Informed Consent Form and Authorization for Adult Subjects and Parents/Legal Guardians and Assent Form For Subjects 16 Years to Age of Majority

Sponsor / Study Title:	**National Institutes of Health (NIH) / "A Randomized Controlled Trial of Pravastatin to Prevent Preeclampsia in High Risk Women"**
Principal Investigator: (Study Doctor)	**«PiFullName»**
Telephone:	**«IcfPhoneNumber»**
Additional Contact(s): (Study Staff)	**«AdditionalStaffMemberContacts»**
Address:	**«PiLocations»**

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

KEY INFORMATION

You are invited to take part in a research study. This research study is studying pravastatin to prevent preeclampsia (high blood pressure with other signs that your organs were not working normally). The Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) and the National Heart, Lung, and Blood Institute (NHLBI), both part of the National Institutes of Health (NIH), are sponsoring this research study.

This study is in addition to your normal prenatal care.

We invite you to take part in this research study because when you were pregnant before, you had preeclampsia and delivered more than six weeks before your due date. Because of this, you are at higher than average risk of having preeclampsia again in this pregnancy. If you consent, you will be in the study from randomization (between 12 weeks 0 days and 16 weeks 6 days along in your pregnancy) until 5 years after your baby is born. You will be randomly assigned (like tossing a coin) to pravastatin capsules or capsules that have no active medicine in them (called placebo).

You will have monthly study visits until delivery. These study visits may be completed in-person or by telehealth (phone or video). At each study visit research staff will:

- Ask you questions about yourself and your pregnancy

- Ask you questions about any side effects of the study drug
- Give you new study drug and take back any unused study drug

At your first visit and at two other visits study team members will take a small amount of blood for research purposes. After delivery, the research staff will collect medical information about you and your baby until you leave the hospital. At six weeks after delivery, the research staff will talk with you to see how you and your baby are doing and ask you questions about any problems after delivery. We will also schedule study visits for 2 and 5 years of age for your child (around 2 hours for each visit). At the 2 year visit, the research staff will review your medical history since delivery , measure your blood pressure, measure your anthropometrics (height, weight, waist circumference, hip circumference), and collect a blood sample. We will check on the health and development of you and your child. After your child's 5-year visit, your time in the study is done.

There are potentially serious or life threatening risks to the study that are described in this consent.

Possible risks from the blood draw include bleeding, bruising, fainting, or soreness, and in rare cases infection.

If you are in the pravastatin group, possible risks to you include muscle or bone pain, bowel or stomach symptoms (for example, heartburn), and/or headache. Rare risks include liver and muscle injury that may be very serious.

There may be risks to your unborn baby from the pravastatin being studied in this research. More information is provided below, and you should ask questions about this, or any other concerns you have, before you decide to participate.

There are no known benefits from participating in this study. It is possible that pravastatin may reduce your chances of developing preeclampsia again, or that it may make your preeclampsia less serious, but you should not expect this.

Participation in this research study is voluntary and if you do not take part, you will receive the routine care usually provided to pregnant women.

Please read this form carefully. Take your time to ask the study doctor or study staff as many questions about the study as you would like. The study doctor or study staff can explain words or information that you do not understand. Reading this form and talking to the study doctor or study staff may help you decide whether to take part or not. If you decide to take part in this study, you must sign your name at the end of this form and date it.

BACKGROUND AND PURPOSE

Preeclampsia is a serious medical condition that can happen when you are pregnant. It usually starts with increasing blood pressure. If your blood pressure becomes very high, or if there are signs that the liver or kidneys or other organs aren't working properly, then it is most likely preeclampsia. Sometimes preeclampsia may become severe and cause seizures, or even in very

rare cases, death. Preeclampsia may also cause serious growth or developmental problems in a developing fetus, and may result in loss of the pregnancy.

There is no cure for preeclampsia other than delivering the baby. However, if preeclampsia starts before the baby is full term and delivery is required, then the baby can have health problems from being born too early. Women who have preeclampsia in one pregnancy are at higher than average risk of having preeclampsia in another pregnancy.

