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UNIVERSITY HOSPITALS CLEVELAND MEDICAL CENTER
CONSENT FOR INVESTIGATIONAL STUDIES

Project Title: The effectiveness of high-dose Synthetic BH4 (Saproterin Dihydrochloride or "Kuvan") in Amish PKU patients

Principal Investigator: Lori-Anne Schillaci, M.D.

PROTOCOL NO.: 1.0
FUNDING: Biomarin Pharmaceutical Inc.

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

Introduction/Purpose

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.

It is important for you to be truthful with your study doctor regarding your health history, in order to avoid harm to yourself by participating in this study.

The study is being funded by Biomarin Pharmaceutical Inc.

The Institutional Review Board at University Hospitals Cleveland Medical Center has approved the information in this consent document and has given approval for the study doctor to do the study. An institutional review board (IRB) is an independent committee established to help protect the rights of research subjects. This does not mean the IRB has approved *your* participation in the study. You must think about the information in this consent document for yourself. You must then decide if you want to be in the study.

BACKGROUND AND PURPOSE

This is a research study to examine Amish people with Phenylketonuria (PKU). PKU is a genetic disorder. It is caused by problems with the enzyme phenylalanine hydroxylase (PAH). This enzyme normally breaks down the amino acid (building block of protein) phenylalanine (Phe). Tetrahydrobiopterin (BH4) is a cofactor ('helper') that helps the enzyme work better. Man-made BH4 (saproterin dihydrochloride) is called "Kuvan". Kuvan is an FDA approved drug. Treatment with Kuvan and a low Phe diet, help improve PAH enzyme activity and lower blood Phe levels in some people.

Previous studies of Kuvan suggested that the more severe the PKU, the less likely Kuvan will help. However, we think that for patients with the more severe PKU, a higher dose of Kuvan given for a longer time than in the previous studies, might work better for these patients. Amish people most often have one particular genetic change causing PKU.

Some people thought that Kuvan probably wouldn't help people with that genetic change. Some doctors have found that people with the same genetic change seen in the Amish, might just need a higher dose of Kuvan and to stay on the medication longer to see if it helps.

We created this research study to find out if Amish people with PKU will have lower Phe in their blood if they take a higher dose of Kuvan for a longer period of time than was previously tested. Even though the FDA has approved Kuvan to treat PKU patients, for this study Kuvan is considered to be an experimental drug.

You are being asked to participate in this research study because you are Amish and you have PKU.

The purpose of this research study is to see if for Amish people:

- a higher dose of Kuvan for one month helps to lower Phe levels in the blood; or if it allows people to eat more protein.
- a higher dose of Kuvan for one month makes them feel better, pay attention better or feel more organized.

NUMBER OF SUBJECTS / LENGTH OF PARTICIPATION

About 25 subjects will participate in this study. Your participation in this study will last approximately 14 weeks and include 5 clinic visits. These clinic visits can occur at University Hospitals Cleveland Medical Center or at the DDC Clinic for Special Needs Children in Middlefield, OH. If you choose to come to University Hospitals Cleveland Medical Center in Cleveland, Ohio, these visits will require a car ride that will take approximately 50 minutes each way. We can help to arrange these car rides if needed. The study will consist of the following periods:

- Part 1 (diet treatment only): 1 clinic visit , one blood draw, and 3 blood spot cards done at home (4 weeks)
- Part 2 (high-dose or low-dose treatment): 2 clinic visits and 3 blood spot cards done at home (4 weeks)
- Wash out period: no treatment, no clinic visits, no blood spot cards (2 weeks)
- Part 3 (high-dose or low-dose treatment): 2 clinic visits and 3 blood spot cards done at home (4 weeks)

Total = 5 clinic visits + 9 home blood spot draws (14 weeks total)

Study Procedures

Before any study-related tests and procedures are performed, you will be asked to read and sign this consent document.

TREATMENT PERIOD 1

You will be asked to come to clinic for a first visit. During this visit the study doctor will explain the requirements of the study to you and your caregiver and determine if you are a good fit for the study.

At the beginning of the visit, you will be given as much time as you need to read this consent form and ask questions about the study. If you agree to take part, you will be asked to sign this consent form. A copy of the signed consent will be given to you.

