Parental Permission, Teen Assent and Authorization Document

Study Title:	**Personalized Immunomodulation in Pediatric Sepsis-Induced MODS (PRECISE)**
Version Date:	**June 24, 2024**
Source of Support:	**National Institute of Child Health and Human Development (NICHD)**

Part 1 of 2: MASTER CONSENT

Parents/Guardians: You have the option of having your child or teen join a research study. This is a parental permission form. It provides a summary of the information the research team will discuss with you. If you decide that your child can take part in this study, you would sign this form to confirm your decision. If you sign this form, you will receive a signed copy for your records. The word "you" in this form refers to your child/teen unless otherwise indicated.

Assent Teen Participants: This form also serves as an assent form. That means that if you choose to take part in this research study, you would sign this form to confirm your choice. Your parent or guardian would also need to give their permission and sign this form for you to join the study.

Consent for Continued Participation (Participants who turn 18 during the study): This is a consent form for continued participation. It provides a summary of the information the research team will discuss with you. If you decide that you would like to continue participating in this research study, you would sign this form to confirm your decision. If you sign this form, you will receive a signed copy of this form for your records.

SUMMARY

You are being invited to take part in a research study. This study is a multi-site study, meaning it will take place at several different locations. Because this is a multi-site study this consent form includes two parts. Part 1 of this consent form is the Master Consent and includes information that applies to all study sites. Part 2 of the consent form is the Study Site Information and includes information specific to the study site where you are being asked to enroll. Both parts together are the legal consent form and must be provided to you.

You are being asked to take part in a research study because you have a severe infection called sepsis, which is causing two or more of your organs to work poorly. We know that when this happens, your immune function may be too low and/or the amount of inflammation in your body may be too high. We can test for these things in the research laboratory. Routine treatment for children with

sepsis does not include medicine to help boost immune function or reduce inflammation. We think that if you get treated with a medicine that matches what your immune system needs (an immune boosting medicine called GM-CSF, or an anti-inflammatory medicine called anakinra, depending on your test results), you will be more likely to recover and you will recover more quickly. If you agree to be in this study, we will take a blood sample in the next day or so, the results of which would determine which medicine you receive. You might receive no medicine at all. Participation in this research study is voluntary and if you chose not to participate, you will continue to receive all of the routine treatment as prescribed by your clinical team.

After the first blood sample, additional blood samples will be collected twice weekly for the next two weeks to see how your body is recovering, for a maximum of 5 blood samples. Each time blood is collected it will be one to one and a half teaspoons of blood. Your parent or guardian will also be asked to complete some surveys while you are in the hospital and then again at 3- and 12-months after discharge from the hospital. These surveys will help us to learn how you and your family are doing after you recover from sepsis. There are no additional visits to the hospital for the purposes of this study.

The main risks of the study are too many or too few white blood cells, allergic reactions, and a low red blood cell count (anemia). These risks will be discussed in more detail later in this form. Although the medications being used in this study are both FDA-approved and have been used safely in many studies of critically ill adults and children, the medications are not yet FDA-approved to help children with sepsis get better faster.

Potential benefits of the study include recovering from your illness faster. Immune function monitoring is not currently done as part of usual ICU care. You don't have to be in the study to get the usual ICU care.

If you are interested in learning more about this study, please continue reading below.

BACKGROUND

You have the option to take part in this research study because you have a serious infection, a condition called sepsis, that is causing two or more of your organs to work poorly. When that happens, it is called multiple organ dysfunction syndrome (MODS). We know that the immune system sometimes does not work properly when a child with sepsis has MODS. In some children, immune system function is too low and they have trouble fighting infection and healing their organs. We believe that these children could benefit from a medicine to help boost the function of their immune system. In other children, there is too much inflammation and we believe that they could benefit from a different, anti-inflammatory medicine. We cannot tell the difference between these children without doing special testing of their immune system. We have developed a blood testing approach that can tell us in about 24 hours how your immune system is working and how much inflammation you have. Routine treatment for children with sepsis does not include treatment to help the immune system. We think that if you get treated with a medicine that matches what your immune system needs it may help you recover more quickly.

