Childhood Liver Disease Research Network

(ChiLDReN)

FibroScan™ in Pediatric Cholestatic Liver Disease

(FORCE)

NCT Number: 02922751

Informed Consent Form

December 12, 2019

E&I Review Services
IRB Study #16096
01/15/2020

CONSENT TO BE PART OF A RESEARCH STUDY

GENERAL INFORMATION ABOUT THIS STUDY AND THE RESEARCHERS

Study Title: Childhood Liver Disease Research Network (ChiLDReN) FibroScan™ in Pediatric Cholestatic Liver Disease (FORCE) Study Protocol

Company or agency sponsoring the study: National Institutes of Health (NIH) / National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)

Data Coordinating Center: Arbor Research Collaborative for Health

Principal Investigator: <<Site Specific>>

Study Coordinator: <<Site Specific>>

KEY INFORMATION ABOUT THE RESEARCH STUDY

You may be eligible to take part in a research study. This form contains information that will help you decide whether to join the study. All of the information in this form is important. Take time to carefully review this information. After you finish, you should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others, such as your friends, family, or other doctors about your possible participation in this study. If you decide to take part in the study, you will need to sign this form. Before you do, be sure you understand what the study is about.

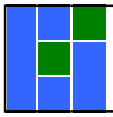
Taking part in this study is completely voluntary. You do not have to participate if you don't want to. You may also leave the study at any time. If you leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled.

This purpose of this research is to learn more about the progression of the growth of scar tissue in the liver (liver fibrosis) in children and young adults with liver disease. We are investigating the use of a painless ultrasound technology to measure changes in the liver that indicate the amount of scar tissue in the liver and changes in that scar tissue over the two years of participation.

You are being asked to take part in this research study because you are already enrolled in one of the ChiLDReN network studies at this hospital (PROBE, BASIC, or LOGIC).

Your participation in this study may be up to two years. Study participation will include:

- Providing a blood sample. It is expected you will donate 3 teaspoons of blood throughout the course of this study. We will try to obtain this blood sample at the same time as other blood samples are being drawn to avoid the need for another needle stick.
- A researcher will feel your abdomen to assess the size of your spleen (the spleen can be enlarged when there is scarring of the liver).
- You will undergo an ultrasound exam utilizing the FibroScan™ machine that will take between 15 and 30 minutes.
- You will come to the clinic for follow-up visits at one year and two years after the first appointment described above. The same tests will occur at each appointment. The staff will make every effort to make sure that all appointments will happen at the same time as clinical visits or research visits for other ChiLDREN studies.



There can be risks associated with joining any research study. The type of risk may impact whether you decide to join the study. For this study, some of these risks may include discomforts associated with obtaining blood and/or FibroScan ultrasound, and the risk of breaching confidentiality. More detailed information will be provided later in this document.

This study may not offer any benefit to you now but may benefit others in the future by allowing future researchers to use your biosamples and associated data that will be stored at the NIDDK repository. More information will be provided later in this document.

The alternative to participating in this study is to not participate. Your care will not be affected if you decide to not take part in this study.

PURPOSE OF THIS STUDY

This purpose of this research study is to learn more about the progression of the growth of scar tissue in the liver (liver fibrosis) in children and young adults with liver disease. We are investigating the use of a painless ultrasound technology (FibroScan) to measure changes in the stiffness of the liver that indicate the amount of scar tissue in the liver and changes in the scar tissue over the two year of this study.

WHO MAY PARTICIPATE IN THE STUDY

Taking part in this study is completely **voluntary**. You do not have to participate if you don't want to. You may also leave the study at any time. If you choose to not be in the study or leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled.

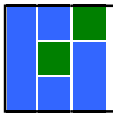
Inclusion criteria:

- Age 21 years or less at the time of enrollment
- Participants enrolled in a ChiLDReN based prospective observational cohort study (PROBE, BASIC, or LOGIC)
- Willingness and ability to participate in the study for up to 24 months
- One of the following three diagnoses
    - Biliary atresia or,
    - Alpha-1 antitrypsin deficiency or,
    - Alagille Syndrome

Exclusion criteria:

- Biliary atresia with known situs inversus or polysplenia/asplenia
- Presence of clinically significant ascites detected on physical examination
- Open wound near expected FibroScan probe application site
- Use of implantable active medical device such as a pacemaker or defibrillator
- Known pregnancy
- Prior liver transplant
- Unable to give informed consent

There will be approximately 550 people taking part in the study. The study is being performed at many major university centers in the United States and Canada.



