INFORMED CONSENT
AND
AUTHORIZATION TO DISCLOSE HEALTH INFORMATION
FOR ADULT SUBJECT / PARENT / LEGAL GUARDIAN

TITLE: Evaluation of Patients with Liver Diseases

INSTITUTE: CALIFORNIA LIVER RESEARCH INSTITUTE (CLRI)

PROTOCOL NO.: CLRI-01

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This form is for use in a research study that may involve subjects who may or may not have the capacity to consent to take part in the study. Accordingly, when the subject cannot legally consent to take part, pronouns "you" and "your" should be read as referring to the subject rather than the person (legally authorized representative) who is signing and dating this form for the subject. In cases where the subject's representative gives consent, the subject should be informed about the study to the extent possible given his/her understanding. During the course of the study, if the subject regains the capacity to consent, informed consent should be completed and the subject offered the ability to leave the study if desired.

If you are the parent or legal guardian of a child who may take part in this study, your permission and the permission of your child will be needed. When "you" appears in this form, it may refer to you or your child.

INTRODUCTION

We invite you to take part in a research study at California Liver Research Institute (CLRI). Before agreeing to participate in this research study, it is important that you read and understand the following explanation of the proposed research study. This consent document describes the purpose, procedures, benefits, risks, discomforts and

precautions of the study. It also describes the alternative procedures that are available to you and your right to withdraw from the study at any time. No guarantees or assurances can be made as to the results of the study.

If you are an employee, your participation or your family member's participation will not place you in good favor with the study doctor, your supervisor, or the study sponsor (for example, increase in salary, promotion, extra vacation, or the like). Not participating will not adversely affect your employment with the study doctor, in particular the position that you currently hold.

If you are not completely truthful with your study doctor regarding your health history, you may harm yourself by participating in this study.

First, we want you to know that: Taking part in this research is entirely voluntary. You may choose not to take part, or you may withdraw from the study at any time. In either case, you will not lose any benefits to which you are otherwise entitled. You may receive no benefit from taking part of this study. The research may give us knowledge that may help people in the future.

Second, some people have personal, religious or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive. If you have such beliefs, please discuss them with your study doctors or research team before you agree to the study.

Background

Now we will describe this research study. Before you decide to take part, please take as much time as you need to ask any questions and discuss this study with anyone, or with family, friends or your personal physician or other health professional.

As a patient with liver disease, or as the parent/guardian of a child with liver disease, or as a healthy volunteer, you are invited to take part in this research study, which will evaluate patients in a careful and thorough manner to gain insight into the natural history of your disease and to provide a better understanding of its causes.

If you are a healthy volunteer: you will have one visit with us with blood draw and fibroscan (a special ultrasound of the liver to measure liver fat and scarring). However, we may call you in the future if further tests are needed. We will also ask you to bring a copy of your previous medical records and blood tests.

If you are a patient with a liver disease: you will be an outpatient and will visit our clinic regularly. On each visit you will be examined by a physician and will have a blood sample taken for routine liver tests. On some occasions, we may take extra blood samples for research blood tests related to your liver disease. Samples of your

serum will also be kept stored for future testing, and these samples will be labeled with your name. While tests may be done on these samples in the future, these tests will be related to hepatitis or liver disease and not to unrelated conditions. If samples of your blood are sent for testing by outside investigators, they will be sent under code so as to protect your confidentiality.

Initially, and at intervals of 1 to 5 years, your doctor may recommend that you undergo an ultrasound examination of the liver in which sound waves are used to measure the size and texture of the liver. If your clinical condition warrants further evaluation, your doctor may recommend to have a liver biopsy. You will be asked to have a liver biopsy only if it is needed for your medical care, and you will be given a separate consent form to sign and date for the biopsy. Furthermore, you may refuse to have a liver biopsy and still be eligible to continue as an outpatient. If you qualify for one of the research treatment studies being carried at the California Liver Research Institute (CLRI), you may be asked to enter that study. In that case, you will have the study explained to you fully and will sign and date another consent form.

If you do not return for routine outpatient visits, we may try to contact you to return for follow up evaluation or to learn of your medical status. If we are unsuccessful at reaching you and cannot track you through your referring physician or next-of-kin, we may request a computer search of the National Death index which is done by the National Center for Health Statistics. If your name appears on the National Death Index we will request copies of medical records, death certificate and autopsy reports.

If you are a patient undergoing bariatric surgery, you are at significant increased risk of non-alcoholic fatty liver disease (NAFLD). NAFLD has spectrums that include simple steatosis (fat accumulation in the liver), which can progress to non-alcoholic steatohepatitis (NASH) (which is fat accumulation in the liver with inflammation and cell injury) with or without fibrosis (scarring of the liver). Therefore, an intraoperative liver biopsy will be performed during the surgery to determine if you have simple steatosis or NASH, and the stage of fibrosis (if any).

NUMBER OF SUBJECTS

The study plans to enroll up to 2,000 subjects.

