Children's Hospital Los Angeles

CONSENT/PERMISSION/ASSENT[1] TO PARTICIPATE IN A RESEARCH STUDY

Brain blood flow and its response to changes to inhaled oxygen levels in subjects with and without sickle cell disease

Subject's Name:			
CHLA #:		Birth Date:	

- **INTRODUCTION**

You are invited to participate in a research study conducted by Dr. John Wood, Dr. Thomas Coates, Dr. Jon Detterich, Dr. Herbert Meiselman, and Dr. Henry J. Forman from the Departments of Cardiology, Hematology, Pediatrics and Radiology at Children's Hospital Los as well as the Department of Physiology, Gerontology, and Biophysics at the University of Southern California. You are invited to participate in this study because you 7 years of age and older and have Sickle Cell Disease, have anemia for other reasons, or have an ethnic background similar to patients with Sickle Cell Disease. We expect to enroll 220 subjects in this research. 100 subjects enrolled in this study will have Sickle Cell Disease, 60 subjects will have anemia for other reasons, and 60 subjects will be gender and ethnicity-matched healthy controls who are free of any diseases or disorders. Participation in this study is completely voluntary. Please read the information below, and ask questions about anything you do not understand, before deciding whether or not to participate.

- **PURPOSE OF THE STUDY**

The purpose of this research study is to try to understand whether we can use sensitive measures of brain blood flow and its response to change to inhaled oxygen levels to determine how the brain protects its oxygen supply. By learning this, we may identify patients at risk for stroke in the future or discover ways to better protect the brain from stroke in sickle cell disease patients.

- **PROCEDURES**

Participation in this research will last up to 30 days.

This research study will be conducted at Children's Hospital Los Angeles in the General Clinical Research Center.

Below is the list of tests and exams that will be done for the study. All tests will be performed at a single location.

[1] This form also serves as the permission form for the parent(s) to read and sign. In this case, "You" refers to your child.

1. **Medical history**: We will ask that you allow us to review and record data from your medical record. This information will help us better understand the MRI data. If you are seen elsewhere you will also be asked to sign a medical release form. We will also ask you questions about your health. This is to find out if you have any serious medical problems that would prevent you from participating in this research study.
2. **Blood Tests**: A regular blood drawing needle will be placed in your arm to sample blood. The blood tests are being done to look at the level of red and white blood cells in your blood (complete blood counts), levels of inflammation in your body, and the types of hemoglobin. In addition we will be doing other tests on the red cell mechanical properties and metabolism that will be sent to special labs at the University of Southern California for processing. The total amount of blood to be drawn will be 3 tablespoons (45 ml).
3. **Urine Sample**: You will be asked to give a urine sample that will be used for research testing. We will collect up to 3 teaspoons (15ml) of urine if a sample is needed.
4. **Brain MRI**: We will have you lie on a padded bed. We will also fit you with a breathing mask connected to the room air. MRI measurements of your brain will be started. The imaging is quite noisy, but you will have to try to hold your head still and not talk. At two separate times, we will switch your breathing source from room air to nitrogen for five breaths and then switch it back to room air. This will cause the oxygen levels in your blood to fall briefly to a level encountered by many people when they sleep but will not reach a dangerous level. We will then switch the mask to pure oxygen for ten minutes. This is not harmful, although some people feel a little excited when they breathe pure oxygen. Then for the rest of the MRI imaging, you will breathe room air. MRI measurements will be made throughout the changes in oxygen levels. The total MRI time including imaging and set up will be approximately 120 minutes.
5. **Heart Monitor/Oxygen Monitor**: There are 2 special devices you will be asked to wear for 24 hours. One is called "Actiheart". This is a small, light device that will be attached to your chest by 2 pads. Through this device we can measure your heart rate continuously for 24 hours. The other special device is called a "Wrist-PAT". This is a small, light device that is worn on your wrist and is the size of a cell phone. A small wire connects this device from your wrist to one of your fingers. Through this device we can measure your blood pressure and oxygen level continuously. Both of these devices will be worn for 24 hours. When you take it off you can either drive back to CHLA and return them in person or you can mail them back in a self-addressed, stamped box to CHLA. You will not have to pay for shipping and handling.
6. **Neuropsych Testing and Questionnaires**: We will ask that you complete neuropsychological assessments, consisting of pen and paper tests designed to evaluate your understanding such as verbal and visual skills, memory, and attention. We will also ask background information about you and your parent or legal guardian. This testing will take up to 4 hours to complete. An examiner will administer the paper and pencil tests to you. Additionally, we will ask you to complete approximately half an hour of questionnaires addressing areas such as attention and social-emotional functioning. If you have sickle cell disease or anemia for which you are transfused, the testing will be scheduled at a time convenient for you but must be done within ten days after your regularly scheduled blood transfusion, in order to reduce the effects of possible fatigue on your test performance. If you are a healthy control the testing will take place within 30 days of the MRI research scan. As always, participants can take as many breaks as needed during the assessment. After the neuropsychological assessment is completed,

you will receive a written report explaining the results. You will be given a copy of the final report. You may choose whether or not to share this report with your medical treatment team, teachers, etc.