Once you have signed the consent form, a blood draw will be performed for genetic testing. This testing is being done to determine the specific genetic mutations present in your *PAH* gene (see genetic testing section below). Knowing your specific mutations will help us figure out which mutations may need higher doses of Kuvan over longer periods of time in the future. At this time, you will also have a blood spot to determine your blood Phe level. If you are female you will also be asked for a urine sample to check if you are pregnant.

You will then begin part 1 of the study. During part 1, you will not receive any medication. You will follow a stable, Phe-restricted diet (including formula) for 4 weeks. You will also be asked to maintain food diaries for 3 days of each week (Specifically, the 3 consecutive days prior to when your weekly Phe level is drawn). Blood Phe levels will be obtained weekly by home blood spot cards. Each blood spot in part 1 will be performed by nursing staff that will travel to your house and perform the blood spots once per week. During these 3 weeks, this nursing staff will also teach you how to perform these blood spots properly yourself.

Genetic testing results will be available 3 weeks after your first blood draw. There is a chance that we will not be able to determine your specific genetic mutations with this testing. If your genetic testing finds only one, or no genetic mutations, you will be not be included in the study after part I. People not found to have two mutations in the PAH gene will not go on to complete parts 2 and 3 of the study.

TREATMENT PERIOD 2 (Part 2)

After part 1 is complete you will continue on to part 2. In part 2, you will be randomly assigned by chance (like the flip of a coin) to receive either high-dose Kuvan (40 mg/kg)

or standard-dose Kuvan (20 mg/kg). Kuvan will either be in tablet or powder form and will be taken by mouth, once daily. Below are your chances of receiving high-dose or low-dose Kuvan.

Treatment	**Chances of Recieving**
Standard-dose Kuvan	½ (50%)
High-dose Kuvan	½ (50%)

You will be required maintain a stable, Phe-restricted diet including formula (the diet that you followed in part 1) during this treatment period. You will be required to attend 2 clinic visits during this part (one at the beginning of the treatment period and one at the conclusion). During these visits the following will take place:

Initial visit:
- Medical history and physical exam
- Food diaries collected for the previous 4 weeks (3 days per week)
- Baseline Phe level drawn by dried blood spot card in office
- Urine pregnancy test (females only)
- Behavioral and quality of life assessment tools (BRIEF, PKU-QOL)
- Provided with high or low-dose medication kits (supply for 4 weeks)
- Provided with instruments for weekly blood measurement – 3 blood spot cards to be performed at home starting week 2 (each Monday) and mailed into the appropriate lab. People or families who are uncomfortable or unable to perform their own blood spots at home will continue to have home nursing visits weekly to obtain the blood spots.

Second visit: conclusion of part 2 after 4 weeks of treatment
- Food diaries collected for the previous 4 weeks (3 per week)
- Behavioral and quality of life assessment tools (BRIEF, PKU-QOL)
- Empty medication bottles/packet kits collected to assess compliance

Study visits are expected to take 2-3 hours.

WASHOUT PERIOD
At the conclusion of part 2 there will be a 2 week 'washout period'. During these two weeks you will not receive any study medication and you will have no clinic visits. You should continue to maintain your stable, Phe-restricted diet.

TREATMENT PERIOD 3 (Part 3)
At the end of the washout period, another 4 week treatment period will begin. Study participants that initially received high-dose Kuvan will receive standard-dose Kuvan for the next 4 weeks and study participants that initially received standard-dose Kuvan will receive high-dose Kuvan for the next 4 weeks. You will again be required to maintain a stable, Phe-restricted diet including your formula (the diet you followed in parts 1 and 2). You will again be required to attend 2 clinic visits during this time (one at the beginning of the treatment period and one at the conclusion). The procedures performed at these visits will be exactly the same as above in Part 2.

This is a blinded study, which means you will not know which of these treatments you have been assigned. In case of an emergency, however, the study doctor can get this information.

DRUG TRANSPORT/STORAGE
At each initial study visit for Part 2 and Part 3, you will be given a 4 week supply of medication for you to take home. Please keep medication in its original container, protect it from getting damp or wet and do not expose it to extreme temperatures.