PROCEDURES

For volunteers: The Fibroscan test is very similar to a regular ultrasound examination. The only difference being the machine uses a special probe that allows the operator/investigator to measure the stiffness and fat amount of the liver. The procedure will be performed in the outpatient clinic usually at the same time of your visit. You or your child will be asked to lie on the examining table and expose the right lower side of your chest. A small amount of ultrasound jelly will be placed on the skin

on your right side over the liver. The tip of the ultrasound probe will be placed between the ribs at the level of the right lobe of the liver. The operator will use ultrasound to locate the best position to perform the test. Once the area of measurement has been located, the operator will press a button and the machine will generate a small vibration that is transmitted to your (or your child's) liver. The machine measures how quickly the wave goes through the liver, which gives a measurement or score for the liver fat and stiffness. The vibration and measurement of liver stiffness will be repeated a total of 10 times. The entire Fibroscan test takes 5 to 10 minutes. In 5 to 10 percent of persons, the test doesn't work. The most common causes for failure include a large amount of fat over the rib cage, a narrow space between the ribs and fluid in the abdomen.

For patients undergoing bariatric surgery: An intraoperative liver biopsy will be performed to determine if the patient has simple steatosis or NASH, and what the stage of fibrosis is. The operating surgeon will take a sample of liver tissue during the bariatric procedure, which will be sent to the department of pathology to determine if you have NAFLD. Also a small piece of this tissue will be saved in our research center for future studies.

Hazards and Discomforts

The only hazards and discomforts of this study are the inconvenience of coming to the outpatient clinic on a regular basis and having frequent blood tests. You will be seen in clinic from 1 to 12 times per year as clinically indicated, and on each occasion you will have blood taken. While most of the blood tests are part of routine care of your liver disease, we may draw extra samples for research purposes. These extra blood samples for research will be used to test for the cause or nature of your liver condition; they will not be used for testing for unrelated medical conditions or for genetic information.

Drawing blood usually causes slight discomfort or pain at the place the needle is inserted in your arm. Occasionally a bruise occurs where the blood is drawn. Some patients faint after blood drawing. No more than 550 mL blood will be drawn during any 8-week period. For children, blood volumes for pediatrics subjects within an 8-week period:

Weight - Blood Volume:
12-20 kg - 10 mL
>20 kg - 20mL

Fibroscan (for volunteers): You (or your child) may experience mild discomfort between the ribs from having the tip of the probe placed there. This discomfort goes away when the probe is taken off the skin. Fibroscan has been performed on thousands of patients and no adverse effects have been reported.

Intraoperative liver biopsy during bariatric surgery: The risk of intraoperative liver biopsy under direct vision is considered to be much lower than percutaneous approaches.Uncommon risks include bleeding, infection perforation of organs and respiratory failure. Intraoperative liver biopsy has been considered as part of the clinical care of patients undergoing bariatric surgery.

BENEFITS

Most of the tests and procedures that will be done in this study are considered as routine medical care for your condition. Any treatment you receive will be the best available, according to standard medical practice. You may not benefit directly from participating. However, you will have a complete medical evaluation of your condition, you will be kept informed of the current knowledge about this disease.

ALTERNATIVES

This research study is not for the treatment of a medical condition. The only alternative is to not participate in this study.

STORAGE AND DISPOSITION OF CLINICAL SAMPLES

Samples of your blood and white blood cells taken during this study will be kept stored in secure locked files or freezers in the California Liver Research Institute (CLRI). Furthermore, information on your medical history and response to treatment will be kept in medical files in the medical record room of the Research Liver Institute (CLRI) as well as in special research files in the California Liver Research Institute (CLRI). The samples will have personal identifiers removed and will be assigned a unique code. These samples and records are stored indefinitely so that they can be analyzed again in the future if new information arises about any type of liver diseases and its treatment or new tests become available that will allow better understanding of your liver condition and response to treatment. The record will be kept confidential and your privacy protected by keeping them in secure and locked places. Serum samples may be sent to outside institutions for further testing. The samples will be anonymized (no personal information) and coded, and the code file will be maintained by the principal investigator and study team on a password protected, encrypted server. The external collaborators will not have access to personally identifiable information and will not have an influence on the analysis of the results or their reporting. The results of this study will likely be published in the medical literature, but you will not be identified individually and any information about you (like name, age, sex, diseases, current medications, and treatment) will not be released to others. You may request copies of your records at any time and may ask us to destroy your samples held in the California Liver Research Institute (CLRI) if you so wish by writing to the study doctor at the address listed on the first page of this form.

OTHER PERTINENT INFORMATION

1. Confidentiality. The CLRI will not release any information about your research involvement without your written permission. However, if you sign and date a release of information form, for example, for an insurance company, the CLRI will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

The Federal Privacy Act protects the confidentiality of your CLRI medical records. However, you should know that the Act allows release of some information from your medical record without your permission, for example, if it is required by the Food and Drug Administration (FDA), members of Congress, law enforcement officials, or authorized hospital accreditation organizations.