A medicine called pravastatin is approved by the United States Food and Drug Administration (FDA) to prevent heart disease in non-pregnant people who have high cholesterol (a waxy substance found in blood). Pravastatin was not approved for use in pregnancy in the past because not enough was known about its safety. However, recent information suggests it may be safer than was believed, and that its use in specific, high risk situations (like preeclampsia) should be investigated.

Although preeclampsia is not heart disease, preeclampsia is similar to heart disease because it has similar disease processes. Pravastatin works well for heart disease, so researchers think it may possibly help in preeclampsia also.

The use of pravastatin in this study is investigational. An investigational use is one that is not approved by the FDA.

Recently, pravastatin was used in two small studies of pregnant women who were at high risk of preeclampsia. The results showed that pravastatin seemed to be safe to take during pregnancy and that it lowered the chance of getting preeclampsia. The results are promising but the studies are too small to be certain. So we do not yet know for sure whether pravastatin can prevent preeclampsia.

In this study, women will either get pravastatin capsules or capsules that have no active medicine in them (called placebo).

About 1,550 women will participate in this study. We will initially enroll 50 women to look at safety measures for you and your child.

WHAT WILL HAPPEN DURING THE STUDY

You will continue your normal prenatal care, and your OB/GYN provider MUST be aware of your participation in this study. It is possible some drugs, including ones available over the counter, that may be needed during pregnancy would interact with pravastatin in ways that could be dangerous. You should make certain anyone who provides you with medical or pregnancy care, or directs you to take any medication or treatment during pregnancy, is aware that you are on this study. Do not take any new medications, prescription or nonprescription, without checking with the study staff.

Your participation, and that of the child you are pregnant with, will last approximately ***5 years and 7 months*** and will include approximately ***12*** study visits to the study center.

You will have a study visit for screening and if eligible, for enrollment into the study. Thereafter, you will have monthly study visits while you are still pregnant and take the study drug until you

deliver. We will then follow up with you and your baby three times after delivery: first at six weeks after delivery, then when your baby is two years old and finally 5 years after delivery, when we will see you and your child for the last time. After that, your time in the study is done.

Screening:
Before any study-related tests and procedures are performed, you will be asked to read, sign, and date this consent document. The following screening tests and procedures will then be performed to determine if you qualify to take part in this study:

- You must be at least 12 weeks pregnant but not more than 16 weeks when you start the study. We will review your ultrasound to confirm how far along in the pregnancy you are. If an ultrasound has not been done, one must be performed to confirm you are eligible.
- We will ask about any medicines you are on to make sure that pravastatin is safe to take.
- You may need to sign a release for medical records if you delivered your baby at another hospital when you had preeclampsia before, so that we can get information about that pregnancy.
- Before you can take part in the study, we need to make sure your liver is working normally by looking at your liver blood tests.
    - If you have had the liver tests within the past 6 months and the results are normal and in your medical record, you do not need to have the test again.
    - If you haven't, or if the results were high, we will take a small sample of your blood – just over a teaspoon, to measure the liver tests.
- If your liver test results are too high and you are less than 16 weeks pregnant, you could have the test repeated to see if you are eligible. If the results are still too high you will not be eligible for the study and the results will be sent to your primary doctor so that he/she can follow up with you.

If you qualify to take part in the study we will ask you to come in to be enrolled. This visit will take approximately 45 minutes to 1 hour. The research staff will do the following:

- Measure your blood pressure, height, and weight.
- Look at your medical records and ask questions. We will get information on your previous pregnancies, whether you drink or smoke, whether you are married or have a partner, how long you went to school, type of medical insurance, medicines you are taking and any medical or pregnancy problems you have now.
- Ask you to sign a release of medical records in case you are hospitalized or deliver your baby at a different hospital.
- Get about 2 tablespoonfuls (27 mL) of blood from your vein.

- Part of the sample will be sent to the lab to measure a test called creatine kinase, an enzyme in the muscles.
- The rest of your sample will be kept for later so that the research team can look for substances in your blood that are related to preeclampsia, as well as your lipid levels (lipids are fat-like substances found in your blood; the best-known is cholesterol).
- If you agree, a teaspoonful of the blood will be saved for DNA analysis. DNA (deoxyribonucleic acid) is the genetic "blueprint" in your body that is unique to every person. These DNA samples may be used by investigators to look at some of your genes, which may be involved in whether the study drug works for you or not.