Data from this study may be used in future research trials related to brain and vascular function. The information that will be shared will not contain any personal information that may identify you.

Completion of failed tests:
When possible, in the event of a failed test (examples: lost lab results, computer failure during procedures, inability to schedule exams/procedures on the same day), you will be asked to return to CHLA at a later time to repeat the failed test.

- **POTENTIAL RISKS AND DISCOMFORTS**

1. **Blood Tests**: The risk of this test can be pain, bruising, infection or puncture of the needle through the vein. Only staff with experience will draw blood from you. Those staff will be a lab tech, nurse or physician. By having only experienced staff draw your blood any complications are reduced.
2. **MRI:** There are no known risks for MRI imaging. If your oxygen levels decrease too far for any reason, we would remove your experimental mask and allow you to breathe regular air. However, we have performed these tests in many subjects with no prior problems.

   It is possible that we may find unexpected results on the MRI, even unwanted findings. Your brain MRI will be read by a board-certified neuroradiologist and the results will be available to you. We can also send results to your physician, if that is your wish.
3. **Heart Monitor (Actiheart)/Oxygen Monitor (Wrist-PAT device):** It is possible that you could have an allergic reaction to the adhesive that holds the pads in place on your chest.
4. **Privacy:** Whenever data (medical information) is being looked at in research there is some risk that nonmedical personnel may learn some private information. To protect you from this all research information on the study will be coded. This code will only be known to the research team. All efforts will be made to minimize this risk
5. **NeuropsychTesting**: Typically, neuropsychological assessment result reports include areas of strength and weakness. There is a possibility you may experience mild discomfort when reading the results from your neuropsychological assessment. Should you experience any discomfort, or have questions regarding the results, you may contact the examiner, a licensed psychologist, on the phone number included in the report.

If the results of any tests and/or procedures done as part of this research tell us something that would be concerning that information will be given to you and to your doctor for follow up.

There may be additional risks to participation in this study that we do not know about and therefore cannot describe.

- **ANTICIPATED BENEFITS TO SUBJECTS**

This study will not provide direct benefit to you.

- **ANTICIPATED BENEFITS TO SOCIETY**

Stroke is extremely common in patients with sickle cell disease. Your participation in this trial may help us understand why this happens and how we might prevent it.

- **ALTERNATIVES TO PARTICIPATION**

The alternative to participating in this study is not to participate. You will receive your standard of care at CHLA.

- **PAYMENT FOR PARTICIPATION**

You will also be paid for your study visits. The money given to you is meant to reimburse you for costs connected with being in the study. This money should be used for time off work and other expenses that may occur such as food or child-care. If you are less than 18 years old your parent or guardian will be paid on your behalf.

You will receive $100.00 in cash upon completion of the MRI study visit and return of the 24-hour recording devices. The devices can be returned either in person or by mail. If returned by mail a self-addressed stamped padded envelope will be provided to you.

You will receive $ 100.00 in cash upon completion of the neuropsych testing.

Total payment for participation in this study is $200.00 in cash.

Should you be asked to return to the clinic in the event that the testing devices failed during the MRI you will be compensated $100.00 in cash to repeat the study procedures again.

In addition, if you need assistance with transportation a taxi can be arranged to bring you to the study visit and take you home. Parking validation will be provided as needed.

- **FINANCIAL OBLIGATION**

This research study is funded by National Institutes of Health and supported in part by the Clinical Translational Science Institute (CTSI) grant awarded to CHLA.

Participants and their families are not responsible for any of the medical costs involved in this study and all exams are free of charge. Neither you nor your insurance company will be billed for your participation in this research.

- **EMERGENCY CARE AND COMPENSATION FOR INJURY**

The investigators and CHLA are not able to offer financial compensation or absorb the costs of treatment should you be injured as a result of participating in this research.

If injury were to occur as a result of participating in this study, the Clinical Trials Unit of the Clinical Translational Science Institute (CTSI) will provide appropriate medical care. However,

the duration and extent of any medical treatment will be determined by the Clinical Translational Science Institute.

If you believe that injury has been suffered as a result of participation in this study, you should contact Dr. John Wood, Dr. Thomas Coates or Dr. Jon Detterich at 323-660-2450. Ask the hospital operator to page one of these doctors to call you back.

- **PRIVACY AND CONFIDENTIALITY**

Members of the research team and, if appropriate, your physicians and nurses will know that you are a research subject. All results will be kept confidential, but may be made available to you, and/or your physician if you wish. No information about you, or provided by you during the research will be disclosed to others without your written permission, except:

- If necessary to protect your rights or welfare (for example, if you are injured and need emergency care); or
- If required by law (i.e., child or elder abuse, harm to self or others, reports of certain infectious diseases).

When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity. Your identification will be protected using a unique identifier for all study related usage of the data. All information collected in this study will also be included in your medical record. You have the right to review all information obtained during this study.

