A Prospective, Blinded, Cross-Over Trial of the Exposure-Response Relationship of Terbutaline Sulfate in Adults with Asthma [TBS02]

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CONSENT TO PARTICIPATE IN A RESEARCH STUDY AND HIPAA AUTHORIZATION

TITLE:	**A Prospective, Blinded, Cross-Over Trial of the Exposure-Response Relationship of Terbutaline Sulfate in Adults with Asthma [TBS02]**
PROTOCOL NO.:	NICHD-2019-TBS02
FUNDING SPONSOR:	The Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) awarded a publicly funded contract to Duke University. The NICHD is a part of the U.S. National Institutes of Health (NIH).
INVESTIGATOR:	<Insert Site PI Name>
STUDY SITE:	<Insert Site name> <Insert Site address>

STUDY RELATED

PHONE NUMBER(S): <Insert Site Contact Name and Phone #> *(24-hour phone number)*

RESEARCH CONSENT SUMMARY

The purpose of this study is to find out if the study drug, terbutaline sulfate (terbutaline), is safe with intravenous (IV) administration (where a small tube called an IV catheter is placed into your vein to allow for medication to be given over 5 minutes) and to determine the IV dose of the drug that works best. Terbutaline has been approved by the U.S. Food and Drug Administration (FDA) for adults and children 12 years and up, by subcutaneous injection (SQ, an injection under the skin). Although it is common for doctors to give terbutaline using the IV route, studies of IV terbutaline have not been performed and submitted to the FDA for approval. The results of this study may be used by the FDA to make decisions about the optimal dose of IV terbutaline in adults and children.

If you participate in this study, you will have a physical exam, breathing assessment with or without albuterol, urine pregnancy test if female and capable of becoming pregnant, electrocardiogram (ECG) and blood draw to determine if you are a good fit for this study. Once confirmed, you will attend four total study visits. During two of the four visits, you will receive a single dose of terbutaline via IV or SQ administration route and complete a series of blood draws, breathing tests, and heart tests (ECG) and urine pregnancy tests if female and capable of becoming pregnant. The two dosing visits will be separated by at least 14 days. The other two visits will occur the day after each of the terbutaline dosing visits and will involve a blood draw and evaluation of any side effects.

Some of the risks associated with terbutaline may include increase in blood pressure, chest discomfort, muscle cramps, weakness, and immediate hypersensitivity. What we learn in this study will be put in a database run by the NIH to be shared for future research. This information will not include anything that identifies you. If you are interested in learning more about this study, please continue to read below.

DETAILED RESEARCH CONSENT

You are being asked for your consent to take part in a research study. A person who takes part in a study is called a "research participant." "Site staff" means any person at the site investigator's location. The "study team" includes people involved with the study at the National Institute of Child Health and Human Development (NICHD), the Investigational New Drug (IND) Sponsor (the person in charge of the study overall), Duke University (Duke Clinical Research Institute [DCRI]), and The Emmes Company, LLC.

Who is paying for this study to be done?

The Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) is paying for this study and may also pay for the site staff through a contract with Duke University.

What should I know about this study?

- Site staff will explain this study to you. This form sums up that explanation. You may take a copy of this form home with you to review before making your decision.
- Taking part in this study is voluntary. Whether you choose to take part is up to you.
- If you choose not to participate in this study or you choose to stop participating at any time, your choice will not be used against you. It will not affect your access to health care at **<Insert Site Name>**. There will not be any penalties or loss of benefits for which you are otherwise entitled.
- If there is anything you do not understand, ask questions. You can ask all of the questions you want before you decide to participate and at any time during the study.
- You may want to talk about the study with your health care provider, friends, or family members before deciding.
- We will tell you about any new information that may affect your health, welfare, or your choice to stay in this study.
- About 12 participants will take part in this study.

Why is this study being done?

The purpose of this study is to learn more about the safest dose of IV terbutaline that works best to treat adults with asthma and to share what we learn with other researchers. We hope results from this study can aid researchers in understanding the best IV dose of terbutaline and use this information in a future study in children. This study is considered investigational. Terbutaline has been approved by the FDA for use in patients 12 years and older by SQ administration. While terbutaline is given via the IV route to treat adults and children with asthma, the FDA has not approved IV terbutaline and the best IV dose of terbutaline is not known.