The drug that we use to **boost the immune system's function** is called GM-CSF. GM-CSF is chemical that is made by our own bodies and it helps the immune system to work better. GM-CSF is also made as a drug and has been approved by the Food and Drug Administration (FDA) for more than 25 years to safely improve immune function in patients with certain types of cancer. We have used GM-CSF in critically ill and injured children too and we know that its use can lead to improved immune function, and we have not seen any bad side effects that came from using it. We do not know if giving GM-CSF to children with low immune function in the setting of sepsis and MODS will help them get better faster, so we are doing this study to find this out.

We also have a medicine, called anakinra, that is used to **reduce inflammation**. It is also made by our bodies, but is made as a drug too. Anakinra works by blocking one of the pathways that causes inflammation in the body. It is very specific for this pathway, so most of the immune system continues to work, while reducing inflammation. Anakinra has been approved by the FDA for 20 years to treat other inflammatory conditions, and it has been used safely in critically ill patients including those with sepsis. We do not know if giving anakinra to children with high inflammation due to sepsis will help them get better faster, so we are doing this study to find this out.

NUMBER OF PARTICIPANTS

This study is being conducted at this hospital and approximately 30 other hospitals that are part of the Collaborative Pediatric Critical Care Research Network (CPCCRN). The study is funded by the National Institute of Health (NIH). A total of about 1,095 participants will take part in this research study around the country over a period of approximately 4 years.

STUDY PROCEDURES

The study involves the following tests and procedures:

Medical Chart Review: Study staff will review your medical chart to decide if you are eligible for this study. If you are eligible, information will be collected from your medical records throughout the study; e.g., age, diagnoses, treatments. We will collect medical information to compare your immune function and its treatment with information about your hospital stay, including the kinds of treatments you receive, how your body responds to them, and how you did during your stay.

Blood Samples and Study Medication Administration: In order to check your immune function, you will have one to one and a half teaspoons of blood drawn within the next day or two. This blood will be used to measure how well your immune system is working and how much inflammation is present in your body. The test that we will use to measure how your immune system is working measures the ability of your blood cells to make a chemical called TNF-alpha. Children whose blood cells cannot make much TNF-alpha have low immune function. We have used this blood test in our research laboratory for many years to check immune function in critically ill children. This test is for research use only and is not used in regular clinical care. The results from this test will not show up in your medical records. We will check the level of inflammation in your blood by measuring chemicals that include ferritin and C-reactive protein (CRP). Levels of these chemicals are high in children with inflammation. We measure these in our research laboratory

as well. We will tell you and your treatment team what the tests show once we know the results, which we expect to get the following day. There are four possible outcomes of your immune testing:

1. **Your immune function is very low, with only moderate inflammation:** We think this means you could benefit from a treatment that will improve your immune function. You will be randomized to receive the drug GM-CSF or saline (salt water) in your IV once a day for 7 days. Randomized means that a computer will randomly pick whether you get GM-CSF or saline during your treatment course. You will have a 50% chance of receiving GM-CSF or saline. Neither you nor your clinical team nor the local research team will be able to tell whether you are getting GM-CSF or saline. The daily dose of GM-CSF that we use, 125 micrograms per square meter of body surface area, is half of the currently FDA-approved dose. This dose was chosen because previous studies showed that it can safely and effectively boost your immune function.

2. **Your immune function is OK but you have moderate inflammation *OR* you have severe inflammation regardless of your immune function:** We think this means you could benefit from a treatment that reduces inflammation. You will be randomized to receive either saline **or** one of four possible dosing levels of anakinra (4, 8, 12, or 16 mg/kg day). You will have about a 50% chance of receiving anakinra and a 50% chance of receiving saline. Neither you nor your clinical team nor the local research team will be able to tell whether you are getting anakinra or saline. The lower two dosing levels are within the currently FDA-approved dosing range. While the remaining two dosing ranges are higher, they are much lower than the doses that have been safely used in adult patients with sepsis. These doses were chosen because they have been safely used to reduce inflammation in other conditions.

3. **Extremely high inflammation:** If your blood test shows extremely high levels of inflammation with a ferritin level greater than 10,000 ng/ml, it would mean that you may have a rare condition called hemophagocytic lymphohistiocytosis (HLH) or macrophage activation syndrome (MAS) and you might require specific treatment for that. We would tell your doctors the results of your tests so that they could repeat them in the clinical laboratory. They would then decide what treatments would be most appropriate for you. You would not receive study drug at all. However, you will remain in the study so we can continue to learn about your immune system, your treatments, and your recovery.