SAMPLE COLLECTION AND STORAGE
Throughout the study, at various time points, blood samples will be collected to help the study doctor and sponsor better understand how, and if, the study drug works. At the initial visit, each participant will have a 'blood draw' where the doctor or nurse will insert a needle into your vein and obtain 2-5mL (1/2-1 teaspoon) of blood. For the remainder of the study, 'blood spots' will be collected through a finger prick where 100 microliters of blood per spot will be placed onto filter paper cards each week. Four spots will be collected with each finger stick and twelve finger sticks will be done over the course of the study for a total of 4,800 microliters (or 4.8 mL or approximately 1 teaspoon). The total blood collected throughout the study will be less than 10 mL (or approximately 2 teaspoons).

Blood samples collected for genetic testing at the initial study visit will be analyzed by the DDC clinic laboratory in Middlefield, Ohio. If you have your initial study visit at University Hospitals Cleveland Medical Center, your blood sample will be mailed to the DDC clinic

for analysis. Blood spot samples collected during clinic visits for Phe analysis will be mailed directly from our clinic to the reference laboratory in Pennsylvania. Our study staff will handle and mail out these samples.

During the weeks that you do not visit our clinic, you will perform blood spot cards at home. In order to teach you to become comfortable performing your own (or your child's) blood spots cards at home, nursing staff (from the DDC clinic) will travel to your house weekly for part 1 of the study (a total of 3 home blood spots). During parts 2 and 3 of the study, you will perform your own (or your child's) blood spots at home. If you are uncomfortable performing these blood spots, blood spots will continue to be collected by home nursing.

Blood spot cards collected at home, by either you or the nurse, will be mailed that day, directly from your home to the reference laboratory in Pennsylvania. Addressed envelopes and stamps will be provided to mail these blood spot cards.

EXPECTATIONS

If you participate in this study, you will be expected to:

- Attend each site visit described above
- Complete laboratory tests and procedures as instructed by the site staff and study doctor, including obtaining blood spots at home once per week (performed by yourself or home nursing staff)
- Complete all surveys given at site visits and bring diet diaries in good condition to each site visit
- Communicate any side effects, changes in your health or behavior or changes in your medication usage to the site staff

If you participate in this study, your caregiver will be expected to:

- Assist the site staff to ensure your compliance with the study requirements and schedule
- Accompany you at each site visit
- Communicate any side effects, changes in your health or behavior or changes in your medication usage to the site staff
- Complete the assessment tools given at each site visit and help maintain and bring diet diaries to each visit.

It should be noted that if a caregiver is answering the assessment surveys at each site visit, it is important for these to be completed by a consistent primary caregiver who is able to reliably and accurate assess the changes in your health, habits, and behavior

throughout your participation in the study.

Risks

Medical treatments often cause side effects. You may have none, some or all of the effects listed below, and they may be mild, moderate or severe. If you have any of these side effects, or are worried about them, talk with your study doctor. Your study doctor will also be looking out for side effects.

There may be side effects that the researchers do not expect or do not know about and that may be serious. Tell your study doctor immediately about any new or unusual symptoms that you experience while in this study.

Many side effects go away shortly after treatment ends. However, sometimes side effects can be serious, long lasting or permanent. If a severe side effect or reaction occurs, your study doctor may need to stop your treatment. Your study doctor will discuss the best way of managing any side effects with you.

RISKS OF STUDY MEDICATION

Kuvan is an FDA approved drug taken by people with PKU at a dose of 20 mg/kg daily. This is the first time it is being given to participants at a dose of 40 mg/kg daily. So, it is not known if there are specific side effects that will show up only at this elevated dose. The study drug must be taken only by you. It must be kept in a safe place out of reach of children and other people who cannot read well or understand that they should not take it.

The most common side effects of Kuvan at a dose of 20mg/kg include:

- Headache
- Nausea (feeling sick in the stomach, queasy)
- Vomiting (throwing up)
- Diarrhea
- Gastritis (inflammation of the stomach lining)
- Upper respiratory tract infection (cold-type symptoms)
- Pharyngolaryngeal pain (throat pain)
- Hyperactive behaviors (such as fidgeting or constant activity)
- Hypophenylalaninemia (low blood phenylalanine)

RISKS OF STUDY PROCEDURES

The insertion of the needle to draw blood is painful; however, this discomfort is brief. For most people, needle punctures to get blood samples to not cause any serious problems; however, they may cause bleeding, bruising, discomfort, infections, dizziness, or fainting.