2. Policy Regarding Research-Related Injuries. If you become ill or are hurt while you are in the study, get the medical care that you need right away. You should inform the healthcare professional treating you that you are participating in this study.

As the risks of this study are minimum. The CLRI will not provide any medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by CLRI.

In no way does signing and dating this consent form waive your legal rights nor does it relieve the investigators, Sponsor or involved institutions from their legal and professional responsibilities

3. Payments. Participants are not paid for taking part in research studies. There is no cost to you for taking part in this study.

4. Getting Answers To Your Questions Or Concerns About The Study. You can ask questions about this consent form or the study (before you decide to start the study, at any time during the study, or after completion of the study). Questions may include:

- Who to contact in the case of a research-related injury or illness;
- Payment or compensation for being in the study, if any;
- Your responsibilities as a study subject;
- Eligibility to participate in the research;
- The study doctor's or study site's decision to exclude you from participation;
- Results of tests and/or procedures;
- Other questions, concerns, or complaints.

Contact the study doctor or study staff listed on the first page of this form with any questions, concerns or complaints.

5. Getting Answers To Your Questions About Your Rights As A Research Subject. This study has been reviewed by an Institutional Review Board (IRB). This Committee reviewed this study to help ensure that your rights and welfare are protected and that this study is carried out in an ethical manner.

For questions about your rights as a research subject, contact:

- By mail:
  Study Subject Adviser
  Chesapeake IRB
  6940 Columbia Gateway Drive, Suite 110
  Columbia, MD 21046
- or call **toll free**: 877-992-4724
- or by **email**: adviser@chesapeakeirb.com

Please reference the following number when contacting the Study Subject Adviser: Pro00018139.

6. New Information About The Study. You will be told about any new information found during the study that may affect whether you want to continue to take part.

Your study doctor may terminate your participation in the program if he/she thinks it is in your best interest or the sponsor decides to end the program.

Consent Document. Please keep a signed and dated copy of this document in case you want to read it again.

COMPLETE APPROPRIATE ITEM(S) BELOW:

Printed Name of Subject: _____

A. Adult Subject's Consent

I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby consent to take part in this study.

Signature of Adult Subject/Legal Representative

Date:_____

Print Name:_____
of Legal Representative

B. Parent's/Legal Guardian's Permission for Minor Subject.

I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby give permission for my child to take part in this study.

Signature of Parent/Legal Guardian

Date:_____

Print Name:_____
of Parent/Legal Guardian

HIPAA Authorization Agreement

Permission to Review, Use and Release Information about You

If you decide to be in this study, the study doctor and research team will use and share health data about you to conduct the study. Health data may include:

- Your name.
- Address.
- Phone number.
- Date of birth.
- Medical history.
- Information from your study visits, including all test results.

Health data may come from your study records or from existing records kept by your doctor or other health care workers.

For this study, the research team may share health data about you with authorized users. Authorized users may include

- Representatives of California Liver Research Institute.
- Representatives of Chesapeake IRB (a Research Ethics Review Board that reviews this study).
- The Food and Drug Administration (FDA) and other US governmental agencies.
- Government agencies to whom certain diseases (like HIV, hepatitis, and STDs) must be reported.
- Governmental agencies of other countries.
- Labs working with the sponsor on this study.
- Other authorized users.

The sponsor and those working for the sponsor may use the health data sent to them:

- For other research activities related to the cause or nature of your liver condition.

Once your health data has been shared with authorized users, it may no longer be protected by federal privacy law.

Your permission to use and share health data about you will not end unless required by state law. If state law applies, your permission to use and share health data about you will end on December 31, 2066.

You may take back your permission to use and share health data about you at any time by writing to the study doctor. If you do this, you will not be able to stay in this study. No new health data that identifies you will be gathered after your written request is received. However, health data about you that has already been gathered may still be used and given to others as described in this form.

Your right to access your health data in the study records will be suspended during the study to keep from changing the study results. When the study is over, you can access your study health data.

If you decide not to sign this form, you will not be able to take part in the study.

STATEMENT OF AUTHORIZATION

I have read this form and its contents were explained. My questions have been answered. I voluntarily agree to allow study staff to collect, use and share my health data as specified in this form. I will receive a signed and dated copy of this form for my records. I am not giving up any of my legal rights by signing this form.

_____ ____/____/____

Signature of Research Subject (if subject is age 18 or older) Date

_____

Printed Name of Research Subject

_____ ____/____/____

Signature of Legally Authorized Representative/ Parent/Legal Guardian (if applicable) Date

_____

Printed Name of Legally Authorized Representative/ Parent/Legal Guardian (if applicable)

Description of the representative's authority to decide for the subject: -

_____

STATEMENT OF PERSON EXPLAINING AUTHORIZATION

I have carefully explained to the subject or the subject's legally authorized representative parent/legal guardian the nature and purpose of this form. I have been available to answer any questions that the subject or the subject's legally authorized representative parent/legal guardian has about this form.

_____ ____/____/____

Signature of Person Explaining Authorization Date

_____

Printed Name of Person Explaining Authorization