Study Treatment:
At the end of the enrollment visit, you will be assigned to one of two study treatments: 20 mg pravastatin or a placebo (a capsule with no active medicine in it). Pravastatin and placebo will be in pill capsules that look exactly the same in size, color, and taste.

You will be randomly assigned by chance (like the flip of a coin) to receive either pravastatin or placebo. You will have a 50% (1 in 2) chance of receiving pravastatin and a 50% (1 in 2) chance of receiving placebo. This is a double-blind study, which means neither you nor the study doctor will know to which of these study drug groups you are assigned. In case of an emergency, however, the study doctor can get this information.

You will be told to take the study drug by mouth once daily (preferably in the evening), with or without food. You will keep taking your assigned study drug until you deliver your baby, unless you choose not to participate in the study anymore, or the study doctor tells you to stop.

Follow-up visits during pregnancy:

After enrollment, the study nurse will see you monthly until you deliver your baby. You may have up to 8 visits during your pregnancy but if you have a problem with the study drug you may be asked to return more often until you get better. Each visit will take about 15-30 minutes. We will try to schedule these visits to coincide with your regular clinic visits, but these study visits are NOT the same as your routine prenatal visits – you need to continue your prenatal care as directed by your pregnancy provider. These study visits may be completed in-person or by telehealth (phone or video). The research staff will do the following:

- Ask whether you have had any problems that might be related to the study drug and ask about how your pregnancy is going. They will ask about any medicines you are on.
- Get your weight and blood pressure, and count the number of study drug in your bottle. They will give you a new bottle of study drug to last to your next visit.
- Get information on your pregnancy from your medical records.

- At a study visit when you are between 23 and 28 weeks and at another visit between 33 and 37 weeks, they will get another 1 tablespoonful (20 mL) of blood from your vein.
    - The blood samples will be stored for future analysis of substances related to preeclampsia, lipid levels, and the amount of study drug in your body.
- If you develop a side effect from the study drug such as muscle or bone pain, you may be asked to return more often until you get better.
- If you go to a hospital, research staff will get information from your medical record.
- If you are on certain medicines, taking pravastatin may alter the way the medicine works. For this reason, it is very important to notify your regular health care provider that you are in this study as well as tell the research team if you start a new medicine. The research team may ask you to change the timing of study drug. We will provide you with an information sheet so that you know which medicines might be affected.

<u>At delivery</u>:

The research staff will collect data on your labor (such as when it starts), delivery, and treatment you need after delivery. They will also collect information on your newborn baby.

If you are one of the first 50 participants, the research staff will collect a small amount of cord blood (one teaspoon; 6 mL of blood, removed from the umbilical cord after the baby has been delivered and it is no longer needed) to check for study drug.

<u>Six weeks after delivery</u>:

Usually, your regular doctor will see you for a check-up at about 6 weeks after delivery. At that time, the research staff would like to talk to you to find out if you needed any other treatment, had to go back to the hospital, or if you or your baby have had any problems since going home.

The research staff may also get information from your medical records on blood pressure, preeclampsia after delivery (which happens occasionally), any infections or other medical problems.

Research staff will contact you at least every six months until your child's five-year visit to make sure that your contact information is still correct.

<u>Two to three years after delivery</u>:

When your child is two years old you will come back for a visit and we will:

- Measure the child's height and weight.
- Assess how well the child sees and hears.
- Assess the development of your child, including language skills, using their hands (fine motor skills), moving (gross motor skills), understanding, and behavior.
- Ask you to fill out a form about your child's behavior.
- Ask you about your medical history since 6 weeks postpartum

- Measure your blood pressure, height, weight, waist circumference, and hip circumference
- Get about 2 tablespoonfuls (20 mL) of blood from your vein.
    - The sample will be used to look for substances in your blood that are related to preeclampsia, as well as your lipid levels (lipids are fat-like substances found in your blood; the best-known is cholesterol) and glucose levels.

This visit will take about an hour and a half. If you are unable to come in for a visit, some of these tests may be done at your home or at another place convenient for you.

Five to six years after delivery:

When your child is five years old you will come back for a visit and we will:

- Measure the child's height and weight.
- Assess your child's IQ and learning skills.
- Test how well the child sees.
- Ask you about your child, including how they behave, how they get things done, and what they do in everyday life.