There may be risks associated with genetic testing; these risks will be discussed in the separate consent for genetic testing.

UNFORESEEN RISKS
Since the study drug is being given at a higher dose than usual, there may be other risks that are unknown. All drugs have a potential risk of an allergic reaction, which if not treated promptly, could become life-threatening.

PREGNANCY / BIRTH CONTROL
Kuvan is rated by the FDA as a category C drug if taken during pregnancy. Adverse events have been observed in some animal reproduction studies. Because of this, it is important that you do not participate in this study if you are pregnant or breast-feeding. It is also important that you do not become pregnant during the course of the study. If you are female and child-bearing is a possibility, you will be required to undergo a pregnancy test prior to starting the study. If you are sexually active and not surgically sterile or post-menopausal, you must use effective contraception approved by the study guidelines. You should discuss methods of effective contraception with your study doctor. Medically acceptable contraceptives include: (1) surgical sterilization, (2) approved hormonal contraceptives such as birth control pills, (3) barrier methods (such as a condom or diaphragm) used with a spermicide, or (4) an intrauterine device (IUD). Barrier contraceptives (condoms or diaphragm) with spermicide, intrauterine devices, hormonal contraceptives (Depo-Provera, Norplant), oral contraceptive pills, and complete abstinence are examples of effective methods.

<u>If you are female and become pregnant while participating in this research project, you should advise your study doctor immediately.</u> Your study doctor will withdraw you from the research project and advise on further medical attention should this be necessary. You must not continue in the research if you become pregnant. You will be referred to appropriate counseling and informed of the possible risks with pregnancy associated with Kuvan. If you have a positive pregnancy test during a study visit and you are younger than 14 years of age the study team is required to tell you, your parent or legal guardian and the Department of Children and Family Services. If you are 14 years of age or older and tell the study team that you are pregnant or have a positive pregnancy test during a study visit, the study team must give this information to your parent/legal guardian if they ask. The study team can help you share this information with your parent or legal guardian.

Benefits

Prolonged increased Phe concentrations are toxic to the brain and lead to the impairment of intelligence and other brain functions. Kuvan has been shown to help maintain reduced blood Phe concentrations in certain people with PKU. There is a possibility that you may decrease your blood Phenylalanine levels and increase your Phenylalanine tolerance by taking Kuvan, but there is no guarantee. Some subjects may not benefit from participation in this study; however, their participation in this study might help in the future treatment of individuals with PKU.

Alternatives to Study Participation

You do not have to be in this study to receive treatment for your PKU**.** You may choose other treatments or procedures to help with your symptoms, such as maintaining a Phe-restricted diet. The study doctor will discuss with you the risks and benefits of the alternative treatments.

Consequences of Withdrawing or Being Discontinued From the Research

Your decision to participate in this study is voluntary. You may choose to not participate or you may withdraw from the study for any reason without penalty or loss of benefits to which you are otherwise entitled and without any effect on your future medical care. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you withdraw from the study prior to its completion, you will be asked to return all study medication to the study doctors.

The study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest
- If new information becomes available
- If you do not follow the study requirements
- If the study is stopped by the sponsor, Institutional Review Board (IRB) or FDA.

Financial Information

Your participation in this study will involve no cost to you. Kuvan will be provided at no cost to you while you are participating in this study. As a participant in the study, we will arrange and cover all travel to and from site visits at University Hospitals Cleveland

Medical Center, as well as, all medical care received at these visits at no cost. You will not be charged for anything else we do that is part of the study.

During the study, you will still have to pay for any medical care that you receive during this time that is not part of the study.

You will not receive any payment for your participation in this study.

Research-Related Injury

In the event that a research activity results in injury, you/your medical insurance may be charged for the cost of diagnosing and treating your condition. You may be responsible for co-pays or deductibles. A research injury is an injury that happens as a result of taking part in this research study. If you are injured by a medical treatment or procedure that you would have received even if you weren't in the study, that is not considered a "research injury". If you/your insurance company does not pay the cost of diagnosing and treating your condition, the cost will be covered by Biomarin Pharmaceutical if they agree the injury was caused by the research or research activity as described in the Protocol and not the fault of the researchers or study staff. There are no plans for payment for lost wages or other expenses. To help avoid injury, it is very important to follow all study directions.