INFORMATION ABOUT STUDY PARTICIPATION

If you agree to participate in this study, you will speak with a researcher who will explain the study to you. You will have an opportunity to ask questions about the study prior to agreeing to participate. You will come to the clinic for follow-up visits at one year and two years after the first appointment. The same tests will occur at each appointment. The staff will make every effort to make sure that all appointments will happen at the same time as clinical visits or research visits for other ChiLDREN studies.

Study participation will include:

Provide a blood sample. It is expected you will donate 3 teaspoons of blood throughout the course of this study. We will try to obtain this blood sample at the same time as other blood samples are being drawn to avoid the need for another needle stick.

A researcher will feel your abdomen to assess the size of your spleen (the spleen can be enlarged when there is scarring of the liver)

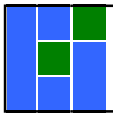
You will undergo an ultrasound exam utilizing the FibroScan™ machine

- You will lie on a table on your back with your right arm out to the side. A trained investigator will apply a water-based gel to your right chest wall and move a small probe over the area to look at your liver.
- After the exam, the gel will be removed with a soft cloth.
- The exam will take between 15 and 30 minutes.
- If you request it, the physician will share the results of the FibroScan™ examination with you, although this is a research finding and it is not used in clinical care.

At any time, you may decide to leave the study. If you withdraw, no more information will be collected from you. When you indicate that you want to leave the study, the investigator will ask if the information/specimens/materials already collected from you can be used.

Your blood samples and data will be sent to the NIDDK Central Repositories, a research resource supported by the National Institutes of Health. The Repository collects, stores, and distributes biological samples and associated data from people with many kinds of disorders, from unaffected family members, and from other healthy people. The purpose of this collection is to make samples and associated data available for use in research for the study of children and young adults who have liver disease after the current study is completed. Sending samples and associated data to the Repository may give scientists valuable research material that can help them to develop new diagnostic tests, new treatments, and new ways to prevent diseases. Your blood samples and de-identified information may be used or shared for future research.

The Repository will take measures to protect your privacy, although no guarantee of confidentiality can be absolute. Before the researchers in this study send samples and associated data to the Repository, each sample will be given a code number. Your name and all personal identifying information, such as address, social security number, and date of birth, will be removed. Therefore, the Repository will not be able to give out your name, or other information that identifies you, to the scientists who receive the samples and associated data. However, the Repository and scientists will have some data about you, such as age, gender, diagnosis, race, and outcomes of the initial study. We will not use your blood for whole genome sequencing or try to identify you by your DNA.



If you agree to have your sample(s) and associated data stored in the Repository, you can change your mind up until the end of the [name of FORCE study]. When study researchers receive written instructions from you, they will destroy your sample and all information that identifies you. After the FORCE study ends, you will not be able to withdraw your sample because the Repository will not know which one is yours. The sample and associated data will stay in the Repository indefinitely.

INFORMATION ABOUT STUDY RISKS AND BENEFITS

Participation in this study will involve research procedures. There are some risks and discomforts that may be associated with this research project including risks and discomforts associated with:

Giving a blood sample: This may include mild pain. A bruise may appear for a few days at the spot where the needle was inserted. There is a slight chance of infection. This is very unlikely. There is also a small risk of dizziness and fainting with blood draws. These risks are made less by the use of trained staff to draw your blood.

Ultrasound: You may experience minor discomfort or soreness over the area where the ultrasound probe touches your abdomen. You may undergo an exam with a probe that has not been FDA-approved for use in children. There is a small risk that you could have an allergic reaction to the water-based gel used to improve the connection between the ultrasound probe and the skin during the exam.

Privacy: There is a potential risk to your privacy when involved in a research study, but all steps will be taken to minimize the risk. Some data obtained for research use will be labeled with your name; however, this information will stay at *<<Your Study Site>>.* Information that is put in the database or that is sent with your samples will be labeled with a study specific identification number.

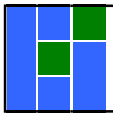
As with any research study, there may be additional risks that are unknown or unexpected. You might become uncomfortable and find the research procedures to be upsetting. You have the option to withdraw from the study at any time.

It is important for you to understand that there is a small chance that some research may yield results that may indirectly have a negative impact on insurability, employability, and/or family relationships of some individuals or groups of people.

The researchers will tell you if they learn of important new information that may change your willingness to stay in this study. If new information is provided to you after you have joined the study, it is possible that you will be asked to sign a new consent form that includes the new information.

The investigator is willing to discuss any questions you might have about these risks and discomforts.

