Title of research study: A Double-Blind Placebo Controlled Phase 2 Trial to Evaluate the Safety, Reactogenicity and Immunogenicity of a Live-Attenuated *Shigella sonnei* Vaccine, WRSs2 and Determine its Efficacy in a Challenge Model of *S. sonnei* 53G in Healthy Adults

Investigator: Dr. Robert Frenck

Contact Info: 513-636-7699

Industry Protocol #: DMID 17-0112

Drug Name: *Shigella sonnei* Vaccine, WRSs2 and *S. sonnei* 53G Challenge

Funding: Division of Microbiology and Infectious Diseases (DMID), National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH)

Key Information:

The following is a short summary of this study to help you decide whether to be a participant in it. More detailed information about the study is listed later in this form. This document does not replace the discussion you should have with the research team about this study including having any questions or concerns answered.

If you are 18 years and older: This is a consent form. It explains this research study. If you decide that you want to be in this research study, then you will sign this form to show that you agree to be part of this study. If you sign this form, you will receive a signed copy of it for your records.

Reason for the study:

The main reason for this research study is to find out if an experimental vaccine called WRSs2 can protect people from getting Shigella. This vaccine was made in the United States at the Walter Reed Army Institute of Research (WRAIR).

Shigella is a bacteria that causes diarrhea in the United States and other countries. Shigella infection is passed easily from person to person, so infections are common. Infections caused by Shigella can range from mild watery diarrhea to severe illness with bloody diarrhea, fever, headaches, and stomach pain. If untreated, Shigella infection, can lead to serious problems in young children, the elderly, and people who have other health problems.

While Shigella can be treated with antibiotics, many strains of Shigella are becoming resistant to antibiotics. Shigella can be prevented by having clean water and with safe food handling. Some parts of the world do not have the resources to improve water and food practices. Therefore, it is important to find other ways to prevent infection. One possible way to prevent Shigella from causing infections and diseases is with vaccines.

In the earlier cohorts of this research study, there were 2 participants that developed diarrhea and vomiting after vaccine, that warranted a reduction in vaccine dose.

Study Procedures:

You will get a handout so you will know what will happen at each study visit. The research staff will explain each visit to you. You will be able to ask questions and

you can take the handout home with you. Your participation will be approximately 8 months with up to 13 outpatient visits, an inpatient stay up to 11 days and a final safety contact.

WHO SHOULD NOT BE IN THE STUDY

You cannot be in this study if you:

- Are younger than 18 years of age or already had your 50th birthday.
- Have problems fighting off infections.
- Are Hepatitis B, Hepatitis C, or HIV positive.
- Are a female who is pregnant or breastfeeding.
- Work in healthcare, daycare or food services and have to return to work within 2 weeks of finishing the challenge.
- Have had a recent Shigella infection or vaccine against Shigella.
- Have a history of irritable bowel disorders.
- Have allergies to components of the Shigella vaccine or ciprofloxacin, or Sulfa drugs.
- You are in another interventional research study.
- Have a BMI that is less than 19 or greater than 40.
- Are taking weight loss medications.

There may be other reasons you cannot be in this study, and the study staff will review these with you.

TO BE IN THIS STUDY YOU MUST BE ABLE TO:

- Not smoke during the inpatient portion of the study (up to 11 days)
- Pass a written test about the study
- Complete the vaccine e-memory aid/memory aid
- Follow rules of conduct during the inpatient admission
- Females need to avoid a sexual relationship that may result in pregnancy or use an acceptable form of birth control during the entire study.
    - Study staff will talk with you more about acceptable forms of birth control

Screening Visit

First you will come to the clinic for a screening visit(s) to see if you qualify to be in this study. You will be asked to read and sign a consent form and will be given a copy. We will ask questions to make sure you are healthy enough to be in the study.