Genetics Studies

Molecular genetic testing will be performed at your first visit. Specifically, testing will include a blood draw for sequencing of the entire PAH gene looking for your specific genetic mutations.The results of the analysis of your DNA done as part of this study will be given to you at the conclusion of the study. Your DNA sample will be identified by a code number, and all other identifying information will be removed. The principal investigator, Lori-Anne Schillaci, MD, will have access to a separate code sheet that links the DNA sample code number with your identity. The benefit of this testing is that your results may identify the two specific genetic mutations causing your condition. Your DNA sample will only be used for the specific purpose described in this consent form. When the study is complete your sample will be destroyed. You will not be allowed to participate in this study if you do not have this genetic testing.

A Federal law, called the Genetic Information Nondiscrimination Act (GINA), effective May 21, 2010, generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

All health insurance companies and group health plans must follow this law by May 21, 2010. All employers with 15 or more employees must follow this law as of November 21, 2009. Be aware that this new Federal law does **not** protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Clinical Trial Information

U.S. NATIONAL INSTITUTES OF HEALTH (NIH) CLINICAL TRIAL DATABASE: A description of this clinical trial will be available on http:///www.clinicaltrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time to find out information about the trial and basic results.

Confidentiality

Records of your participation in this study will be held confidential except when sharing the information is required by law or as described in this informed consent. The study doctor, the funding company or persons working on behalf of the funding company, and under certain circumstances, the United States Food and Drug Administration (FDA) and the Institutional Review Board (IRB) will be able to inspect and copy confidential study-related records which identify you by name. This means that despite taking the appropriate precautions, absolute confidentiality cannot be guaranteed and there is a risk that confidentiality may be lost. If the results of this study are published or presented at meetings, you will not be identified.

Privacy of Protected Health Information

The Health Insurance Portability & Accountability Act (HIPAA) is a Federal law that helps to protect the privacy of your health information and to whom this information may be shared within and outside of University Hospitals. This Authorization form is specifically for a research study entitled "The effectiveness of high-dose Synthetic BH4 (Saproterin

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Project Title: The effectiveness of high-dose Synthetic BH4 (Saproterin Dihydrochloride or "Kuvan") in Amish PKU patients

Principal Investigator: Lori-Anne Schillaci, M.D.

Dihydrochloride or "Kuvan") in Amish PKU patients" and will tell you what health information (called Protected Health Information or PHI) will be collected for this research study, who will see your PHI and in what ways they can use the information. In order for the Principal Investigator, Lori-Anne Schillaci, M.D., and the research study staff to collect and use your PHI, you must sign this authorization form. You will receive a copy of this signed Authorization for your records. If you do not sign this form, you may not join this study. Your decision to allow the use and disclosure of your PHI is voluntary and will have no impact on your treatment at University Hospitals. By signing this form, you are allowing the researchers for this study to use and disclose your PHI in the manner described below.

Generally the Principal Investigator and study staff at University Hospitals and Case Western Reserve University who are working on this research project will know that you are in a research study and will see and use your PHI. The researchers working on this study will collect the following PHI about you name, birth date, address, phone number, medical record number. This PHI will be used to identify you and contact you throughout the study if needed. Your access to your PHI may be limited during the study to protect the study results.

Your PHI may also be shared with the following groups/persons associated with this research study or involved in the review of research: Biomarin Pharmaceutical, the funding company for this study; other staff from the Principal Investigator's medical practice group, including Dr. Katherine Dempsey, Ms. Heidi Reilly, the metabolic dietician involved with this study, and Ms. Valeria Sency, a clinical nurse involved with this study; as well as persons associated with University Hospitals, including the Center for Clinical Research and the Law Department; Government representatives or Federal agencies, when required by law.

Your permission to use and disclose your PHI does not expire. However, you have the right to change your mind at any time and revoke your authorization. If you revoke your authorization, the researchers will continue to use the information that they previously collected, but they will not collect any additional information. Also, if you revoke your authorization you may no longer be able to participate in the research study. To revoke your permission, you must do so in writing by sending a letter to Dr. Lori-Anne Schillaci, 11100 Euclid Avenue, Cleveland, Ohio, 44106, Lakeside suite 1500; If you have a complaint or concerns about the privacy of your health information, you may also write to the UH Privacy Officer, Management Service Center, 3605 Warrensville Center, MSC 9105, Shaker Heights, OH 44122 or to the Federal Department of Health and Human Services (DHHS) at DHHS Regional Manager, Office of Civil Rights, US Department of

Health and Human Services Government Center, JF Kennedy Federal Building, Room 1875, Boston, MA 02203. Complaints should be sent within 180 days of finding out about the problem.