The visit will take about 2 hours. If you are unable to come in for a visit, some of these tests may be done at your home or at another place convenient for you.

EXPECTATIONS

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

- Take the study drug
- Attend your follow-up study visits (in-person or by telehealth)
- Report to the research team any problems you think you are having from taking part in the study or taking the study drug
- Tell us if your regular doctor prescribes any new medication

RISKS, SIDE EFFECTS, AND/OR DISCOMFORTS

It is possible that being in this study could involve risks to you or your baby.

For Pravastatin:

Pravastatin is in a class of drugs called statins. Statins are considered safe in non-pregnant patients.

The FDA advises that statins should not be given to pregnant women because there was no information about the risks to the fetus or likely benefits to pregnant women. It is possible pravastatin may harm an unborn baby, but researchers now think this may be unlikely based on what limited research and information are available.

Side effects are usually mild and last only a short time.

Frequent

The most commonly reported side effects are:

- Muscle or bone pain
- Bowel or stomach problems such as:
    - Nausea
    - Vomiting
    - Diarrhea
    - Stomach pain
    - Constipation
    - Gas
    - Heartburn

Rare

- In research studies about 12 in 1000 of the subjects taking pravastatin for a long time (years) had an increase in their liver enzymes indicating harm to the liver.
- Less than 1 in 1000 subjects had some muscle weakness and pain as well as an increase in the muscle enzymes indicating muscle injury.

The effects of using pravastatin for a long duration during the second and third trimesters of pregnancy on fetal and neonatal health and growth are unknown. No studies have found that pravastatin is linked to an increased risk of birth defects. However, in general, very few women have taken pravastatin in pregnancy and fewer still have been exposed during the second or third trimester of pregnancy. In this study, the study drug will be started at 12 weeks of pregnancy or later. At this point in the pregnancy, your baby's major organs will have mostly formed so that major birth defects are thought to be less likely.

Safety data for birth defects are limited and there could be other risks affecting how your child may develop. Studies in rats showed that very high levels of pravastatin changed brain development, behavior, and the ability to learn in rat babies. Doses in the rat similar to what you will receive did not cause any change in behavior or development problems.

Recently 40 women participated in two small studies and were randomized to pravastatin or placebo. The most common side effects of women who received pravastatin in pregnancy were muscle or bone pain, bowel or stomach symptoms (for example, heartburn), and headache. **There were no serious side effects on the mothers or babies, however, long-term developmental effects of the study drug on children exposed were not done. Therefore, the long-term risks of pravastatin to children, exposed during their mother's pregnancy, are unknown.**

If you take part in this research study, we will ask you about your symptoms at every study visit. If you have any symptoms between visits, please report them promptly to the research team. If you experience a symptom, you may be asked to come back more often.

Placebo Risk:
If you receive placebo (the inactive substance) as part of this study, your chance of developing preeclampsia would not improve.

RISKS OF STUDY PROCEDURES

- Blood samples: Possible side effects from blood drawing include faintness, inflammation of the vein, pain, bruising, or bleeding at the site of puncture. There is also a slight possibility of infection.
- Loss of confidentiality: There is a minimal risk of breach of confidentiality regarding the collection of medical record information. All research information about you or your baby will be handled in a confidential (private) manner consistent with other hospital medical records.

Certain medications should not be taken or should be taken at specific times if you are also taking the study drug. You will be provided a subject instruction sheet that includes specific information. Also inform research staff if your regular doctor prescribes any new medication.

UNFORESEEN RISKS
Since the use of the study drug is investigational, there may be other risks to you or your baby that are unknown. These may be minor or severe. They may find out new risks while the study is going on. If this happens, the research staff will tell you the new information, whether it may affect you, and what, if anything, to expect.

ALTERNATIVES TO PARTICIPATION
You do not have to be in this study to receive treatment to try to avoid preeclampsia**.** Your options may include:

- Baby aspirin: Most doctors now recommend you take baby aspirin during your pregnancy if you have had preeclampsia in a pregnancy before. Taking only baby aspirin is another option if you choose not to take part in this study (if you participate you would continue to take the aspirin in addition to pravastatin/placebo).