What is involved in this study?

How long will I be in the study?

We expect that your minimum participation in this study will last about 17 days, however, it could last up to 82 days if needed. If you experience a severe side effect to terbutaline, you may be followed for up to an additional 7 days, or until the side effects or symptoms have resolved.

What will happen in the study?

We will record your sex, date of birth, race, ethnicity, and information on how to contact you. We will record information from your medical record at this location. Examples include your medical history, visits to the emergency room or a hospital stay, past breathing tests, current and past medicines, physical exam and imaging results, laboratory results, recent asthma symptoms/attacks (cough, wheezing, difficulty breathing, etc.), and smoking history. If you are seen at another location, we may ask you to sign a form to allow us to get records of the above information from them.

Each participant will receive two doses of terbutaline. You will be put into a study group, Group A or Group B, by chance, like flipping a coin. The group you are in will determine the order of the route of administration - the way in which you will receive each terbutaline dose during your study visits.

- Group A will receive the 1st dose of terbutaline through an IV administration (where a small tube called an IV catheter is placed into your vein to allow for medication to be given over 5 minutes) during their first visit, and then receive the 2nd dose by SQ administration at a follow-up visit at least 14 days later.
- Group B will have the same procedures except the SQ dose will occur first and the IV dose will occur at least 14 days later.

Administration of drug can be delayed if you are showing signs of worsening asthma symptoms, respiratory illness; if you have a fever; if your heart rate, blood pressure, or oxygen saturation levels are not normal; if you are taking certain medications; or if you have had certain foods and/or drinks prior to your terbutaline dose. We will need to reschedule your visit.

Each of the two times you receive terbutaline you will be monitored closely in the clinic for approximately 8 hours to collect your vital signs and heart rate, conduct breathing tests and ECG, and to draw blood (to measure the blood levels of terbutaline and/or reevaluate kidney function as needed).

Screening Visit: (The following procedures must occur within 21 days before Visit 1 dosing, and lasts approximately 1.5 hours.)

The site staff will:

- Collect information about your age, gender, race, ethnicity;
- Collect a urine sample from you for a pregnancy test if you are capable of becoming pregnant;
- Collect a blood sample to perform a kidney function test called “Estimated Glomerular Filtration Rate” (eGFR) that helps determine whether your kidneys are functioning normally;
- Ask about your medical history, medications you are taking, smoking history, and confirm with your medical records;
- Perform a physical exam (including height and weight);
- Perform an ECG. An ECG measures your heart’s electrical activity by attaching soft electrodes (small sticky pads) with a gel to your chest, arms, and legs;
- Record your vital signs, including your blood pressure, heart rate, temperature, and oxygen level;
- Perform a breathing test (spirometry) , that measures the amount of air you inhale and exhale;
- Conduct eligibility assessments, such as multiple breathing tests (spirometry) with inhaled albuterol, that measures airway reactivity for the study if there is no documentation in your medical records in the last 12 months
- Review eligibility criteria for the study to ensure you are eligible to participate;
- Discuss medications and foods to avoid before terbutaline dosing (see attachment).

Visit 1: (Visit 1 day 1 and will last approximately 8 hours)

The site staff will:

- Collect a urine sample from you for a pregnancy test if you are capable of becoming pregnant;
- Review eligibility criteria for the study to ensure you are eligible to participate;
- Ask you about the current medications you are taking;
- Review requirements for getting terbutaline, such as making sure that you are not taking any other excluded medications, food, or drink that could interact with terbutaline;

- Record your vital signs, including your blood pressure, heart rate, temperature (taken at the beginning of the visit), and oxygen level;
- Put you into a study group, either Group A or Group B, by chance;
- Perform a breathing test (spirometry) that measures the amount of air you inhale and exhale. You will be asked to do this test 10 times (occurs before and after receiving terbutaline). It requires you to breathe forcefully several times into a tube attached to a machine, called a spirometer;
- Give you the terbutaline;
- Collect up to nine blood samples, approximately 18 mL total (about 1 tablespoon);
- Review and record your medical condition and update any changes in your study records;
- Perform an ECG after you have received the terbutaline;
- Schedule Visit 2 for the next calendar day and Visit 3.