4. **Your immune function is OK and you have little or no inflammation:** If your immune function is found to be OK, and you have only mild (or no) inflammation, you will not receive any study drug at all. However, you will remain in the study so we can continue to learn about your immune system, your treatments, and your recovery.

Being in this study will not change the care that you would otherwise receive during your illness.

Additional Sample Collections: Regardless of what your initial blood tests show, we would like to understand how your immune function and levels of inflammation get better over time. We

will collect another one to one and a half teaspoons twice weekly for the next two weeks for a total of 5 blood samples at most, including the initial immune function testing. We will use these blood samples to learn more about how your body is recovering from infection and responding to treatments. This could include understanding how chemicals in the bloodstream, chemicals in blood cells, and even your DNA are related to how you are recovering. If you are discharged from the hospital before then, you do not have to come back for blood draws. We will try to collect these samples from tubes that you already have in an artery or vein, and/or coordinate the sampling with a time when your treatment team is getting blood for clinical reasons. It may be, though, that we need to use a needle in a blood vessel to get one or more of these samples if there is no other way to get them. If you are in one of the groups that does *not* get study drug, we will *not* use a needle to get those additional blood samples and we would stop taking blood samples if you leave the intensive care unit before the sampling period is over. If you have a breathing tube in place, we will also collect a small amount of fluid from the breathing tube on the same days that we collect blood samples, including the initial sample. This fluid is removed as part of routine care and is usually thrown away, but we will save some of it to help understand how your lungs are doing.

Questionnaires at Time of Study Entry, 3-Months and 12-Months: We will ask your parent or guardian to complete surveys about how you and your family are doing while you are in the hospital. We will contact them and/or send a link to complete the same surveys at about 3- and 12- months after discharge of the hospital to learn about how you and your family are doing. This will help us understand if being in this study helped your recovery from sepsis. We anticipate that these questions will take about 30-60 minutes to answer. Once you are discharged from the hospital there will be no follow-up visits, tests, or drugs that are needed for the purposes of this study.

ALTERNATIVE PROCEDURES

Your participation in is this study is voluntary. It is not necessary to be in this study to get care for your illness. Monitoring of immune function is not currently done as part of routine ICU care. There are no other treatments designed to increase immune function or reduce inflammation that are routinely used in children with sepsis.

RISKS

Taking part in a research study can involve risks. If you have any questions about any of the possible risks listed below, you should talk to the study doctor or your regular doctor.

Risks associated with GM-CSF treatment (if you receive GM-CSF): GM-CSF, in the dose used in this study, has been safely given to critically ill adults and children in several other small studies. No bad side effects from GM-CSF treatment were seen in these studies. There are a couple of side effects that we will be looking for, however. There is no way to say without a doubt that you will or will not experience any of these or other side effects:

- Too many white blood cells: One way that GM-CSF works is to help the body to make more white blood cells. If there are way too many white blood cells (more than 100,000 cells/mm^3), it can be harmful. If we see that your white blood cell count is greater than 50,000 cells/mm^3 we will not give the study drug. We expect this to happen in less than 10% of patients.
- Allergic reactions: Allergic reactions can happen with any drug. If you are known to be allergic to GM-CSF then you cannot be in the study. We expect this to happen very rarely if at all (in less than 1% of patients).

Risks associated with anakinra treatment (if you receive anakinra): Anakinra has been safely used in many studies of critically ill adults and children in doses that are the same or higher than those used in this study. There are, however, a few side effects that we will be looking for. There is no way to say without a doubt that you will or will not experience any of these or other side effects:

- Too few white blood cells: Anakinra use has rarely been associated with a large drop in white blood cell count. A drop in white blood cell count can be seen with sepsis alone, but if we see a severe drop in your white blood cell count on two consecutive days we will stop the study drug. We expect to see this rarely if at all (in less than 1% of patients).
- Risk of new infection: For some conditions, anakinra has been used long-term, for months or even years. Patients who receive anakinra over a long period of time may be at increased risk for developing new infections. This has not been seen when anakinra is used for short periods of time like in this study. While new infections sometimes happen in children with sepsis, we do not expect this risk to be increased in children who receive anakinra.
- Allergic reactions: Allergic reactions can happen with any drug. If you are known to be allergic to anakinra then you cannot be in the study. We expect this to happen very rarely if at all (in less than 1% of patients).

It is important that you give the research study staff a complete medical history. Not giving them this information could harm you. If any of the problems listed above require treatment, your clinical team will treat them. If you are worried about anything while in this study, please call the Principal Investigator of this study or his study staff.