Please talk to the study doctor about your options before you decide whether or not you will take part in this study. Your choice not to take part will have no effect on the benefits to which you are otherwise entitled. This study will not alter you, your fetus' or your infant's clinical care.

NEW FINDINGS
Any new important information that is discovered during the study and which may influence your willingness to continue participation in the study will be provided to you.

BENEFITS
You may benefit as a result of your participation in this study. There is, however, no guarantee that you will benefit from your participation in this study. Information learned from the study may help other people in the future.

Ask the study doctor for your estimated recovery time from the study treatment or procedures done during your participation in this study.

COMPENSATION FOR PARTICIPATION

If you agree to take part in this research study, we will pay you for travel and/or parking at each study visit. In addition, you will receive a maximum of $450 to compensate for your time and effort ($200 at delivery, $100 for the 2-year follow-up visit and $150 for the 5-year follow-up visit) in the form of gift cards, baby related gifts, or money.

You will be paid _____ ***[“after each visit,” “annually,” “bi-weekly,” etc.]***

If you have any questions regarding your compensation for participation, please contact the study staff.

CONFIDENTIALITY

The medical information collected on you for this research study will come from your medical record and from information you give the research staff. If we lose track of you, study staff may collect information from the internet including social network sites in order to find your contact information.

The information collected for this research study will be entered into an electronic database at the data coordinating center (George Washington University Biostatistics Center in Rockville, Maryland). The database has information from all of the participants. Your information in the database will only be used for statistical analysis and if the results of this study are published or presented at meetings, you will not be identified. The information at the data coordinating center does not include your name, address, social security number, hospital number, date of birth, or any other personal identifiers. Instead, the data center will use a unique code for each person consisting of a set of numbers. The key to the code linking the data and blood samples to you will be kept here in a secure manner. Only the research study staff employed for this study at this center will have access to the key to the code.

The blood collected during this study will be stored here first and then stored at a National Institutes of Health sample storage facility. All blood samples are stored with a barcode number that is linked to your unique study code. No personal identifiers are included on the sample.

Blood that is collected will be sent to the laboratories for analysis of substances in the blood related to preeclampsia. Other samples will be sent to other laboratories to measure markers related to preeclampsia, lipid levels, and study drug concentrations. These research test results will not be reported to you and will not be put in your medical record. These tests are being done only for research purposes.

The results of this research study will be provided to the sponsor, NIH (and/or their representatives). In addition, data from this study will be put in an NIH data and sample repository that will be available to other research investigators. This data set will be de-identified (will not contain any identifying subject data). When the data set is shared, it will be done without obtaining additional permission from you. Each person’s data will be given a new

code by the data coordinating center, so that no one, including the research staff at this center, will have a link between the subject's identifying information and data in the repository.

ClinicalTrials.gov is a website that provides information about federally and privately supported clinical trials. 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.

Access to medical and research records:

To the extent allowed by law, we limit your personal information to people who have to review it. We cannot promise complete secrecy. The following individuals and/or agencies will be able to look at and copy your medical and research records at this hospital:

- The study doctor, study staff and other medical professionals who may be evaluating the study.
- The Institutional Review Board (IRB), which is a group of people who are responsible for making sure the rights of participants in research are respected.
- The United States Food and Drug Administration (FDA) and/or the Office for Human Research Protections (OHRP) and or Department of Health and Human Services (DHHS)
- The National Institutes of Health (NIH) which sponsors this study, including persons or organizations working with the sponsors, such as the data coordinating center, the George Washington University Biostatistics Center in Rockville, Maryland.

A copy of your medical chart or your baby's medical chart also may be sent to research investigators at one of the other enrolling centers, the data coordinating center or NIH for review. If your chart is sent, all identifying information, such as your name, address, social security number, hospital number, and date of birth first will be removed.

AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

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

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

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

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

- Representatives of the Sponsor
- Representatives of Advarra IRB (an Institutional Review Board that reviews this study).
- The Food and Drug Administration (FDA) and other US federal and state agencies.
- Government agencies to whom certain diseases (like HIV, hepatitis, and STDs) must be reported.
- Governmental agencies of other countries.
- Outside individuals and companies, such as laboratories and data storage companies, that work with the researchers and sponsor and need to access your information to conduct this study.
- Other research doctors and medical centers participating in this research, if applicable.
- A data safety monitoring board which oversees this research, if applicable.