Visit 2: (1 day after Visit 1; will last approximately 1 hour)

The site staff will:

- Collect a blood sample; approximately 2 mL (about $^{1}/_{6}$ of a tablespoon)
- Review your medical condition and update any changes in your study records.

Visit 3: (should occur between day 16 and day 60; and will last approximately 8 hours)

The site staff will:

- Collect urine sample from you for a pregnancy test, if applicable, if you are capable of becoming pregnant;
- Review requirements for getting terbutaline, such as making sure that you are not taking any other excluded medications, food, or drink that could interact with terbutaline;
- Ask you about the current medications you are taking;
- Record your vital signs, including your blood pressure, heart rate, temperature (taken at the beginning of the visit), and oxygen level;
- Collect a repeat blood sample to perform a test (eGFR) that helps determine whether your kidneys are functioning normally (if previous lab results were not normal);
- Perform breathing tests (spirometry) that measure the amount of air you inhale and exhale. You will be asked to do this test 10 times (occurs before and after receiving terbutaline). It requires you to breathe forcefully several times into a tube attached to a machine, called a spirometer;

- If the site staff determines you are eligible to receive the second dose of terbutaline, the drug will be given based on your original assignment to Group A or B;
- Collect up to nine blood samples, approximately 18 mL total (about 1 tablespoon);
- Perform an ECG after you have received the terbutaline;
- Review and record your medical condition and update any changes;
- Schedule Visit 4 for the next calendar day.

Visit 4: (1 day after visit 3; will last approximately 1 hour)

The site staff will:

- Collect a blood sample; approximately 2 mL (about $^{1}/_{6}$ of a tablespoon);
- Review your medical condition and update any changes;
- Give you end of study/discharge information.

Follow-Up Contact (approximately 48 hours (± 24 hours)) after you receive your final terbutaline dose, a phone call or in-person visit will take place. We will ask you about your general health and the presence or absence of any new symptoms. These questions will last approximately 5-10 minutes.

Sample Collection and Testing

Blood will be collected from a vein located in either your hand or arm and may involve the use of an IV line that is inserted and used to draw blood.

Blood samples will be collected up to twenty-two times from you. Over the course of the whole study, approximately 102 mL (about 7 tablespoons) of blood will be collected. No more than 49 mL (approximately 3 tablespoons) of blood will be collected at a single study visit. This total volume also includes an additional amount of blood that is discarded prior to collecting each PK sample. We will use this blood for the tests we explain below.

eGFR Tests

Blood will be collected from a vein located in either your hand or arm and may involve the use of an IV line that is inserted and used to draw blood. Blood will be drawn at screening and at Visit 3 (if retesting is needed) to determine whether your kidneys are functioning normally prior to terbutaline administration.

Pharmacokinetic (PK) Tests

These blood samples will be used to perform PK tests to measure the amount of terbutaline in your blood. This information helps researchers understand how much medicine to give and how often it should be given.

- Visits 1 and 3

- Blood will be collected from a line that will be inserted into your arm prior to terbutaline administration and used to draw blood. Approximately 2 mL (about $^1/_6$ of a tablespoon) of blood will be collected at each of the 9 study time points [5 minutes, 15 minutes, 30 minutes, 45 minutes, 1 hour, 2 hours, 3 hours, 4 hours, 6 hours after terbutaline administration] for a total blood amount of 18 mL (about 1 tablespoon) at each visit.

- Visits 2 and 4
  - Approximately 2 mL (about $^1/_6$ of a tablespoon) of blood will be collected from a hand or arm stick at each visit.

When participants receive IV terbutaline at either Visit 1 or Visit 3, they will have two separate IV lines placed (one in either the hand or arm). One IV line will be used to administer terbutaline and can be removed after the drug is administered. The second IV line will be used to collect the PK blood samples and can remain in place for the duration of the study visit.