Questions may include:

- Age, race and ethnic group
- Any past or present illnesses, hospitalizations, surgeries and medicines you are taking including past vaccines

- We will measure your blood pressure, temperature, heart rate, height and weight.
- We will perform a physical examination
- We will collect urine for protein and test for opiates (like heroin, morphine and codeine).
- Trained staff will collect about 1½ tablespoons of your blood from a vein to test for:
  - Healthy immune system, liver, kidneys and blood counts
  - Shigella titer to see if you have already had this infection
  - We will collect blood to see how your body will respond before the Shigella vaccine is given
  - Hepatitis B, Hepatitis C, HLA-B27, HIV infection*
    * If you have a blood test that is positive for Hepatitis B, Hepatitis C, or HIV, the results must be reported to the local health authorities according to state law. You will also be given information about the disease, a chance to ask questions, and a list of doctors who are experts in these diseases.
- You will be given a kit and instructions on collecting a baseline stool (poop)
- Females of child-bearing potential will have urine tested for pregnancy
- If you qualify for the study, we will ask you to bring another stool collection to your next screening and clinic visits.

<u>These are the things that will happen to you while in the study:</u>

Medical History: We will ask you about your past and present illnesses, hospitalizations, surgeries, medicines and vaccinations

Physical Exam and Vital Signs: We will measure your temperature, heart rate, blood pressure, height and weight. You may also have a physical exam if anything has changed in your health since your last visit.

Blood Tests: Trained staff will collect your blood from a vein at each study visit to see if the study vaccines or Shigella bacteria have caused any changes in your blood counts, or your liver and kidney tests throughout the study. We will also collect blood to see how your body has responded to the vaccine or Shigella bacteria. Extra tubes of blood will be collected at some of the study visits that may be used in future research to test for how the body responds to the Shigella vaccines. Blood collection schedule and amounts of blood being taken are listed on the handout you have been given.

Stool Tests: You will be given a stool (poop) kit and instructions on collecting a sample to bring to the vaccination visits and to most of your study visits. In the event you are unable to provide a stool (poop) sample, you will be asked to do a rectal swab.

Secondary Research: By agreeing to take part in this study you also give permission to allow extra tubes of blood (approximately 16 tablespoons over the course of the study) and any leftover blood or stool samples from any study visits to be stored indefinitely for secondary research at Cincinnati Children's or another facility that the National Institutes of Health chooses. Secondary research is research that is not part of this study but may be performed during the study or in the future. These samples will be labeled with a code and will not include your name or any other information that would identify you. Samples will be used for research only. They will not be sold or used to make new cell lines or for genetic testing. They may be used to help develop new vaccines, or in new or different laboratory tests, or to study other infections. There will be no identifying information used in reporting or publications of any future testing results. The results of this testing will not be reported to you or your doctor and will not benefit you. The samples might be shared with researchers at other study centers.

If you do not want to allow your samples to be used for future research, do not participate in this study. If after you enroll and later change your mind and decide to withdraw consent for future research, no extra samples will be collected. There will be no further use of any of your future research samples, if you withdraw from future research.

Pregnancy Test: If you are a woman and able to have children, we will test your urine before each vaccine visit and upon admission to the research unit to be sure you are not pregnant.

Written Test: After the study staff has explained the study to you, **you must pass a written exam about the study with a score of at least 70%.** You will be given up to 2 attempts to pass successfully. If you are unable to pass this test, you will not be allowed to be in the study.

Vaccination: Everyone in the study will drink either the WRSs2 vaccine or a placebo twice as described below. The placebo contains no vaccine; however, it will look and taste the same as the vaccine. Neither you nor the study staff will know if you have been given vaccine or placebo. If there is an emergency, your study doctor will be able to find out.

There are 2 groups in this study. You will be put into one of three groups by chance (like flipping a coin).

Vaccine Groups:

	Day 1	Day 29
Group 1	WRSs2 vaccine	WRSs2 vaccine
Group 2	Placebo	Placebo

Before each vaccine:

You will have a light breakfast early in the morning and then you will have nothing to eat or drink for 90 minutes before and 90 minutes after drinking the vaccine.

Just before drinking the vaccine or placebo, you will be given a cup of sodium bicarbonate water (like baking soda water) to drink to help coat the stomach.

You will stay in the research clinic **for at least 90 minutes** after each vaccine to be watched for any immediate reactions

e-Memory Aid: You will be given a memory aid, thermometer, and study contact information. You will be asked to fill out the memory aid every day for 7 days after each vaccine. The study staff will give you instructions and teach you how to do this. You will be asked to record any new medicines and to take your temperature about the same time every day and complete online or write it down. You will also complete online or write down any symptoms you have. The message sent to you will state that your memory aid is overdue and will indicate the day(s) that you have missed. You will be asked to call us if you have any concerns, symptoms of illness, any severe reaction that you enter on your memory aid, have changes in your health, visit the emergency room or are hospitalized, become pregnant, or have any concerns.