Risks associated with study blood draws: If you already have a tube in a blood vessel that permits blood sampling as part of clinical care, we will draw blood from that tube. Accessing a blood drawing line to obtain blood can increase the risk of getting a bloodstream infection, but the team will be careful to avoid this. Whenever possible, we will collect research samples at the same time that blood is drawn for clinical reasons so that we minimize the number of times the blood drawing line is entered.

If those blood drawing lines do not work well or have come out we may need to use a needle to get blood. Drawing blood by placing a needle in a vein may cause pain, lightheadedness and fainting, bleeding, bruising, or swelling at the puncture site. Infection is a rare possibility.

Risk of needing a new IV catheter: If you end up in the GM-CSF or anakinra part of the study, you will need to have an IV tube (catheter) available through which to give the study drug. If for some reason you do not have an IV catheter available during the time period in which you are getting the study drug, a new one would need to be placed. Getting new IV catheters is common in patients with sepsis. Getting IV catheters may cause pain, lightheadedness and fainting, bleeding, bruising, or swelling at the puncture site. Infection is a rare possibility.

Risk of developing anemia: Many patients who are critically ill require a blood transfusion as part of their treatment. Any time we draw blood from a patient it can contribute to a low red blood cell count (or anemia). The volume of blood taken for the purposes of this study, however, is very small compared to the amount taken in the course of routine ICU care. We will stop drawing blood from you if your doctor(s) feel that we should stop. Being in this study should not significantly increase your risk of needing a transfusion.

Risks associated with data collection: As with any study that involves collecting data, loss of confidentiality is possible. Every precaution will be taken to secure participants' personal information. At the time of participation, each participant will be assigned a study identification number. This number will be used on data collection forms, blood samples, and in the study database instead of names and other private information. A separate list that links each participant's name to the study identification number will be securely maintained for future reference and communication.

Unforeseeable Risks: In addition to the risks listed above, you may experience a previously unknown risk or side effect.

Reproductive Risks: If a person is known to be pregnant or lactating, she cannot participate in this study. If a person is discovered to be pregnant or lactating after starting in the study, participation in the study would stop including stopping the study drug.

BENEFITS

Potential Benefits for You: We know that patients with sepsis who have low immune function and/or high levels of inflammation are at risk for getting new infections, having longer periods of time with organ failure, and/or death. We think that treatment with a medicine like GM-CSF or anakinra that matches what your immune system needs will improve your immune function and/or reduce your inflammation, if present. This could make it easier for you to recover from your illness.

Potential Benefits for Others: We also might learn something that could help other critically ill children with sepsis in the future.

RIGHT OF THE INVESTIGATOR TO WITHDRAW PARTICIPANTS

The investigator can withdraw your child without your approval. If at any time the investigator believes participating in this study is not the best choice of care, the study may be stopped and other care prescribed. If unexpected medical problems come up, the investigator may decide to stop your participation in the study.

NEW INFORMATION

Sometimes during the course of a research project, new information becomes available about the drugs that are being studied. If this happens, your research doctor will tell you about it and discuss with you whether you want to continue in the study. If you decide to continue in the study, you may be asked to sign an updated consent form. Also, on receiving new information the research doctor might consider it to be in your best interests to withdraw you from the study. He/she will explain the reasons and arrange for your medical care to continue.

OPTION TO STORE SAMPLES FOR FUTURE RESEARCH

After your blood and breathing tube samples are used for this study, there may be some unused parts of the samples that are left over, including your DNA. These samples may be useful to new research performed in the future. Use of your samples for future research may help researchers learn more about how to prevent, find, and treat various diseases and conditions, even diseases and conditions that are different from yours.

How we will handle your samples: Samples saved for future research will be stored at Nationwide Children's Hospital or a network-approved biorepository. Your samples and related information will be coded so your name is not on them. Future researchers will not be given your name but will only be given information like your age and what disease or condition you have. At the end of the study, the identifying code assigned to your samples will be deleted.

Your samples and information will be used only for research and will not be sold, but for-profit research may be done. No royalties or payment will be made if any commercial product is developed from your blood obtained from you during this study.

If you decide at any time that you do not want your samples or related information stored for future research, you must contact the principal investigator listed on this consent document, to have your samples and information destroyed. However, if we have already deleted the identifying code or shared your samples or information for a future project, we will not be able to destroy any of the samples or information that are no longer in our possession.