Urine Pregnancy Tests

Participants capable of becoming pregnant will be asked to provide a urine sample to conduct pregnancy testing at screening, Visit 1 and Visit 3.

Breathing Tests and ECG

All participants will have one breathing test (spirometry) performed at screening. Some participants may have additional breathing tests performed at screening, to confirm airway reactivity. These additional breathing tests will be done after an albuterol dose and again at 15 minutes, 25 minutes, 35 minutes, and 45 minutes, if needed.

Breathing tests (spirometry) will also be performed at Visits 1 and 3, before each dose of terbutaline and again at 5 minutes, 15 minutes, 30 minutes, 45 minutes, 1 hour, 2 hours, 3 hours, 4 hours, and 6 hours after the terbutaline dose.

An ECG will be performed at Screening and 6 hours after each dose of terbutaline, at Visits 1 and 3.

Are there benefits to taking part in this study?

There may be no direct medical benefits to you from taking part in this study. On the day of dosing, terbutaline may open your airways and make your breathing feel better. We hope the information learned from this study will benefit adults and children in the future.

What are the discomforts or risks of the study?

Risk of Terbutaline Sulfate Administration:

There is a risk of cardiovascular side effects in some patients, including fast heart rate, palpitations (pounding in your chest), increase of blood pressure, chest discomfort,

muscle cramps, and weakness while taking terbutaline; although such effects are uncommon after SQ terbutaline at the recommended doses. If these symptoms occur the drug may need to be discontinued. In addition, other types of medicines like terbutaline have been reported to produce cardiac ECG changes; however, the clinical significance of these ECG findings is unknown.

There have also been rare reports of seizures in patients receiving terbutaline. Seizures did not recur in these patients after the drug was discontinued. Other side effects include tremors, nervousness, dizziness, drowsiness, difficulty falling asleep or staying asleep, headache, nausea, sweating, and dry mouth. Pain at the injection site has also been reported.

Serious but rare allergic reactions including rash, itching/swelling of face, tongue, throat, and trouble breathing may occur. Changes in blood sugar in patients with diabetes have been reported after terbutaline administration.

The use of terbutaline with certain medicines is not recommended and these medicines (as listed in the attachment provided by site staff) are not allowed while you are on study. Large doses of IV terbutaline have been reported to make pre-existing diabetes worse.

Risks of Blood Drawing:

There are small risks to having blood drawn. These risks may include some pain, discomfort, or bruising where the blood is drawn. There is a small chance of infection and bleeding problems. Fainting or feeling dizzy may also occur.

Risks of ECG*:*

Possible side effects of the ECG are skin irritation, itching, and redness from the ECG sticky pads.

Risks of Breathing Tests (Spirometry):

Possible rare side effects when spirometry is performed repeatedly can include fatigue, dizziness, rapid heart rate, and cough.

Risks of Inhaled Albuterol:

Albuterol at the prescribed doses is generally very safe. The most frequent side effect of treatment with inhaled albuterol is tremor (shakiness). Possible side effects include insomnia and nausea. Less common side effects may include; dizziness, pain, anxiety, palpitations (heart is pounding or racing), rapid heart rate and serious but rare allergic reactions to albuterol. Your study physician will discuss drug side effects with you.

Risk of Loss of Confidentiality:

There is a risk of loss of confidentiality. Every effort will be made to protect your information, but this cannot be guaranteed.

For Women, Risks Related to Pregnancy:

Serious adverse reactions, including death, have been reported following terbutaline administration when given to pregnant women to postpone delivery.

You cannot be enrolled in this study if you are:

- Pregnant
- Planning to become pregnant during the study
- Nursing a child
- Capable of becoming pregnant, and unwilling to agree to the use of effective contraception during study participation

If you are pregnant or nursing a child during the study, there may be risks to you, the embryo, fetus, or nursing child.

If you are capable of becoming pregnant, you must use an acceptable method of birth control, from screening until end of study.