After Each Vaccine (given about a month apart):

You will:

- Return to clinic 3 days, 7 days, and 14 days after each vaccine to check on your safety
- Be asked questions about your health, and medicines you are taking
- Have blood collected to check your health and to see how your body is responding to the vaccine
- Bring in a stool samples to be checked for Shigella
- Fill in the memory aid

You may also have a brief physical exam with vital signs if needed.

Admission to the Overnight Research Unit

On arrival to the overnight unit the study team will:

1. Ensure continued eligibility

2. Obtain a nasal swab for COVID-19 antigen testing. If you are found to be positive for COVID-19, you will be immediately escorted out of the challenge unit and will not be administered the dose of Shigella.

If you are negative on the COVID-19 antigen test, you will be admitted to our overnight unit. The day following admission, you will receive a dose of Shigella. You will not be able to eat or drink anything for 90 minutes before and after receiving the Shigella. The study staff will explain this in further detail at your visit.

While you are in the overnight unit, we will:

- Watch you carefully for any signs of illness
- Check your weight, vital signs and ask how you are feeling
    - Do a brief physical exam if you are feeling unwell
- Study your body's response to the Shigella bacteria and to see if the Shigella vaccines prevented you from getting sick.
- **Collect every stool** you have, and the study staff will check for diarrhea and send samples for testing
- Check your blood, urine, and stool to see how you are responding to the Shigella bacteria
    - Ask you to use swabs if you are unable to collect a stool sample
- On the 5th day after drinking the Shigella, give you antibiotics to clear the bacteria from your body.
    - You may be given antibiotics prior to the 5th day if the study doctor determines it is medically necessary.
- COVID-19 testing may be repeated if you develop COVID symptoms. If you are found to be positive, you will be quarantined to your room until you have recovered sufficiently from the Shigella infection to allow you to be safely sent home.

When Can I Go Home?

You can go home after:

- You have completed all of your antibiotics
- You are feeling well.
- The Shigella infection has been cleared from your body.

You will be asked to come back to the outpatient clinic for safety follow up and specimen collection. You will be given a handout with the schedule of outpatient clinic visits. We will contact you after about 6 months to make sure you are doing okay.

Unscheduled Visits: You may be asked to come back to the clinic at other times if the study doctor decides you should be seen. Your medical history, medicines, memory aid and any safety questions may be reviewed. The study doctor may examine you and your vital signs and, blood may be drawn to be sure you are safe.

Risks to Participate:

During study visits, the most common risks are from blood draws.

The bad things that can happen from blood draws are pain or bruising where the needle goes into the vein or feeling faint when the blood is drawn. Although it is rare, it is possible to develop a blood clot in the vein you have your blood collected from and some people have gotten an infection from having their blood drawn. To minimize some of these risks, trained staff collecting samples will clean your skin properly and apply pressure at the site after the blood draw is complete.

COMMON RISKS OF BLOOD DRAWS, SOME MAY BE SERIOUS
• Pain • Bruising where blood is collected from • Feeling light-headed or fainting • Blood clot in the vein you have your blood collected from • Infection where blood was collected from

The WRSs2 Vaccine and Shigella Challenge germs used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood, causing side effects. The table below shows the most common and most serious side effects that researchers know about. We do not know all of the side effects that may occur.

The summaries below show the most common and most serious side effects of this vaccination and Shigella infection that researchers know about. We do not know all of the side effects that may occur.

Vaccine

After the vaccine you may have:

COMMON RISKS OF VACCINATION WITH WRSs2 VACCINE

- Tiredness
- General unwell feeling
- Headache
- Body aches/muscle/joint pain
- Fever, chills/shivering/sweating
- Upset stomach, mild diarrhea

These reactions are usually worse in the first 24 hours after vaccine and typically go away without treatment.

Allergic Reactions

Vaccines can cause a severe allergic reaction. Such reactions are rare and would happen within a few minutes to a few hours. Signs of a severe allergic reaction can include hives, swelling of the face and throat, difficulty breathing, a fast heartbeat, dizziness, and weakness. If allergic reactions are not treated right away, they could become serious or lead to death, but the study doctors do not expect this. We will observe you for reactions for 90 minutes after each vaccine and there will be medicines available to treat allergic reactions.

