Chou if you have any questions about how this study is funded.

What if you have questions about the study?

If you have questions about this study or how your samples/data are going to be used, call the study doctor, Dr. Stella Chou at 215-590-0947. You may also talk to your own doctor if you have questions or concerns.

The Institutional Review Board (IRB) at The Children's Hospital of Philadelphia has reviewed and approved this study. The IRB looks at research studies like these and makes sure research subjects' rights and welfare are protected. If you have questions about your rights or if you have a complaint, you can call the IRB Office at 215-590-2830.

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.

What happens if you are injured during the study?

If you are hurt or get sick from something that was done as part of this study, doctors at the clinic or hospital can arrange for emergency medical care. The Hospital does not offer financial compensation or payment for injuries due to participation in this research.

You and your insurance company will be billed for the costs of any care or injuries.

If you think you have been injured from taking part in this study, call Dr. Dr. Stella Chou at 215-590-0947. She can go over things with you, let you know of resources that may be available and give you information on what you need to do.

In case of injury resulting from this study, you will not lose any legal rights by signing this form.

Optional Consent for Use of Identifiable Data or Specimens for Future Research

As part of the study, we will collect data and blood samples from you. We may wish to use and share this information or samples in a future study about sickle cell disease or red cell transfusions.

Research could occur at CHOP, or at outside institutions, which could include for profit companies. The information and samples will be given a unique code and may include information that can identify you. Information that can identify you or the blood samples may be kept permanently in a computer database and laboratory at CHOP or at the New York Blood Center. A Master List that links the data and the blood samples to you will be stored in a password protected database at CHOP.

We may not ask for your consent before using or sharing your identifiable specimens or data. You will not receive any results or financial benefit from the future research done on your specimens or data. We may share your identifiable specimens or data with outside researchers who will use them for future research.

If you leave the study, you can ask to have the data collected about you removed or the samples destroyed. You can also ask us to remove information that identifies you from the data or samples. This may not be possible if your samples and data have already been shared.

Please indicate whether you will allow the identifiable data and samples to be used for future research by putting your initials next to one of the following choices:

_____ (initials) NO, my identifiable data and specimens may not be used for future research. They may be used for this study only.

_____ (initials) YES, my identifiable data and specimens may be used for other future research studies.

Consent to Take Part in this Research Study and Authorization to Use and Disclose Health Information for the Research

The research study and consent form have been explained to you by:

Person Obtaining Consent	Signature of Person Obtaining Consent
	Date

By signing this form, you are indicating that you have had your questions answered, you agree to take part in this research study and if you are giving permission for a child or consent for an adult to participate in this research study, you are legally authorized to consent to the child's or adult's participation. You are also agreeing to let CHOP use and share the health information that will be collected for this study, as explained above. If you don't agree to the collection, use and sharing of health information, you cannot participate in this study.
NOTE: *A foster parent is not legally authorized to consent for a foster child's participation.*

Name of Subject	
Signature of Subject (18 years or older)	Date
Name of Authorized Representative (if different than subject)	Relation to subject: ☐ Parent ☐ Legal Guardian ☐ Legally Authorized Representative
Signature of Authorized Representative	Date

Assent to Take Part in this Research Study

For children (or adults with diminished capacity) capable of providing assent:

I have explained this study and the procedures involved to _____ in terms he/she could understand and that he/she freely assented to take part in this study.

_____
Person Conducting Assent

_____ _____
Signature of Person Conducting Assent Date

This study has been explained to me and I agree to take part.

_____ _____
Signature of Subject (optional) Date

For children (or adults with diminished capacity) unable to assent:

I certify that _____ was not capable of understanding the procedures involved in the study sufficiently to assent to study participation.

_____
Person Responsible for Conducting Assent

_____ _____
Signature of Person Responsible Date