Your samples may be used for whole genome or whole exome sequencing. We will not be able to share results of future studies, including genetic studies, with you or your doctors.

Risk of Genetic Testing: You should be aware that there might be potential social and economic disadvantages, which can be associated with the gathering of genetic information. A federal law, called the Genetic Information Nondiscrimination Act (GINA), 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.

However, since the genetic testing performed as a part of this study is solely for research purposes only and the significance of the results of this genetic analysis is not known, we will not share the results of these genetic tests with anyone, including you, your family members, or any healthcare providers. Since genetic information divulged to the wrong source could affect you and your family, we are careful not to share this information with anyone. If you choose to participate in this study, you will be assigned a random number as your study ID. This study ID will only be linked to you within the study and no one outside of the study will know it was you who participated in this study. If any results from the genetic testing are shared, it will be in a coded form using this study ID. In this form, your genetic information may be used for future research or analysis by researchers in a controlled access government health research database, but again, we will not give them your name, address, phone number, or any other personally identifiable information.

Consent for saving your samples: You can choose to allow your leftover samples to be saved for this future research. This is optional and you can still be in the main part of this study if you say no. No matter what you decide to do, your decision will not affect your medical care.

Initial your choice below:

_____YES. I agree to allow all of my leftover samples, **including DNA**, to be kept and used for future research that may be unrelated to the PRECISE study.

_____YES. I agree to allow my leftover samples, **except for DNA**, to be kept and used for future research that may be unrelated to the PRECISE study.

_____NO. I do not agree to allow any of my leftover samples to be kept and used for future research.

Consent to be contacted for future research studies: Researchers in the future may design new studies for which you could be eligible. These studies may be related to the PRECISE study or unrelated to the PRECISE study. We would like to know if it would be OK to contact you in the future to see if you would like to participate in those studies.

Initial your choice below:

_____YES. I agree to be contacted about *any* future research studies for which I may be eligible.

_____YES. I agree to be contacted *only* about future research studies that are related to the PRECISE study.

_____NO. I do not agree to be contacted about any future research studies for which I may be eligible.

COSTS AND COMPENSATION TO PARTICIPANTS

While you are in this study, the cost of your usual medical care - procedures, medications and doctor visits - will continue to be billed to you or your insurance. There will be no additional costs to you for your participation in this study. You will receive up to $50 to compensate you for your time when completing the follow-up surveys at the 3- and 12-month time points. You will receive $25 for each follow-up period once we receive your answers to the surveys. Any tests that are performed or medications administered solely for the purposes of being in this study will be paid for by the research doctor. The National Institutes of Health is providing funding for this study.

SINGLE IRB CONTACT

Institutional Review Board: The University of Utah Institutional Review Board (IRB) is serving as the single IRB (SIRB) for this study. Contact the SIRB if you have questions, complaints or concerns which you do not feel you can discuss with the investigator. The University of Utah IRB may be reached by phone at (801) 581-3655 or by e-mail at irb@hsc.utah.edu.

Parental Permission, Teen Assent and Authorization Document

Study Title:	**Personalized Immunomodulation in Pediatric Sepsis-Induced MODS (PRECISE)**
Principal Investigator:	**Mark W. Hall, MD** **Nationwide Children's Hospital** **(614)722-3438**

Part 2 of 2: SITE SPECIFIC INFORMATION

This part of the consent form includes information about the site that is asking you to participate in this study and is specific to participation at your site only. Before making your decision, both the site-specific information and the general study information should be reviewed with you. Your medical record will contain a note saying you are in a research study and may contain some research information about you. Anyone you authorize to receive your medical record will also get this information.

AUTHORIZATION FOR USE OF PROTECTED HEALTH INFORMATION

The purpose of the authorization is to allow protected health information (PHI) to be used for the research described in this consent and authorization form. The following pieces of PHI will be collected for this research study:

1. Name
2. Medical record number
3. Date of birth
4. Admission and discharge dates from the hospital and ICU
5. Zip code
6. Parent/guardian name(s)
7. Parent/guardian email address(es)
8. Parent/guardian telephone number(s)
9. Parent/guardian mailing address(es)

Efforts will be made to keep your study-related information confidential. However, there may be circumstances when this information must be released. For example, personal information regarding your participation in this study may be disclosed if required by state law. Your records may be reviewed by the following groups (as applicable to the research):