Shigella Risks

In previous studies, the solution of Shigella bacteria caused Shigella illness in about 50%-70% of study participants. People who got sick were given antibiotics and the symptoms went away in 1-2 days. The most common symptoms of a Shigella infection are:

COMMON RISKS OF SHIGELLA INFECTION

- Loose or watery diarrhea with stomach ache and cramping
- Bloody diarrhea
- Headache
- Muscle and joint pain
- Feeling tired
- Fever

To minimize the risk of transmission of Shigella bacteria to others, frequent handwashing is advised.

Antibiotic Risks

Shigella symptoms can be treated with antibiotics. For this study you will be treated after 5 days with an antibiotic called ciprofloxacin (Cipro). The study staff can give you antibiotics sooner than 5 days if they think you need it. Antibiotics may cause nausea, diarrhea, abnormal liver tests, vomiting and rash. Most symptoms are mild to moderate, require no treatment, and go away after the antibiotics are stopped. Fluoroquinolones, including ciprofloxacin, are associated with an increased risk of tendonitis and tendon rupture in all ages, **and in high-risk patients can increase risk of aortic tear or rupture**. Other symptoms rarely seen include hypersensitivity, dizziness, pseudomembranous colitis, and peripheral neuropathy.

If you are allergic to ciprofloxacin, Bactrim (trimethoprim-sulfamethoxazole) will be given. Bactrim can cause nausea, vomiting, loss of appetite, and allergic skin reactions like rash and itching.

Post-infectious irritable bowel syndrome (IBS)

There may be an increased chance of developing a bowel disorder called post-infectious irritable bowel syndrome (IBS) following diarrheal illness caused by Shigella. About 10% (1 in 10 people) can have stomach pain several times a month after being sick from Shigella. These symptoms usually go away within 3 to 6 months. IBS can cause discomfort and changes in your normal bowel patterns such as diarrhea, constipation, bloating, abdominal pain and gas and it is not known for certain how long these symptoms may last.

Rarely (less than 2%) patients may develop arthritis with swelling of the eyes and urethra that starts about 1-3 weeks after the onset of Shigella infection. This usually happens in people with a certain genetic condition which is why people with HLA B27 cannot enter the study.

If you are too sick to drink or pee during the overnight admission, one of the study doctors will check you to see if you need fluids given in your veins (intravenous - IV). It is possible you may get sick enough that we may need to transfer you to a local adult hospital for additional care. If this happens you will not be billed for such services.

Blood collection and IV placement

You may have pain or bruising at the site where the needle went into your arm or hand. You may feel lightheaded right afterwards or faint, but these symptoms do not last long.

There is a rare chance you could get an infection at the blood draw site. The study staff will make sure to use a sterile needle and follow guidelines to prevent infection.

Nasal Swab

A nasal swab may cause some discomfort. Rarely, nosebleeds can occur as a result of nasal swabs. If this occurs, it is typically temporary. All nasal swabs collected in this study are the type that are inserted to the middle portion of your nose, rather than deeper into the nasal passages.

What are the risks if you get pregnant during this study?

We do not know what the Shigella vaccine may do to an unborn baby. Because of this, you should not get pregnant at any time during the study.

If you become pregnant during the study, you should notify the study staff right away. We will ask to stay in contact with you until the end of your pregnancy.

Benefits to Participate:

There is no direct benefit to you for being in this study. When we finish the study, we hope that we will know more about Shigella infections, and this may help other people with Shigella infections later on.

Other Options:

Participation in research is completely voluntary. If you decide to be in this study, you may change your mind at any time during the study and you can stop being in the study. Take all the time you need to make your choice. You can ask questions at any time. It is also okay to ask more questions after you decide to be in the study.

Stopping the Study Early: You may decide at any time not to be in the study.

If you choose to stop being in the study during the outpatient part of the study, you may be asked to come back to the clinic for a final visit. Your medical history, medicines, memory aid and any safety questions may be reviewed. The study doctor may examine you and your vital signs and, blood may be drawn to be sure you are safe. If you choose to stop being in the study during the inpatient part of the study, you will be asked to begin antibiotics and should have two stools done 6 hours apart that are negative for Shigella before being discharged from the unit. You should agree to complete the antibiotics at home and are encouraged to complete all outpatient visits. You will be provided with instructions about how to prevent the spread of infection to close contacts. You may be asked to have blood collected for health and safety labs and for presence of antibodies to *Shigella*.