Acceptable methods of contraception include:

- Partner vasectomy
- Bilateral tubal ligation
- Intrauterine devices (IUDs)
- Hormonal methods (birth control pills, implants, injections, patches, vaginal rings)
- Use of a combination barrier (such as the use of condoms or diaphragm and vaginal spermicide)

Please speak to the study doctor or staff about acceptable methods of birth control. You should not participate in this study if you are capable of becoming pregnant and cannot use one of the above birth control methods. Some methods of birth control do not work as well when you are taking certain drugs. Be aware that women can still become pregnant even if using an acceptable birth control method. You will be notified of the results of any pregnancy tests performed while you are participating in this study, as applicable, based on your state and/or local laws and regulations. If you become pregnant while you are in this study, you should report this immediately to the study team and you will not receive any further terbutaline. With your permission, the study doctor or study staff will ask about your health and collect information from you through the outcome of your pregnancy. The study team may share this information with the study sponsor, the Data Safety Monitoring Board (DSMB), and with the Institutional Review Board (IRB), a group of people who review research studies to protect the rights and welfare of research participants.

Unforeseen Risks

There may be other risks to the participant from this research that are not known or foreseeable at this time.

What other choices are there besides taking part in this study?

This study is not designed to diagnose, treat, or prevent any disease. Your alternative is to not take part in the study. Even if you do not participate, you will have access to standard medical care at **<Insert Site Name>**.

Will I be paid for taking part in this study?

You will be reimbursed for time and travel an amount of $**<insert compensation>** for each study visit (including sample collection, length of visit, or completed study visit) in the form of a **<insert form of payment>**. You may be paid up to a maximum total of $**<insert compensation>** for study participation.

Will I receive any payment if there is a commercial profit?

Your study data and/or samples will not be sold to anyone. However, the use of study data and/or samples may result in commercial profit. You will not receive any payment if there is commercial profit.

Will I have to pay to take part in this study?

There will be no additional costs to you as a result of being in this study. Any study specific procedures or study specific tests will be provided to you free of charge. However, your insurance company will be charged for the routine medical care you would receive whether or not you participate in this study. You may wish to contact your insurance company to talk about this further.

What if I am injured because of taking part in this study?

If you are injured or get sick because of being in this study, seek immediate medical attention, and then call the site investigator named on the first page of this form. The investigator will provide you with treatment or refer you for treatment; your insurance will be billed for this.

Who will pay if I am injured?

There is no plan by the study site to provide free medical care or money for injuries to participants in this study. There is no plan by the National Institute of Child Health and Human Development (NICHD), Duke University (Duke Clinical Research Institute [DCRI]), or Duke University Health System to provide any reimbursement or payment for any study-related injury costs. You are not giving up any of your legal rights by signing this permission form.

Confidentiality

What happens to my study data and samples?

All data we record as part of this study will be stored in a secure database on a server in the United States (U.S.). All study data in the database and samples will be given a unique code number and will not be labeled with your name or initials, social security number, address, or telephone number. The database will include your sex, date of

birth, race, ethnicity, and dates of study visits. Only the site staff, study team, and their authorized representatives and others listed under the “authorization” section below will have access to information that may identify you including the list that can match your name to the unique code number. Separate from the study database, electronic copies of documents may also be sent to The Emmes Company, LLC, that contain your identifying information. These electronic copies will be checked for accuracy and then immediately destroyed following review. All study members who access your information will keep this list confidential and secure.

All participants’ de-identified study data and remaining de-identified study samples will be submitted to a U.S. NIH storage location such as the NICHD Data and Specimen Hub or DASH (https://dash.nichd.nih.gov) from which the data will be shared with other researchers.

Your study data, study samples and health information stored in these databases will not be labeled with your name or other information that could be used to identify them. Researchers approved to access information in these databases will agree not to attempt to identify you.

De-identified samples may also be used by researchers in the future to conduct tests separate from those being done in the current study. These researchers may conduct whole genome sequencing (WGS); by doing WGS, these researchers may have information that is unique to you.

The purpose of sharing this information is to make more research possible that may improve adult and child health. This will be done without obtaining additional permission from you.

The data and samples collected in this study may be kept forever. We may publish the results of this study. However, we will not include your name or any other identifying information.

What is a Certificate of Confidentiality?