You will not receive any direct benefit for participating, but your sample and associated data may benefit the future health of the community at large or some particular group. Because other researchers will not have access to your identity, neither you nor your physician will get the eventual results of studies that might be performed using your sample. It is possible that data resulting from use of your sample may eventually be used in a research publication. In that event, your name or other identifying information will not be included, as this information will not be available to the researchers.



ALTERNATIVES TO PARTICIPATING IN THE STUDY

Participation in this study and donation of samples to the Repository are completely voluntary and your alternative is not to participate. You will receive the same treatment whether or not you take part in this study and there will be no penalty or loss of benefits to which you are otherwise entitled. Ask the researchers or your doctors about other options that you may have.

ENDING THE STUDY

You are free to leave the study at any time. If you leave the study before it is finished, there will be no penalty to you. If you choose to tell the researchers why you are leaving the study, your reasons for leaving may be kept as part of the study record. If you decide to leave the study before it is finished, please notify one of the persons listed in Contact Information section of this consent.

There is no risk of harm to you if you decide to leave the study early.

There are many reasons why the researchers may need to end your participation in the study. Some examples are:

- 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 the study.
- You receive a liver transplant.
- Pregnancy.
- You do not follow instructions from the researchers.
- The study is suspended or canceled.

FINANCIAL INFORMATION

You will not be paid to take part in this study.

For this study, you will not be charged for the cost of the special research laboratory tests and studies conducted only for research purposes. However, you or your health insurance company will be responsible for costs related to the standard diagnosis, treatment and follow-up of your liver condition, including: clinic visits, blood tests, operations, biopsies, medicines, vitamins, immunizations and special feeding formulas. It is important to understand that some insurance companies may not cover all of the above listed costs. If your insurance company does not cover these treatments or procedures, you will be required to pay for them. Ask the researchers if you have any questions about bills, fees, or other costs related to this study.

By signing this form, you do not give up your right to seek payment if you are harmed as a result of being in this study.

Sometimes, research results in findings or inventions that have value if they are made or sold. These findings or inventions may be patented or licensed, which could give a company the sole right to make and sell products or offer testing based on the discovery. Some of the profits from this may be paid back to the researchers and the organizations doing this study, but you will not receive any financial benefits. Biospecimens may be used for commercial profit and you will not share in this profit.

CONFIDENTIALITY OF SUBJECT RECORDS AND AUTHORIZATION TO RELEASE YOUR PROTECTED HEALTH INFORMATION

There is the possibility of a breach of confidentiality and your participation could become known outside the research study. Personal identifiers (other than date of birth and gender) will be removed from all information stored in the study database.

Protected Health Information (PHI) is any health information through which you can be identified. Protected Health Information is protected by federal law under the Health Insurance Portability and Accountability Act of 1996 (HIPAA). A decision to participate in this research means that you agree to let the research team use and share your PHI for the study explained above. Study PHI will be kept in your research record and only the research team will have access to this information.

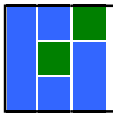
This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the SPONSOR which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of child abuse and neglect. If you tell us or we learn something that makes us believe that you or others have been or may be physically harmed, we may be required to report that information to the appropriate agencies. The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document.

Department of Health and Human Services (DHHS) personnel may request identifying information for purposes of performing audits, carrying out investigations on DHHS grant recipients, or evaluating DHHS funded research projects.

Once you are enrolled into this research study, you will be assigned a unique Research ID Number. All information and samples (blood) will be labeled with this de-identified number. Only the research team will keep a list that matches your name with this Research ID number. Information sent to the Data



Coordinating Center and specimens sent to the NIDDK repository will contain the de-identified number. This way only the research team at this clinical site will be able to identify you.

The Repository will take measures to protect your privacy, although no guarantee of confidentiality can be absolute. Before the researchers in this study send samples to the Repository, each sample will be given a code number. Your name and all personal identifying information such as address, social security number, and date of birth, will be removed. Therefore, the Repository will not be able to give out your name, or other information that identifies you to the scientists who receive the samples. However, the Repository and scientists will have some data about you, such as age, gender, diagnosis, race, and outcomes of the initial study.

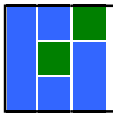
The only identifiable information in the research file is your date of birth and gender. This information is necessary to perform statistical analysis on the data, such as to calculate growth rates and age at onset of the illness. This information in the research file is no longer protected by HIPAA.

You will not be identified in any reports or publications that arise from this study. We will take every precaution to protect your confidentiality.

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.