- The Collaborative Pediatric Critical Care Research Network (CPCCRN) Data Coordinating Center at the University of Utah, the research data coordinating center that is responsible for collecting results and findings from all the researchers;
- Researchers at Nationwide Children's Hospital and their auditors/monitors, the laboratory who will analyze and store your samples and the central pharmacy that provides study drug to the study sites;
- The University of Utah Institutional Review Board, the central committee that reviews all human subject research for CPCCRN;
- The Principal Investigator and study staff at Nationwide Children's Hospital;
- Independent Auditor(s), representative(s) from any of the above groups who might audit the study to further verify accuracy of the study results;
- The Office for Human Research Protections (OHRP), the federal government office that oversees human subject research;
- The Food Drug Administration (FDA), the federal government office that oversees research medications;
- National Institutes of Health (NIH), a federal agency that needs to confirm the accuracy of the results submitted to the government.

Because of the need to give information to these people, absolute confidentiality cannot be guaranteed. Information given to these people may be further disclosed by them and no longer be protected by federal privacy rules.

If you have a bad outcome or adverse event from being in this study, the Principal Investigator and staff or other health care providers may need to look at your entire medical records. We expect that the results from this study may be published in the future but your identity will not be revealed.

There is a risk that someone could get access to the information (data) we have collected about you. If those data suggested something serious about your health, it could be misused. We cannot guarantee that this will fully protect you. Your privacy and the confidentiality of your data are very important to us. We will make every effort to protect them.

If you do not sign this form, you may not join this study. This authorization does not have an expiration date. You have a right to information used to make decisions about your child's health care. However, your child's information from this study will not be available during the study.

Certificate of Confidentiality

By law, we are required to protect your health information. The investigator and staff involved with this study will keep your personal health information collected for the study strictly confidential. To help us protect your privacy, the National Institutes of Health have issued a Certificate of Confidentiality for this study. With this certificate, the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the certificate to resist any demands for information that would identify you, except as explained below.

The certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the certificate to withhold that information.

The Certificate of Confidentiality does not prevent the researchers from disclosing voluntarily, without your consent, information that would identify you as a participant in the research project. However, there are no conditions under which the researchers plan to voluntarily disclose your identity.

Public Use Data Set At the end of the study, the Data Coordinating Center at the University of Utah will prepare a de-identified public use dataset. This dataset will include information collected from you during the study. De-identified means that there will be no way for the researchers or users of the de- identified dataset to trace the information back to you. The NIH requires CPCCRN to prepare a public use dataset for other researchers to use. Even though the dataset is de-identified, users of the public use dataset are required to obtain IRB approval and follow regulatory and privacy laws associated with the research. This dataset will be shared with and managed by the NIH.

ClinicalTrials.gov A description of study 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.

What if I decide to not participate after I sign the Consent and Authorization Form?

You can tell us anytime that you do not want to be in this study and do not want us to use your health information. You can also tell us in writing. If you change your mind, we will not be able to collect new information about your child, and your child will be withdrawn from the research study. However, we can continue to use information we have already started to use in our research, as needed to maintain the integrity of the research.

Your signature on this form would mean:

- The research study was explained to you.
- You had a chance to ask all the questions you have at this time. All your questions have been answered in a way that is clear.
- You understand that the persons listed on this form will answer any other questions you may have about the study or your rights as a research study participant.
- You have rights as a research participant. We will tell you about new information or changes to the study that may affect your health or your willingness to stay in the study.

WHO TO CONTACT

If you have any questions about anything while on this study, or if you have been injured by the research, you may contact Dr. Hall at (614)722-3438, Monday-Friday, between 8am to 4pm.

If you have questions, concerns, or complaints about the research; if you have questions about your rights as a research volunteer; if you cannot reach the Principal Investigator; or if you want to call someone else, call (614) 722-2708, Nationwide Children's Hospital Institutional Review Board, (the committee that reviews all research involving human subjects at Nationwide Children's Hospital).

RESEARCH RELATED INJURY

If you are hurt by the study drug or procedures that are part of this study, you will receive treatment at Nationwide Children's Hospital.

In most cases, this care will be billed to your health insurance company or whoever usually pays for your health care at the usual charges, but some insurance companies will not pay for care related to a study. If the care is provided at Nationwide Children's Hospital, we make no commitment to pay for the medical care provided to you. No funds have been set aside to compensate you in the event of injury. If no one else pays for your care, you may have to pay for the cost of this care. This does not mean that you give up any of your legal rights to seek compensation for your injuries.