The study data and specimens are covered by a Certificate of Confidentiality (CoC) from the NIH. The CoC further protects your privacy. It keeps the courts and other agencies from forcing the U.S. study team to share information or body fluid samples that may identify you during a legal proceeding unless you agree to this. If you want your study information shared with insurers, medical providers, or others not connected with this research, you must ask the investigator to release it.

Information and body fluid samples can only be shared without your permission if:

1. There is a law that requires us to share this with an agency. An example of this would be to report abuse or contagious diseases; or
2. The information is used for other research, as allowed by federal rules.

We must share information for program reviews with the NIH or the U.S. FDA who may request these.

This Certificate does not keep you from sharing information about yourself or your participation in this research.

What information will be in my records at the study location?

Study data entered into your medical records will be kept per the study site policies. Other study records will be kept until the FDA has completed their review of the results or for a minimum of 2 years after the study has ended, whichever is longer. A copy of this signed form may go into your medical record. This will allow the health care providers caring for you to know what tests you are receiving as part of the study and to know how to take care of you if you have other health problems or needs during the study. It is possible that you may not be able to see the information that has become part of your records until the entire study is over.

Authorization for the use and disclosure of protected health information

The U.S. government has a Privacy Rule to protect the privacy rights of patients. The Privacy Rule protects the confidentiality of personal health information (PHI) that can be linked to a specific individual. The information protected under the Privacy Rule is often referred to as “protected health information” or PHI. This section, called an “Authorization,” explains how your PHI will be used and shared, and it also describes your rights.

Your PHI, which may include your date of birth, sex, dosing information, medical records, medical history, and the dates or results of any tests, therapies, or procedures that you have for your medical care will be shared by site staff with individuals and organizations that oversee this study, including:

- Site staff (named on the first page of this form),
- The study team and their authorized representatives, including laboratories that may be hired to perform tests,
- Government agencies, such as the U.S. FDA and NICHD, a part of the NIH, who will obtain information from this study under the data collection authority given to them under U.S. law,
- The Institutional Review Board (IRB) reviews the ethical conduct of this study. The IRB or ethics committee is a group of scientists and non-scientists who review the ethics of research. The goal of the IRB or ethics committee is to protect the rights and welfare of study participants.

The sponsor and the groups above will use your health information:

- to complete this research
- to evaluate the results of the study
- to check that the study is being done properly

- to obtain marketing approval for new products resulting from this research

We try to make sure that everyone who sees your PHI keeps it private, but we cannot guarantee this. If your information is shared by any of the groups named above with anyone outside the study team, it may be further shared by them and may not be covered by federal privacy laws. Except when required by law, we will only use or share information outside the study team in a way that nobody can tell it is your information.

There is no expiration date for the use of this information as stated in this Authorization, but you have the right to stop this Authorization at any time.

You do not have to sign this, but if you want to be in this study, you must sign/date this form. By agreeing to be in this study, you are giving permission (also called authorization) for us to use and disclose your PHI as described in this form. If you refuse to allow the study team to share your PHI, you will not be able to be in the study. However, not signing this form will not affect your access to medical care.

If you do not stop this Authorization, it will remain in effect indefinitely.

You have the right to stop this Authorization at any time. Your decision to stop your Authorization will not involve any penalty or loss of access to treatment or other benefits to which you are otherwise entitled. If you decide you no longer want to participate in this study, but do not stop your Authorization, new health information may be collected until this study ends.

To stop this Authorization, you should inform the site investigator, as named on the first page of this form of your decision in writing. Stopping your Authorization will prevent sharing of PHI in the future but will not affect any PHI that has already been gathered or shared.

You have the right to review and copy your health information. However, your access to this information may be delayed until the study is complete.

Will I see any study results?

At the end of your participation, we will share a summary of your study results with you, including maximum lung function improvement following each dose.

You may be contacted by the study team conducting this research in the future to be provided with overall study results (summary results from all participants). This means you will not know the results as they relate to you specifically. You can contact the site staff if you have any questions about study results availability.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov as required by U.S. law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

You will not be provided with overall results from future studies that use de-identified data and specimens from this study that have been submitted to an NIH storage location such as DASH.

Who can answer my questions about this study?

If you have questions about this study, complaints, or concerns that you were harmed as a result of participation, call the site staff at the phone number listed on the first page of this form.