The study doctor, the sponsor (NIH), or any regulatory authority may also decide it is in your best interest to end your participation in the research study at any time.

Cost to Participate:

There are no costs for you to participate in this study.

Payment:

If you agree to take part in this research study, we will pay you for your time and effort. The handout you receive will show you how much you will be reimbursed for each visit.

You will receive payment for this study in the form of a reloadable debit card (Clincard). We will give you a handout that will explain how to use the card. Because you are being paid for your participation, Cincinnati Children's is required by the Internal Revenue Service (IRS) to collect and use your social security number (SSN) or taxpayer identification number (TIN) to track the amount of money that we pay. You will need to complete a Federal W-9 form for this income tax reporting. This form requires your Social Security number. This form will be given to the Cincinnati Children's business office. It will not be kept as part of your study chart. If you move, you will need to complete another W-9 with an updated address.

You will be reimbursed for your travel expenses to your study visits as outlined in the handout provided with this consent form.

Tissues or body fluids collected for this research may result in the development of a product that could be patented/licensed and sold. You will not be paid if this happens.

Additional Study Information:

The following is more detailed information about this study in addition to the Key Information.

If I have Questions or would like to know about:

Who to talk to…	**You can call …**	**At …**
• Emergencies • General study questions • Research-related injuries • Any research concerns or complaints •	**Dr. Robert Frenck**	Phone: 513-803-5085
• Emergencies • General study questions	**Tena Pham**	Phone: 513-636-7699

Who to talk to…	You can call …	At …
• Research-related injuries • Any research concerns or complaints		
• Your rights as a research participant	**Institutional Review Board** This is a group of scientists and community members who make sure research meets legal and ethical standards.	Phone: 513- 636-8039

Total number of participants:

We expect 120 people or more from the Cincinnati area will be screened for this research study.

Change of Mind/Study Withdrawal:

You can leave the research at any time; it will not be held against you.

The person in charge of the research study or the sponsor can remove you from the research study without your approval.

If you stop being in the research, specimens may not be destroyed, and data already collected may not be removed from the study database. You will be asked whether the investigator can collect data from your routine medical care. If you agree, this data will be handled the same as research data.

The study doctor will tell you if they find out about new information from this or other studies that may affect your health, safety, or willingness to stay in this study.

Privacy:

Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete privacy. Organizations that may inspect and copy your information include the IRB and other representatives of this organization.

You will be registered in the Cincinnati Children's Hospital Medical Center's (CCHMC) computer system as a research patient. Privacy and confidentiality will be protected the same as other patients at CCHMC.
We will keep a copy of this consent form in your research chart. To keep

your information private and confidential, CCHMC and/or the study doctor will:

- use code numbers instead of your name in your study chart
- limit the people who can see your study records
- not identify you in any records or articles published about the study findings

By signing this consent form, you are giving permission for parts of your medical and research records related to this study to be reviewed by:

- Cincinnati Children's Hospital Medical Center (CCHMC)
- The study doctor and CCHMC research staff who are part of the study
- The CCHMC Institutional Review Board and the Office for Research Compliance and Regulatory Affairs
- The sponsor: National Institutes of Health (NIH) or authorized representative
- The Department of Defense (DOD) or their representatives
- Your personal healthcare provider

The Food and Drug Administration (FDA) may review your records since they are in charge of studies of experimental unapproved vaccines.

A description of this clinical trial will be available at 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. The clinicaltrials.gov identifier is NCT#.

To help us protect your privacy, we have a Certificate of Confidentiality from the National Institutes of Health (NIH). The researchers can use this Certificate to legally refuse to give information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify you, except for reporting of communicable diseases to State and local health departments.

The Certificate of Confidentiality:

- Will not be used to prevent disclosure to state or local authorities for information required by local or state law.
- Cannot be used for information in your medical records.

- Does not prevent disclosure of your information to the NIH, Food and Drug Administration (FDA), or federal funding agency.
- Does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research.

If you give your consent to release information to a medical care provider, an insurer, or other person to receive research information, then the researchers will not withhold that information.