COST AND COMPENSATION

While you are in this study, the cost of your usual medical care - procedures, medications and doctor visits - will continue to be billed to you or your insurance. There will be no additional costs to you for your participation in this study. You will not receive any payments for taking part in this study. Any tests that are performed as a result of being in this study will be paid for by the research doctor. The National Institutes of Health is providing funding for this study.

For your time and inconvenience, you (study participant) will receive $25 per survey completion up to a total of $50. You will be issued a debit card specially designed for clinical research. When a survey has been completed, funds will be approved and automatically loaded onto your card.

PARENT/GUARDIAN CONSENT:

I confirm that I have read this parental permission document and have had the opportunity to ask questions. I will be given a signed copy of the parental permission form to keep.

I agree to allow my child to participate in this research study and authorize you to use and disclose health information about my child for this study, as you have explained in this document.

_____
Child's Name

_____
Parent/Guardian's Name

_____ _____
Parent/Guardian's Signature Date\Time

_____
Relationship to Child for Parent/Guardian

_____
Name of Person Obtaining
Authorization and Consent

_____ _____
Signature of Person Obtaining Date\Time
Authorization and Consent

TEEN ASSENT:

I confirm that I have read this assent document and have had the opportunity to ask questions. I will be given a signed copy of the assent and authorization form to keep.

_____
Printed Name of Child

_____ _____
Signature of Child Date\Time

_____
Name of Person Obtaining Assent

_____ _____
Signature of Person Obtaining Assent Date\Time

CONSENT TO CONTINUED PARTICIPATION:

I understand that I am currently participating in a research study. I further understand that consent for my participation in this research study was initially obtained from my parent/guardian as a result of my not yet being 18 years of age and was unable to provide direct consent at the time that this initial consent was requested.

I am now 18 years of age and am able to provide direct consent for continued participation in this research study. I confirm that I have read this consent document and have had the opportunity to ask questions. I will be given a signed copy of this consent document to keep.

_____

Printed Name of 18 year old participant

_____ _____

Signature of 18 year old participant | Date\Time

_____

Name of Person Obtaining Consent

_____ _____

Signature of Person Obtaining Consent | Date\Time

INTERPRETER STATEMENT: (For Non-English Speaking Participants Only)

I confirm that I was present as an interpreter for the duration of the consent process for this research study. I confirm that I am qualified and have the necessary skills to provide interpretation between the participant's language and English. By signing this form, I confirm that I provided a full and complete interpretation of the exchange between the researcher obtaining consent and the participant, to the best of my ability.

_____

Name of Interpreter

_____ _____

Signature of Interpreter Date\Time

Reporting Race and Ethnicity Data
Per the NIH POLICY ON REPORTING RACE AND ETHNICITY DATA: SUBJECTS IN CLINICAL RESEARCH (NOT-OD-01-053)

Date of Birth	**Sex/Gender** ☐ **Male** ☐ **Female**

Ethnicity

Do you consider yourself to be Hispanic or Latino? (See definition below). Select one. **Hispanic or Latino**. A person of Mexican, Puerto Rican, Cuban, South or Central American, or other Spanish culture or origin, regardless of race. The term, "Spanish origin," can be used in addition to "Hispanic or Latino."

☐ **Hispanic or Latino**
☐ **Not Hispanic or Latino**

Race

What race do you consider yourself to be? Select one or more of the following.

☐ **American Indian or Alaska Native.** A person having origins in any of the original peoples of North, Central, or South America, and who maintains tribal affiliation or community attachment.

☐ **Asian.** A person having origins in any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent, including, for example, Cambodia, China, India, Japan, Korea, Malaysia, Pakistan, the Philippine Islands, Thailand, and Vietnam. (Note: Individuals from the Philippine Islands have been recorded as Pacific Islanders in previous data collection strategies.)

☐ **Black or African American.** A person having origins in any of the black racial groups of Africa. Terms such as "Haitian" or "Negro" can be used in addition to "Black" or "African American."

☐ **Native Hawaiian or other Pacific Islander.** A person having origins in any of the original peoples of Hawaii, Guam, Samoa, or other Pacific Islands.

☐ **White.** A person having origins in any of the original peoples of Europe, the Middle East, or North Africa.

☐ Check here if you do not wish to provide some or all of the above information.