Your health data will be used to conduct and oversee the research, including for instance:

- To see if the study drug works and is safe
- To compare the study drug to other drugs
- For other research activities related to the study drug

This permission does not end unless you cancel it, even if you withdraw from the study. In California and any state that requires an expiration date, the Authorization will expire 50 years after you sign this authorization document. You can cancel this permission any time. Even if you cancel this authorization, the researchers may still use and disclose protected health information (PHI) they already have obtained about you as necessary to maintain the integrity or reliability of the research. However, no new PHI or new biological specimens will be collected from you after you revoke your authorization.

To cancel your permission, you will need to send a letter to the Principal Investigator, listed on the first page, stating that you are canceling your authorization. This letter must be signed and dated and sent to the Principal Investigator's address. If you are unable to write a letter, ask one of the research staff to provide you with a letter that must be signed, dated, and sent to the above address. A copy of this cancellation will be provided to the Principal Investigator and his or her research team. Not signing and dating this form or later canceling your permission will not affect your health care treatment outside the study, payment for health care from a health plan, or ability to get health plan benefits.

Your protected health information will be treated confidentially to the extent permitted by applicable laws and regulations. Federal law may allow someone who gets your health information from this study to use or release it in some way not discussed in this section and no longer be protected by the HIPAA Privacy Rule.

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

By signing and dating this form you authorize the Principal Investigator and members of the research team to use and share with others (disclose) your PHI for the purpose of this study. If you do not wish to authorize the use or disclosure of your PHI, you cannot participate in this study because your PHI is necessary to conduct this study. You will receive a signed and dated copy of this form for my records.

_____

Printed Name of Subject

_____ _____

Signature of Subject Date

_____

Parent/Legal Guardian Printed Name (if subject is under the age of majority)

_____ _____

Parent/Legal Guardian Signature Date

CERTIFICATE OF CONFIDENTIALITY

This research is covered by a Certificate of Confidentiality from the National Institutes of Health (NIH). The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the NIH or for information that must be disclosed in order to meet the requirements of the FDA. You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

COMPENSATION FOR INJURY

If you become ill or are injured while you are in the study, get the medical care that you need right away. You should inform the healthcare professional treating you that you are participating in this study. If you tell the study staff that you think you have been injured then

they will help you get the care you need. You should promptly notify the Principal Investigator in the event of any illness or injury as a result of being in the study.

Care for such injuries will be billed in the ordinary manner to you or your insurance company. The NIH has not made any provision for monetary compensation in the event of injury resulting from the research. In the event of such injury, treatment will be provided, but it is not provided free of charge. Since this is a research study, payment for any injury resulting from your participation in this research study may not be covered by some health insurance plans.

COSTS

The study drug, study-related procedures, and study visits will be provided at no charge to you or your insurance company.

You and your insurance company will be charged for the health care services that you would ordinarily be responsible to pay. In some cases, insurance will not pay for services ordinarily covered because these services were performed in a research study. You should check with your insurance to see what services will be covered by your insurance and what you will be responsible to pay. The contact information for your insurance is usually found on your insurance card. Research staff will help you if you have questions or if you are unable to find the contact information.

FUTURE RESEARCH STUDIES

You are also being asked if any samples of your blood or DNA remain after the study tests described above, and if you agree, they may be used for future research studies or distributed to another investigator for future research studies without additional informed consent. Before they are available to investigators outside of this research study group, the samples will be relabeled so that they cannot be linked back to your unique code at this center but can be linked to the dataset in the NIH data and sample repository. The samples will be sent to the same NIH repository, where they will be stored indefinitely. They will be accessed only by researchers approved by the NIH.

You may decide not to allow your samples be stored and used for future research. Your decision will have no impact on your ability to participate in the main study and will have no impact on any other benefits to which you would otherwise be entitled. Please indicate your preference below:

If the subject is under the age of majority, both the subject and the subject's parent/legal guardian must initial.