The researchers and staff agree to protect your health information by using and disclosing it only as permitted by you in this Authorization and as directed by state and Federal law. University Hospitals is committed to protecting your confidentiality. Please understand that once your PHI has been disclosed to anyone outside of University Hospitals, there is a risk that your PHI may no longer be protected; however other Federal and State laws may provide continued protection of your information.

Summary of your rights as a participant in a research

Your participation in this research study is voluntary. Refusing to participate will not alter your usual health care or involve any penalty or loss of benefits to which you are otherwise entitled. If you decide to join the study, you may withdraw at any time and for any reason without penalty or loss of benefits. If information generated from this study is published or presented, your identity will not be revealed. In the event new information becomes available that may affect the risks or benefits associated with this study or your willingness to participate in it, you will be notified so that you can decide whether or not to continue participating. If you experience physical injury or illness as a result of participating in this research study, medical care is available at University Hospitals Cleveland Medical Center (UHCMC) or elsewhere; however, UHCMC has no plans to provide free care or compensation for lost wages.

Disclosure of your study records

Efforts will be made to keep the personal information in your research record private and confidential, but absolute confidentiality cannot be guaranteed. The University Hospitals Cleveland Medical Center Institutional Review Board may review your study records. If this study is regulated by the Food and Drug Administration (FDA), there is a possibility that the FDA might inspect your records. In addition, for treatment studies, the study sponsor and possibly foreign regulatory agencies may also review your records. If your records are reviewed your identity could become known.

Contact information

_____ has described to you what is going to be done, the risks, hazards, and benefits involved. The Principal Investigator, Dr. Lori-Anne Schillaci, can also be contacted at (216) 844-3936, option 2. If you have any

questions, concerns or complaints about the study in the future, you may also contact them later.

If the researchers cannot be reached, or if you would like to talk to someone other than the researcher(s) about; concerns regarding the study; research participant's rights; research- related injury; or other human subject issues, please call the University Hospitals Cleveland Medical Center's Research Subject Rights phone line at (216) 983-4979 or write to: The Chief Medical Officer, The Center for Clinical Research, University Hospitals Cleveland Medical Center, 11100 Euclid Avenue, Lakeside 1400, Cleveland, Ohio, 44106-7061.

Signature

Signing below indicates that you have been informed about the research study in which you voluntarily agree to participate; that you have asked any questions about the study that you may have; and that the information given to you has permitted you to make a fully informed and free decision about your participation in the study. By signing this consent form, you do not waive any legal rights, and the investigator(s) or sponsor(s) are not relieved of any liability they may have. A copy of this consent form will be provided to you.

x	
Signature of Participant	Date
x	
Printed Name of Participant	

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[USE THIS FOR STUDIES ENROLLING DECISIONALLY IMPAIRED ADULTS]

x	
Signature of Participant	Date
x	
Printed Name of Participant	
If participant does not have the capacity to consent and protocol is approved for inclusion	
x	
Signature of Legally Authorized Representative (LAR) or Next of Kin	Date
x	
Printed name of Legally Authorized Representative (LAR) or Next of Kin	
If Next of Kin, please mark ONE relationship from list below (in decending order of priority):	

	Spouse		Adult Child		Custodial Parent		Adult Sibling		Adult relative (related by blood or adoption)

[USE THIS FOR STUDIES ENROLLING MINORS where the IRB has determined ONE PARENT SIGNATURE is sufficient]

x	
Signature of Participant	Date
x	
Printed name of minor if used to obtain assent	
x	
Signature of Parent/Legal Guardian	Date
x	
Printed name of Parent/Legal Guardian	
x	
If Legal Guardian, indicate relationship to child	

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Study personnel (only individuals designated on the checklist may obtain consent)

x	
Signature of person obtaining informed consent	Date
x	
Printed name of person obtaining informed consent	