Samples and/or data collected for or generated from this study could be shared and used for future research. Samples and /or data may be shared with other collaborators at Cincinnati Children's and possibly with outside collaborators, who may be at another institution or for-profit company.

If information that could identify you is removed from your information or samples collected during this research, that information or those samples could be stored and used for future research studies or distributed to another investigator for future research studies without your additional informed consent.

The sponsor, monitors, auditors, the IRB, the Food and Drug Administration will be granted direct access to your medical records to conduct and oversee the research. By signing this document, you are authorizing this access. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

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.

If injured while in the study:

If you believe that you have been injured as a result of this research, you should contact Dr. Frenck as soon as possible to discuss the concerns. Treatment for injuries is available at Cincinnati Children's. If you go to the Emergency Room or to another hospital or doctor, it is important that you tell them that you are in a research study. If possible, you should give them a copy of this consent form.

Cincinnati Children's follows a policy of making all decisions about compensation for the medical treatment of physical injuries that happened during or were caused by research on an individual basis.

In general, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH or the Federal Government.

Return of results:

Most tests done on samples or images obtained in research studies are only for research and have no clear meaning for healthcare. If the research with your information or samples gives results that do have meaning for your health, the researchers will contact you and ask you if you would like to know what they have found. You can say No to hearing about the results at that time if you desire.

AUTHORIZATION FOR USE/DISCLOSURE OF HEALTH INFORMATION FOR RESEARCH

To be in this research study you must also give your permission (or authorization) to use and disclose (or share) your "protected health information" (called PHI for short).

What protected health information will be used and shared during this study?

Cincinnati Children's Hospital Medical Center (Cincinnati Children's) will need to use and share your PHI as part of this study. This PHI will come from:

- Your Cincinnati Children's medical records
- Your research records

The types of information that will be used and shared from these records include:

- Laboratory test results, diagnosis, and medications
- Reports and notes from clinical and research observations
- Imaging (like CT scans, MRI scans, x-rays, etc.) studies and reports
- If applicable, information concerning HIV testing or the treatment of AIDS or AIDS-related conditions, drug or alcohol abuse, drug-related conditions, alcoholism, and/or psychiatric/psychological conditions (but not psychotherapy notes).

Who will share, receive and/or use your protected health information in this study?

- Staff at all the research study sites (including Cincinnati Children's)
- Personnel who provide services to you as part of this study
- Other individuals and organizations that need to use your PHI in connection with the research, including people at the sponsor and organizations that the sponsor may use to oversee or conduct the study.
- The members of the Cincinnati Children's Institutional Review Board and staff of the Office of Research Compliance and Regulatory Affairs.
- The Department of Defense (DOD) or their representatives

How will you know that your PHI is not misused?

People that receive your PHI as part of the research are generally limited in how they can use your PHI. In addition, most people who receive your PHI are also required by federal privacy laws to protect your PHI. However, some people that may receive your PHI may not be required to protect it and may share the information with others without your permission, if permitted by the laws that apply to them.

Can you change your mind?

You may choose to withdraw your permission at any time. A withdrawal of your permission to use and share your PHI would also include a withdrawal from participation in the research study. If you wish to withdraw your permission to use and share PHI you need to notify the study doctor, listed on the first page of this document, in writing. Your request will be effective immediately and no new PHI about you will be used or shared. The only exceptions are (1) any use or sharing of PHI that has already occurred or was in process prior to you withdrawing your permission and (2) any use or sharing that is needed to maintain the integrity of the research.

Will this permission expire?

Your permission will expire at the end of the study.

Will your other medical care be impacted?

By signing this document, you agree to participate in this research study and give permission to Cincinnati Children's to use and share your PHI for the purpose of this research study. If you refuse to sign this document, you will not be able to participate in the study. However, your rights concerning treatment not related to this study, payment for services, enrollment in a health plan or eligibility of benefits will not be affected.

SIGNATURES

The research team has discussed this study with you and answered all of your questions. Like any research, the researchers cannot predict exactly what will happen. Once you have had enough time to consider whether you/your child should participate in this research, you will document your permission by signature below.

You will receive a copy of this signed document for your records.

_____
Printed Name of Research Participant

_____
* If signed by a legally authorized representative, a description of such representative's authority must be provided

_____ _____
Signature of Individual Obtaining Consent Date