❒**YES** I agree to have my samples stored and used for future research.
_____ **(subject's initials)**
_____ **(subject's parent/legal guardian initials – if applicable)**

❒**NO** I do not agree to have my samples stored and used for future research.
_____ **(subject's initials)**
_____ **(subject's parent/legal guardian initials – if applicable)**

However if the researchers decide that there is no more use for your samples, you agree that they may be thrown away.

COMMERCIAL PROFIT

Your biospecimens collected during this study may be used for commercial profit (even if identifiers are removed) and **you will not share in this profit**.

CONSENT FOR OPTIONAL MATERNAL DNA:

I give permission to have my genetic material (DNA) from my blood sample collected and stored for future analysis related to the study drug used in this study and/or pregnancy complications.

If the subject is under the age of majority, both the subject and the subject's parent/legal guardian must initial.

❒**YES** I agree to have my DNA collected and stored as described above.

_____ **(subject's initials)**

_____ **(subject's parent/legal guardian initials – if applicable)**

❒**NO** I do not agree to have my DNA collected and stored as described above.

_____ **(subject's initials)**

_____ **(subject's parent/legal guardian initials – if applicable)**

GENOME SEQUENCING

Researchers can look closely at large amounts of your genetic information by sequencing, or "reading", every letter in your DNA (your genome). Reading a person's entire genetic code is called whole genome sequencing. The research **might include** whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).

CONSENT FOR FUTURE CONTACT

We may want to continue follow-up of you or your child after 5 years. To protect your confidentiality and respect your privacy, the research team needs your permission to contact you. Please indicate your preference below:

If the subject is under the age of majority, both the subject and the subject's parent/legal guardian must initial.

❒**YES** I agree to have a member of the research team contact me for future research studies.

_____ **(subject's initials)**

_____ **(subject's parent/legal guardian initials – if applicable)**

❒**NO** I do not agree to have a member of the research team contact me for future research studies.

_____ **(subject's initials)**

_____ **(subject's parent/legal guardian initials – if applicable)**

WHOM TO CONTACT ABOUT THIS STUDY

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the Investigator at the telephone number listed on the first page of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research subjects. If you have any questions about your rights as a research subject, and/or concerns or complaints regarding this research study, contact**:**

- By mail:
  Study Subject Adviser
  Advarra IRB
  6100 Merriweather Drive, Suite 600
  Columbia, MD 21044
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00033875.

VOLUNTARY PARTICIPATION / WITHDRAWAL

Your decision to participate in this study is voluntary. You may choose to not participate or you may withdraw from the study for any reason without penalty or loss of benefits to which you are otherwise entitled and without any effect on your future medical care. However, please note that the FDA requires that any information collected up to the point of your withdrawal cannot be removed from the study.

The study doctor or the sponsor can stop your participation at any time without your consent for the following reasons:

- If it appears to be medically harmful to you;
- If the study is canceled; or
- For administrative reasons.

If you leave the study for any reason, the study doctor may ask you to have some end-of-study tests for your safety.

CONSENT

I have read and understand the information in this informed consent document. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I voluntarily agree to participate in this study until I decide otherwise. I do not give up any of my legal rights by signing and dating this consent document. I will receive a copy of this signed and dated consent document.

_____

Subject's Printed Name (if subject is age of majority or older)

_____ _____

Subject's Signature (if subject is age of majority or older) Date

_____

Printed Name of the Person Conducting the Consent Discussion

_____ _____

Signature of the Person Conducting the Consent Discussion Date

STATEMENT OF ASSENT (if applicable)

I would like to be in this study.

_____
Printed Name of Minor Participant (if subject is under age of majority)

_____ _____
Minor Assent Signature (if subject is under age or majority) Date

_____
Printed Name of the Person Obtaining Assent

_____ _____
Signature of the Person Obtaining Assent Date

STATEMENT OF PARENTAL / LEGAL GUARDIAN PERMISSION (if applicable)

I have read and understand the information in this informed consent document. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I voluntarily agree for my child to participate in this study until I decide otherwise. I do not give up any of my or my child's legal rights by signing this consent document. I will receive a copy of this signed and dated consent document.

_____

Parent/Legal Guardian Printed Name (if subject is under the age of majority)

_____ _____

Parent/Legal Guardian Signature Date

_____

Printed Name of the Person Conducting the Consent Discussion

_____ _____

Signature of the Person Conducting the Consent Discussion Date