Authorized representatives of the Department of Health and Human Services (DHHS), the Clinical Translational Science Institute (CTSI), and the CHLA Institutional Review Board may need to review records of individual subjects. As a result, they may see your name and your child's name but they are bound by rules of confidentiality not to reveal your identity to others.

A copy of this consent form will be placed in your medical record.

- **PARTICIPATION AND WITHDRAWAL**

Your participation in this research is VOLUNTARY. Your choice about whether or not to participate will have no effect on your care, services or benefits at Children's Hospital Los Angeles. If you agree to participate, but later decide to withdraw from this study, you may do so without affecting your rights to health care, services or other benefits at Children's Hospital Los Angeles. Please contact the Principal Investigator if you wish to withdraw from the study.

- **WITHDRAWAL OF PARTICIPATION BY THE INVESTIGATOR**

The investigator may withdraw you from participating in this research if necessary to protect your health or if other situations arise that make it necessary to do so. If you become ill during the research, you may have to drop out, even if you would like to continue. The investigators, Dr. John Wood, Dr. Thomas Coates, Dr. Herbert Meiselman or Dr. Jon Detterich will make the decision and let you (and your parents) know if it is not possible for you to continue. The decision may be made either to protect your health and safety, or because it is part of the research plan that people who develop certain conditions may not continue to participate.

- **NEW INFORMATION**

If there is significant new information found during the course of the study or the research plan is changed in a way that might affect your decision to continue participating in the study, you will be informed and your consent to continue participating in the study may be requested.

- **HOW TO OBTAIN INFORMATION**

Daytime, Monday through Friday, 8:00 A.M. through 4:30 P.M. you may call Dr. John Wood at 323-361-5470 or Dr. Thomas Coates at 323-361-2352.

Evenings, nights, weekends or holidays you may call the hospital number, 323-660-2450 and ask for either the Division of Cardiology or Hematology Service doctor on-call.

- **FINANCIAL INTEREST OF THE INVESTIGATOR**

Funding for this research study is provided by the Clinical Translational Science Institute (CTSI) grant awarded to CHLA and by the National Heart Lung and Blood Institute of the National Institute of Health. The amount of funding is not based on the number of research subjects enrolled. If your physician is an investigator for this study he is interested in both your healthcare and the conduct of this research. You are not under any obligation to participate in a research study conducted by your physician.

- **RIGHTS OF RESEARCH SUBJECTS**

You may withdraw from this study at any time and discontinue participation without penalty. You are not waiving any legal claims, rights or remedies because of your participation in this research study. If you have questions regarding the rights of research subjects or if you have complaints or concerns about the research and cannot reach the Principal Investigator; or just want to talk to someone other than the Investigator, you may call Children's Hospital Los Angeles, Human Subjects Protection Program office at (323) 361-2265.

SIGNATURE OF RESEARCH SUBJECT (If the subject is 14 years or older)

Your signature below indicates

- You have read this document and understand its meaning;
- You have had a chance to ask questions and have had these questions answered to your satisfaction;
- You consent/assent to your participation in this research study; and
- You will be given a signed copy of this form.

_____
Print Name of Subject

_____ _____
Signature of Subject Date

SIGNATURE OF PARENT(S)/LEGAL GUARDIAN(S) (If the subject is a minor)

Your signature(s) below indicates

- You have read this document and understand its meaning;
- You have had a chance to ask questions and have had these questions answered to your satisfaction;
- You agree to your child's participation in this research study;
- You agree to your own participation in this research study; and
- You will be given a signed copy of this form.

_____ _____

Print Name(s) of Parent(s)/Legal Guardian(s)

_____ _____

Signature of Parent/Legal Guardian Date

_____ _____

Signature of Parent/Legal Guardian Date

SIGNATURE OF INDIVIDUAL OBTAINING CONSENT

I have explained the research to the subject and/or the subject's parent(s)/legal guardian(s) and have answered all of their questions. I believe that they understand all of the information described in this document and freely give consent/permission/assent to participate.

_____

Print Name of Individual Obtaining Consent

_____ _____

Signature of Individual Obtaining Consent Date

SIGNATURE OF WITNESS

My signature as Witness indicates that the subject and/or the subject's parent(s)/legal guardian(s) voluntarily signed this consent/permission/assent form in my presence.

_____

Print Name of Witness

_____ _____

Signature of Witness Date

SIGNATURE OF INTERPRETER

_____
Print Name of Interpreter

_____ _____
Signature of Interpreter Date

Study Team Instructions: Only complete the section below if assent is required and either only verbal assent was obtained from the subject or assent was not obtained from the subject.

Please check appropriate box and sign below.

☐ The undersigned, _____, hereby certifies that verbal assent was obtained from the subject.

☐ Assent was not obtained from the subject. (Please state the reason. Examples include: subject is an infant; subject is comatose; subject lacks cognitive abilities to understand the information; etc.)

_____

_____

Date:_____

Time:_____ Signature_____

Routing of signed copies of the form:
1) Give to the subject if at least 14 years old (copy)
2) Give to the parent/legal guardian if subject is a minor (copy)
3) Place in the CHLA Medical Record (copy)
4) Place in the Principal Investigator's research file (original)