



CHILDREN'S NATIONAL MEDICAL CENTER

Research Center for Genetic Medicine
111 Michigan Avenue, NW
Washington, DC 20010
(202) 476-6011

CONSENT TO PARTICIPATE IN A CLINICAL RESEARCH STUDY AND AUTHORIZATION TO USE PROTECTED HEALTH INFORMATION

Patient with a Leukodystrophy

TITLE OF STUDY: New Diagnostic Approaches In Leukodystrophy

PRINCIPAL INVESTIGATOR: Adeline Vanderver, MD; Department of Neurology

"You" refers to "You" or "Your Child" throughout this document

INTRODUCTION: We would like to invite you to be part of a research study at Children's National Medical Center. Before you decide if you would like to participate, we want you to know why we are doing the study. We also want you to know about any risks (anything unexpected that might happen) and what you will be expected to do in the study.

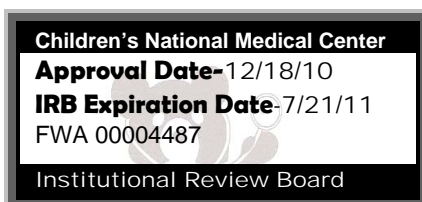
This form gives you information about the study. Your doctor will talk to you about the study and answer any questions you have. We encourage you to discuss this study with your family and anyone else you trust before making your decision. We will ask you to sign this form to show that you understand the study. If your child is seven years old or older, we may talk to your child about the study and ask your child to sign a form like this one but shorter. We will give you a copy of this form to keep. It is important that you know:

- You do not have to join the study;
- You may change your mind and stop being in the study any time you want
- If we make any important change to the study we will tell you about it and make sure you still want to be in the study.

IRB Protocol No.: { 3415 }

Date: 11.10.10

Page 1 of 13





A. PURPOSE OF STUDY

Your physician suspects that you may have a leukodystrophy. Leukodystrophy is a disease that affects the white matter. The white matter is the area of the brain through which messages are sent. A substance called myelin allows messages to move quickly through this area and causes the area to look white in color, which is why it is called white matter. Leukodystrophies can have many causes, some known and some yet to be recognized. Many patients have leukodystrophies for which there are no specific tests to help establish the cause or diagnosis. Even patients who have a leukodystrophy that has a recognized cause may not be easy to diagnose with the tests currently available. There is a need for better testing techniques in leukodystrophies.

The purpose of this study is to establish new tests for leukodystrophies.

B. PROCEDURE

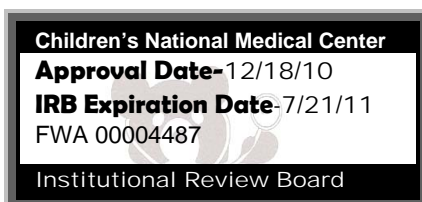
If your physician believes that you have a leukodystrophy, we would like to include you in this study to improve the diagnosis and understanding of the leukodystrophies.

This study uses blood, and excess urine, cerebrospinal fluid and tissue samples to help identify genes and proteins related to leukodystrophy. Genes carry the instructions for how everything in our body works. Proteins are created from the instructions in the genes and carry that message to the body. If we can identify genes altered in patients with a specific disease we may be able to identify the gene causing the disease or genes that can be targeted for future types of treatment. If we can identify proteins that are changed in patients with a specific disease we may be able to identify the process causing the disease and these can also be targeted for future types of treatment.

If you agree to participate, your physician will be asked to complete a questionnaire regarding your symptoms. He or she will also be asked to send any medical records and MRI images related to your diagnosis of leukodystrophy. After we review these records we will contact your physician to let them know if you fit the inclusion criteria for this study (any known or unknown form of leukodystrophy).

If we ask that you be included in our study, this may include the following things:

IRB Protocol No.: { 3415 }
Date: 11.10.10
Page 2 of 13





We may ask that you visit Children's National Medical Center in Washington DC for a clinical evaluation. This means that we would ask you to come to our hospital to be seen by Dr. Vanderver. This would include a physical examination. In some cases it is not necessary or possible for patients to travel for this research study. Dr. Vanderver and your doctor may discuss this in individual situations.

If you give a urine sample for testing, we may ask to keep some extra fluid in our research.

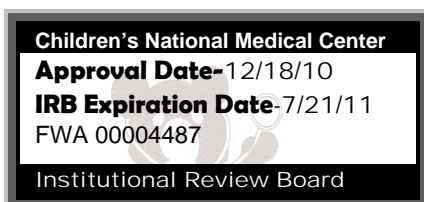
Also, if you have a spinal tap or lumbar puncture as part of the tests done by your doctor, we would like to keep any extra fluid for use in our research. We will use the fluid to look at what proteins are found in the cerebrospinal fluid (fluid from the lumbar puncture) in patients with leukodystrophies. We will not ask you to have a spinal tap for this study alone.

If you have a skin biopsy as part of the tests done by your doctor, we would like to ask that a culture of skin cells be sent to us for use in our research. The skin cells may be grown from the skin biopsy (so that we end up with many more cells than what was originally taken) this allows us to use the cells for research without using up the cells obtained during the original biopsy. We will use the skin cells to look at what proteins and genes are activated or inactivated in certain diseases. We will not ask you to have a skin biopsy for this study alone.

In addition, you may be asked to give a blood sample for DNA testing of genes known to cause different forms of leukodystrophy and also for testing of all the genes using special techniques to see which genes are activated or inactivated in certain diseases. We may keep fluid, DNA or cells from this blood sample.

We may use advanced techniques to test your DNA for genetic causes of leukodystrophy. The new DNA sequencing technology looks at all the human genes we know about; this is known as genome sequencing. We are looking to see if any of these genes have changes that might explain your condition. Just like with any other type of genetic testing we do as part of this study, if we are able to find a genetic change that we believe is the cause of your leukodystrophy, your sample will be sent to a clinical testing center for verification, and you will receive that information. In addition to providing information about leukodystrophies, genome sequencing may lead to the discovery of gene changes that are known to cause or contribute to other

IRB Protocol No.: { 3415 }
Date: 11.10.10
Page 3 of 13





diseases, gene changes that are not known to cause disease (normal variations), or gene changes of new or uncertain clinical importance. If we find a gene change that has serious health implications unrelated to our study of leukodystrophy, and for which there is an immediate and accessible treatment, we will repeat the test for that specific gene variant in a clinical laboratory. We will ONLY give you results about specific abnormal gene variants that we think are important to your health and/or the health of your relatives, and that have been confirmed in a clinical laboratory. This type of finding is very rare, and most people will not receive this type of information from this study. Information about genes and how they relate to disease is always changing, and we will only provide this genetic information to you based on knowledge we have at the time of this study.

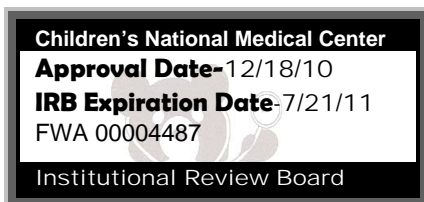
Your DNA, cerebrospinal fluid or skin culture sample(s) will be stored in a confidential manner in Dr. Vanderver's laboratory. They will be stored with an identifying number on them. Dr Vanderver and members of her research team can look up that number in a confidential database to know that sample belongs to you, but no one else can. The sample(s) will be kept until the end of this study. In the future, researcher's may want to use your sample in other similar studies that try to find out more about your specific kind of leukodystrophy or other similar diseases. Because these diseases are rare, your donation of samples is very precious to researchers. If at any point you decide that you no longer want the sample(s) kept, you may contact Dr. Vanderver at 202- 476-6011 to withdraw from the study and the sample(s) will be destroyed. If you are signing this consent for a minor, this person may decide at age 18 if he/ she wishes to continue to participate in the study if no diagnosis has been made.

No treatment methods are being tested in this study.

C. POTENTIAL RISKS/DISCOMFORT

1. For DNA-based studies, we require one sample of blood (about 2 teaspoons). The needle puncture in one's vein from the blood draw may result in bleeding, pain, discomfort, or infection. The procedure is to be performed by individuals trained and experienced in obtaining blood samples so as to minimize these risks.
2. Cerebrospinal fluid is obtained during a lumbar puncture or spinal tap. This procedure may result in bleeding, pain, headache or infection. The procedure is performed by individuals experienced in performing lumbar punctures.

IRB Protocol No.: { 3415 }
Date: 11.10.10
Page 4 of 13





3. Skin cultures are obtained from skin biopsies. This procedure may result in bleeding, pain, headache or infection. The procedure is performed by individuals experienced in performing skin biopsies.
4. Other samples may be collected when laboratory work or testing is being done.
5. A genetic counselor, employed by Dr. Vanderver's laboratory, will be available to discuss any concerns that you may have.
6. The information being collected in this study is confidential but not anonymous. You may worry about how this information may affect your/your child's health/life insurance and or future employment. All records will be kept in a locked file cabinet or in a password protected web-based database at Children's National Medical Center and will not be discussed or released to anyone but your referring physician without your express written consent.
7. There is a chance that you may feel stress from participating in our research. Knowing that you have a leukodystrophy can lead to feelings of anxiety or sadness. Stress may also occur in knowing that you have a genetic condition, but that the doctors don't have a cure or treatment for these conditions. We have a genetic counselor who can answer questions you have about the research. If you are upset, you should talk to your doctor about this. If you are unsure if you want to be in this research study, the genetic counselor can help you decide if you want to participate.

Genetic testing may provide information about how health or illness is passed on to you by your parents or from you to your children. This knowledge may affect you emotionally. Other family members may also feel stress, anxiety or depression because how this genetic information affects them. Some genetic testing can also determine if people are directly related, meaning that it can show that a person was adopted, or that their biological parent is not their legal parent. If this information wasn't previously known, this may cause distress. The genetic counselor can help you understand what the genetic information from this study could mean for you and your family.

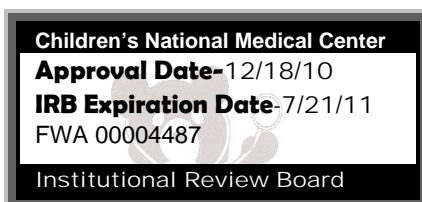
D. VOLUNTARY PARTICIPATION

There will be no penalty or loss of benefits to which you are otherwise entitled if you decide to withdraw from the study.

E. POTENTIAL BENEFITS

By having samples from individuals with genetic diseases and their family members, our laboratory has identified previously unknown genetic changes in genes and proteins. Through this study, we expect to continue to identify new

IRB Protocol No.: { 3415 }
Date: 11.10.10
Page 5 of 13





genetic changes associated with disease. This enables us to develop accurate tests and is a place to start in the development of a rational genetic therapy for diseases. If we find any results through our research that might help you/ your child directly, we will let your doctor know so that he (she) can tell you. In addition, there is the potential benefit of diagnosis when you are examined by a physician will special expertise in leukodystrophy.

F. ALTERNATIVES TO PARTICIPATION

No treatment is offered or recommended for participants in this study. If you decline participation in this study, your medical care here at Children's National Medical Center (CNMC) will not be affected.

G. QUESTIONS – WHO TO CALL

We want you to ask questions about any part of this study or consent form either now or at any time in the future. If you have research or medical questions about this study, call the Principal Investigator, Dr. Adeline Vanderver, at 202-476-6011. If you believe you have been injured as a result of being in this study, you should call the Principal Investigator, Dr. Adeline Vanderver, at 202-476-6011. If you have any questions or concerns about your rights in this research study at any time, please call Children's Hospital's Manager of Customer Relations, at (202) 476-5000 or call the Chief Academic Officer of the Children's National Medical Center at (202) 476-5000.

H. CONFIDENTIALITY

We will keep the records of this study confidential. We will not tell anyone you are in the study. Only the people working on the study will know your name. They will keep this information in case we have to find you later for medical reasons. The federal government can review the study records and medical records to make sure we are following the law and protecting the people in the study and to make sure our results are correct. Your medical record is confidential, but just like any medical record; there are some exceptions under state and federal law.

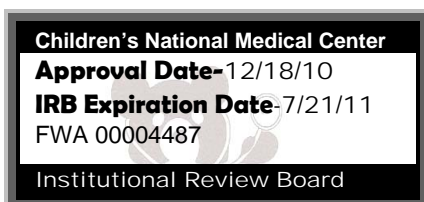
HEALTH INSURANCE PORTABILITY AND ACCOUNTABILITY

In 1996 the government passed a law known as The Health Insurance Portability and Accountability Act (HIPAA). This privacy law protects your individually identifiable health

IRB Protocol No.: { 3415 }

Date: 11.10.10

Page 6 of 13





information (Protected Health Information or **PHI**). The privacy law requires you to sign an agreement so researchers can use or share your PHI for research purposes. This describes to you how information about you may be used or shared if you are in a research study. It is important that you read this carefully and ask a member of the research team to explain anything you do not understand.

I authorize Dr. Adeline Vanderver and her research staff to create, access, use, and disclose my PHI for the purposes described below.

Protected Health Information that may be used and shared includes:

- Information that identifies you such as name, address, telephone number, date of birth, Social Security number, and other details about you
- Information that relates to your health or medical condition from your medical records
- Information obtained from the study procedures outlined in this consent form, for example: things done to see if you can join the study such as physical exams, blood and urine tests, x-rays and other tests, and any other medical information we learn from you about your health history and family history
- Laboratory results obtained on specimens collected from you (blood, urine, tissue)

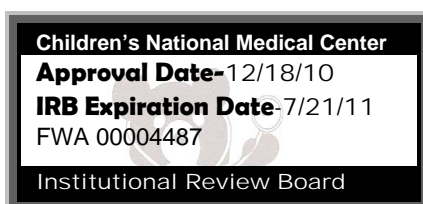
The Researchers may use and share my Protected Health Information with:

- ◆ The Principal Investigator, other Investigators, Study Coordinators, and all administrative staff in charge of doing work for the study;
- ◆ Government agencies that have the right to see or review your PHI, including but not limited to the Office of Human Research Protections and the Food and Drug Administration;
- ◆ Children's National Medical Center Institutional Review Board;
- ◆ Audit Committee of the Children's National Medical Center Institutional Review Board;
- ◆ Quality Improvement Program Coordinator and other staff in the Office for the Protection of Human Subjects at Children's National Medical Center.

In addition to the above people and organizations, the Researchers may also use and share my Protected Health Information with:

- The Patient Advocate or Research Ombudsman (person who watches out for your

IRB Protocol No.: { 3415 }
Date: 11.10.10
Page 7 of 13





best interest)

- Any other outside entity who will receive health information
Please list: physician/ genetic counselor referring patients into the study

Also, your primary physician will be contacted if during the course of the study the researcher learns of a medical condition that needs immediate attention.

Should your health information be disclosed to anyone outside of the study, your information may no longer be protected by HIPAA and this Authorization. However, the use of your health information will still be regulated by applicable federal and state laws.

Banking of Tissue/DNA Specimens:

We would like to store tissue/DNA specimens collected from you in this study in a tissue bank for future research as identified below. The tissue specimens may consist of any one or more of the following:

- ◆ DNA (blood or saliva)
- ◆ Blood fluid (plasma or serum)
- ◆ Blood cells (lymphocytes or white blood cells)
- ◆ Urine
- ◆ Cerebrospinal fluid (CSF)
- ◆ Skin fibroblasts

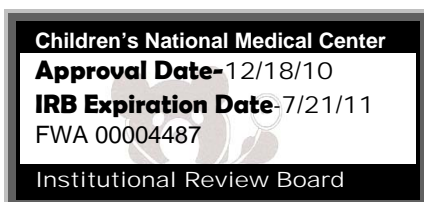
The tissue bank is maintained by Dr. Adeline Vanderver's Laboratory within the Center for Genetic Medicine, a branch of the Children's National Medical Center.

By signing this document, you indicate your approval of any or all of the following:

My tissue/DNA may be stored in the above named bank for future analysis related to this study.

My tissue/DNA may be stored in the above named bank for future analysis related to [leukodystrophy research](#).

IRB Protocol No.: { 3415 }
Date: 11.10.10
Page 8 of 13





If you would like to be contacted with results of this study that might affect your health, please indicate how to best be contacted you by providing your permanent address, phone number, and email address. If you prefer that we do not contact you directly, but prefer that we contact your physician, please indicate your physician's contact information below. (In the case of someone under the age of 18 years, we will contact the parents until the minor reaches adulthood.)

Please indicate below what your preferences to be contacted are by checking the box next to the desired choice.

Please contact me directly

Please **do not** contact me directly, I would like all information sent directly to my doctor.

Permanent Address: _____

Street
Address _____

City State Zip code

Phone () _____

Fax () _____

Email Address _____

When selecting the physician to place as the contact it is often helpful to select someone who is working with the participant closely regarding his/her diagnosis of leukodystrophy.

Physician Name: _____
Last First Middle Initial

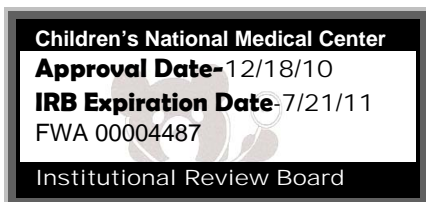
Address: _____

Street
Address _____

City State Zip code

Phone () _____

IRB Protocol No.: { 3415 }
Date: 11.10.10
Page 9 of 13





Fax (_____) _____

Email Address _____

I may change my mind at a later time and request that my tissue specimen be destroyed. If I change my mind and want to request that my tissue be destroyed, I must do so in writing to Dr. Vanderver, at phone number 202-476-6011; fax 202-476-6014.

Storage of PHI in a Database:

We would like to store personal health information collected from you in this study in a database for future research. The database is maintained by [Dr. Adeline Vanderver's Laboratory](#) within Children's National Medical Center with the branch of Center for Genetic Medicine, Children's Research Institute.

By signing this document, you indicate your approval of any or all of the following statements:

My personal health information may be stored in the above named database for future analysis related to this study.

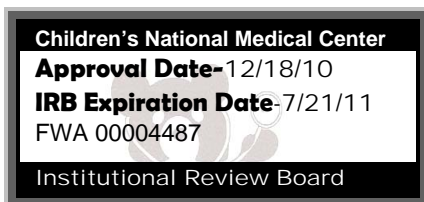
My personal health information may be stored in the above named database for future analysis related to [leukodystrophy research](#).

If you agree to participate in this research study, the research team, may use Personally Unidentified Study Data. The Personally Unidentified Study Data does not include your name, address, telephone, or social security number. Instead, the researcher assigns a code to the Personally Unidentified Study Data. Personally Unidentified Study Data may include your date of birth, initials, and dates you received medical care. Personally Unidentified Study Data may also include the health information used, created, or collected in the research study. The research team may share the Personally Unidentified Study Data with others to perform additional research, place it into research databases, share it with researchers in the U.S. or other countries, or use it to improve the design of future studies. They may also publish it in scientific journals, or share it with business partners

IRB Protocol No.: { 3415 }

Date: 11.10.10

Page 10 of 13





and to file applications with U.S. or foreign government agencies to get approval for new drugs or health care products.

You do not have to sign this Consent/Authorization. If you decide not to sign the Authorization, you will not be allowed to participate in the research study.

After signing the Consent/Authorization, you can change your mind and:

- ◆ Revoke this Authorization. If you revoke the Authorization, you will send a written letter to: Dr. Adeline Vanderver to inform him of your decision.
- ◆ If you revoke this Authorization, researchers may only use and disclose the PHI that was collected for this research study before you revoked the Authorization.
- ◆ If you revoke this Authorization your PHI may still be used and disclosed if you should have an adverse event (unexpected side effect).
- ◆ If you change your mind and withdraw the Authorization, you will not be allowed to participate in the study.

You will not be allowed to review the information collected for this research study until after the study is completed. If you are not allowed to review your information during participation in the study, when the study is over you will have the right to access the information.

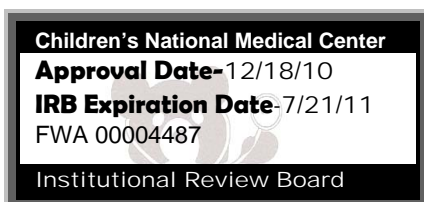
This Authorization does not have an expiration date.

If you have not already received a Notice of Privacy Practices from Children's National Medical Center, you may request a copy and will be given one. If you have any questions or concerns about your privacy rights, you may contact the Children's Hospital Privacy Officer at 202-884-4550.

I. COMPENSATION

Children's National Medical Center cannot promise that the risks we have told you about or other unknown problems will not happen. If you think that something unexpected happened because your child was in the study, please call the Chief Academic Officer of the Children's National Medical Center at (202) 476-5000. We will give your child any emergency treatment needed.

IRB Protocol No.: { 3415 }
Date: 11.10.10
Page 11 of 13





J. ADDITIONAL ELEMENTS

The National Institutes of Health supports a Research Subject Advocate or RSA for the research study that you are being asked to join. The RSA, Dr. Tomas Silber, is here to help you with your questions or concerns about taking part in this research. Dr. Silber does not work for the doctors who are doing this research and they do not pay him. He is here only to help and protect you during any research.

You may contact Dr. Silber at any time. This can be before you decide to take part in the research, during the study, or even after you finish the study. You can call Dr. Silber at 202-476-3066 or reach him by e-mail at tsilber@cnmc.org.

K. CONSENT

I am the participant or I am authorized to act on behalf of the participant. I have read this information and will receive a copy of this form after it is signed.

By signing this form, you agree that you have talked to your/your child's doctor about the study and understand it, and want yourself/your child to be in the study. The different parts include:

1. Collection of medical records, MRI and clinical examination
2. Collection of a blood sample for genetic tests
3. Saving additional cerebrospinal fluid for protein and other tests
4. Saving skin culture for protein and genetic tests
5. Saving additional urine for protein and other tests

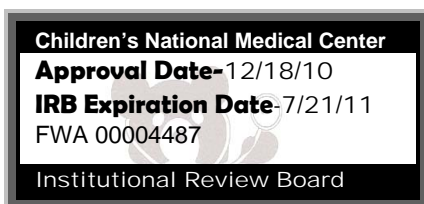
You agree that we have talked to you about the risks and benefits of the study, and about other choices. You may take yourself/your child out of the study at any time and no one will mind and nothing will change about your/your child's medical care other than not being in the study. Copies of this form will be:

- (1) kept in the study file by the Principal Investigator;
- (2) put in your/your child's medical record; and
- (3) given to you to keep.

Please call the Principal Investigator, Dr. Adeline Vanderver, at 202-476-6011 if you have any questions.

Printed Name of Participant: _____

IRB Protocol No.: { 3415 }
Date: 11.10.10
Page 12 of 13





Medical Record Number: _____
Printed Name of Parent(s)/Guardian(s): _____

Signature of Participant: _____ Date: _____
(Participant must be 18 years of age or older)

Signature of Parent(s)/Guardian(s): _____ Date: _____
[Note: signature of both parents required if more than minimal risk and no direct benefit, unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child]

Witness (to signatures): _____ Date: _____
(may be investigator)

Translator's Signature (if, applicable): _____
Language: _____

INVESTIGATOR'S AFFIDAVIT: I certify that I have explained to the above individual(s) the nature and purpose of the study, potential benefits, and possible risks associated with participation in this study. I have answered any questions that have been raised.

Printed Name of Individual Obtaining Consent: _____

Title: _____ Signature: _____ Date: _____

IRB Protocol No.: { 3415 }
Date: 11.10.10
Page 13 of 13