There are many reasons why information about you may be used or seen by the researchers or others during or after this study. Examples include:

- The researchers may need the information to make sure that you can take part in the study.
- The researchers may need the information to check your test results or look for side effects.
- A monitor from the Data Coordinating Center may review your medical records and consent forms to check that the data that you provide are being recorded correctly and to monitor the progress and safety of the study.
- University and government officials and representatives from the NIH (study sponsor) or the Institutional Review Board may review your medical records to make sure that the study is done properly.
- Study sponsors or funders, or safety monitors or committees, may need the information to:
    - Make sure the study is done safely and properly
    - Learn more about side effects
    - Analyze the results of the study
- Representatives from Echosens, the manufacturer of the FibroScan machine, may need the information to help us interpret the scan results.
- Your date of birth and gender must be shared with the Data Coordinating Center and the Data Safety and Monitoring Board, which oversees the safety of the study. This protected health information (PHI) will be used for statistical analysis of medical data.
- Insurance companies or other organizations may need the information in order to pay your medical bills or other routine medical costs not related to your participation in the study.
- The researchers may need to use the information to create a databank of information about your condition or its treatment.



- All data and samples are stored in a central repository under contract with NIH. The data and the samples do not contain any personal identification.
- Federal or State law may require the study team to give information to government agencies. For example, to prevent harm to you or others, or for public health reasons.

Your participation is voluntary; you may choose not to participate in this research study or to withdraw at any time. Your choice will not affect the commitment of your health care providers to care for you and there will be no penalty or loss of benefits to which you are otherwise entitled. If you decide to end your participation in the study, please contact the Principal Investigator.

If you agree to have your sample(s) and associated data stored in the Repository, you can change your mind up until the end of the study. When study researchers receive written instructions from you, they will destroy your sample and all information that identifies you. After the study ends, you will not be able to withdraw your sample because the Repository will not know which one is yours. The sample and associated data will stay in the Repository indefinitely.

Samples and data that you provide may be used at any time in the future for research into liver disease. Both samples and data will be stripped of all personal identifiers. These samples and data may be used by researchers approved by NIH who may not be part of the current study.

It is not possible to undo or disallow research that has already been performed. Specimens and data that have been stripped of personal identifiers cannot be retrieved.

It is important to understand that once your medical records have been disclosed as described above, they may no longer be protected directly by federal privacy regulations issued under HIPAA. However, as long as the information is held in any part of the institution, it is protected by the institution's privacy policies. For more information about these policies, please ask your doctor for a copy of the Site's Notice of Privacy Practices.

You will not be informed of the details of any specific research studies or results that might be conducted using your identifiable private information or identifiable biospecimens, including the purposes of the research.

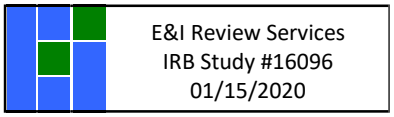
The results of this study could be published in an article but would not include any information that would let others identify you.

Your permission expires at the end of the study, unless you cancel it sooner. You may cancel your permission at any time by writing to the researchers listed in Contact Information section of the consent. If you withdraw your permission, you will no longer be eligible to participate in this study.

CONTACT INFORMATION

Please contact the researchers listed below to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Talk about study-related costs to you or your health plan



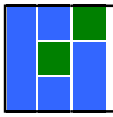
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study
- To provide input about the study

Principal Investigator:
Mailing Address:
Telephone:

Study Coordinator:
Mailing Address:
Telephone:

You may also express a concern about this study by contacting the Institutional Review Board listed.
Ethical & Independent Review Services
816-421-0008
www.eandireview.com
Reference E&I study 16096

If you are concerned about a possible violation of your privacy, contact the Institution's Privacy Officer at_____.



SIGNATURES

Consent to Participate in the Research Study

I have read the information printed on this form. I have discussed this study, its risks and potential benefits, and my other choices with <<Study Team Member Name/s>>. My questions so far have been answered. If I have more questions or concerns about the study or my participation as a research participant, I may contact one of the people listed in the Contact Information section (above). I will receive a copy of this form at the time I sign it and later upon request. (Note: In addition to the copy you receive, copies of this document will be stored in a separate confidential research file.)

Adult Consent

- **I consent to participate in this study._____Initials**
- **I consent to provide blood and information (this information does not contain my name or other identifying information) to the NIDDK Repository. _____Initials**
- **I do not agree provide blood to the NIDDK Repository._____Initials**

Legal Name: _____

Signature:_____

Address:_____

Date of Signature (mm/dd/yy): _____

Principal Investigator or Designee

I have provided this participant information about this study that I believe to be accurate and complete. The participant was told about the nature of the study, including risks and benefits of participating.

Name:_____

Title:_____

Signature: _____

Date of Signature (mm/dd/yy): _____