This study is being overseen by an IRB. An IRB is a group of people who perform independent review of research studies. You may contact them at <insert IRB email address> or talk to them at <insert IRB phone #> if:

- You have questions, concerns, or complaints that are not being answered by the site staff.
- You are not getting answers from the research team.
- You cannot reach the research team.
- You want to talk to someone else about the research.
- You have questions about your rights as a study participant.

Can I be removed from this study without my approval?

You may be removed from this study by the site investigator or the sponsor without your approval. Possible reasons for removal include:

- Your condition changes, and the study is no longer in your best interest
- The entire study is stopped by the FDA, NICHD, or the IND sponsor
- The investigator is no longer participating in the study
- You do not follow the study rules

You will be removed from this study if you become pregnant. We request that you let the site staff know and inform your doctor. No further samples will be collected from you.

How will I be informed about new information?

We may learn new information during the study that you may need to know. We may also learn about things that might make you want to stop participating in the study. If this happens, you will be notified about any new information in a timely manner. You may also be asked to sign a new consent form that describes these new findings if you decide to continue in the study.

What happens if I agree to participate in this study, but I change my mind later?

If you decide that you no longer want to participate in this study, call the site staff at the phone number listed on the first page of this form to inform them. You will be followed for an additional 7 days for safety. You will be contacted at the end of the 7-day window to ask if there were any issues or problems.

No additional samples will be collected and no new information about you will be collected for study purposes unless you have a side effect related to being in this study. If a side effect occurs, the site staff may need to contact you or review your medical records.

Any information and study samples collected before your withdrawal will remain a part of the study records.

Future Contact for New Research Opportunities

At the end of this consent form, you will have the chance to tell us whether or not you will allow the study staff to contact you in the future about opportunities for additional research studies that you may be eligible to participate in. If you choose not to allow us to contact you in the future, you can still participate in this research study.

Optional: Decision to Allow Contact for Opportunities for Additional Research Studies	
Please **initial** the appropriate line to indicate whether or not you agree to allow contact about opportunities for additional research studies.	
The information below can only be completed by the participant capable of providing consent.	
Initials	**Yes,** I give study staff permission to contact me about opportunities for additional research studies.
Initials	**No,** I do not give study staff permission to contact me about opportunities for additional studies.

Statement of Consent:

<table>
<tr><th colspan="2">STUDY STATEMENT OF CONSENT</th></tr>
<tr><td colspan="2">By signing this form, I confirm that:
I have read this consent form and was given enough time to consider the decision for me to participate in this study.
The purpose of this study, procedures to be followed, risks, and benefits have been explained to me.
I have been encouraged to ask questions, and my questions have been answered to my satisfaction.
I have been told whom to contact if I have questions, to talk about problems, concerns, or suggestions related to this study.
I have read this form and agree to give consent for my participation in this study and for the use of associated protected health information.
I understand that participation in this study is voluntary, and I may choose to stop participation in this study at any time without any penalty or loss of access to treatment or other benefits to which I am otherwise entitled.
I have been told that I will be given a signed and dated copy of this consent form.</td></tr>
<tr><td colspan="2">The information below can only be completed by the participant capable of providing consent.</td></tr>
<tr><td colspan="2">By signing below, I certify that I am the participant named above.</td></tr>
<tr><td colspan="2">Printed Name of Participant</td></tr>
<tr><td>Signature of Participant</td><td>Date:

Time:
☐ AM / ☐ PM
(check one)</td></tr>
</table>

STUDY STATEMENT OF PERSON OBTAINING CONSENT (As applicable)		
My signature below documents that: I have fully explained the study described by this form in a language the person signing this form understood or via translation. I have answered their questions and will answer any future questions to the best of my ability. I will tell the person(s) signing this form of any changes in procedures or in the possible harms/possible benefits of the study that may affect their willingness to provide permission to stay in the study. Consent was freely given, and I will provide the person signing this form with a signed copy of this form.		
The information below can only be completed by the person obtaining consent.		
Printed Name of Person Obtaining Consent	Signature of Person Obtaining Consent	Date: