UPMC LIFE CHANGING MEDICINE

Magee-Womens Hospital of UPMC
Department of Obstetrics, Gynecology, & Reproductive Sciences

CONSENT TO ACT AS A SUBJECT IN A RESEARCH STUDY

TITLE: Impact of Pregnancy on Buprenorphine Pharmacokinetics and Pharmacodynamics

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Your doctor may be involved as an investigator in this research study. Before agreeing to participate in this research study, or at any time during your study participation, you may discuss your care with another doctor who is not associated with this research study. You are not under any obligation to participate in any research study offered by your doctor.

Introduction

You are invited to take part in a research study. This consent form provides information about the risks and benefits of the study. A member of the study team is available to answer your questions and to provide further explanations. You are free to choose whether or not you will take part in the study. If you agree to take part in the research, you will be asked to sign this consent form. This process is known as informed consent.

Why is this research being done?

The purpose of this study is to look at how a drug called buprenorphine is handled in the body after sublingual (under the tongue) administration during pregnancy and the postpartum (after birth) period. Buprenorphine is used for substitution therapy in opioid-dependent patients. Currently, only buprenorphine and a drug called methadone are approved by the FDA (U.S. Food and Drug Administration) for substitution therapy in opioid-dependent patients. Even though buprenorphine (marketed as Subutex® or Suboxone®) reduces the rates of opioid use, the appropriate dose (how much) and dosing interval (how often) during pregnancy and in the postpartum period has not been clearly established.

University Of Pittsburgh Institutional Review Board
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It appears that buprenorphine also may reduce the risk of Neonatal Abstinence Syndrome (NAS), but the other factors that determine whether or not a baby develops NAS are not well defined. NAS is a group of problems that occurs in a newborn who was exposed to addictive opiate drugs while in the mother's womb. This study also will evaluate several factors that might predict which babies will get NAS and which will not.

Who is being asked to take part in this research study?

You are being invited to participate because you are pregnant with one baby, have been prescribed buprenorphine by your care provider, and are currently taking it twice a day, three times a day, or four times a day.

This study will take place at OPRC (Obstetric-Fetal Pharmacology Research Center) Network hospitals and facilities throughout the United States. The OPRC Network includes 3 hospitals: Magee-Womens Hospital (MWH), Northwestern University, and the University of Texas Medical Branch in Galveston. The OPRC also will use DM-STAT (Data Management and Statistical Analysis) in Massachusetts as the Data Coordinating and Analysis Center for this research study. We will enroll up to 40 women, ages 18 to 45, at MWH. The length of time for your participation in this study ranges from as early as 5 weeks of pregnancy until as late as 18 weeks after delivery of your baby, for a total of up to a little more than 12 months.

What procedures will be performed for research purposes?

Whether or not you choose to participate in this research study, both your buprenorphine treatment and prenatal care will remain the same. This means that both you and your care provider will continue to decide your buprenorphine treatment and manage your pregnancy. The procedures that we will perform as part of this research study will relate to the measurement of the amount of buprenorphine in your blood during pregnancy and in the postpartum period, and how your body reacts to buprenorphine. However, this information will not be used to change your buprenorphine prescription, as only your care provider will change your prescription.

If you decide to take part in this study and once you sign this consent form, you will meet with a member of the study team at MWH for a Baseline Screening Visit. This study visit will confirm your eligibility to participate in the research study and should take about 1 hour to complete.

Baseline Screening Visit:

1) We will review your medical records and ask you questions about your background (such as age and race); your pregnancy and medical history, including your current pregnancy, height, weight, and any medications you are taking; and your social history (such as your alcohol, tobacco, and illicit drug use).
2) You will be asked to sign routine medical record release forms. If you deliver your baby at another hospital, these forms allow us to collect information from your medical records at another hospital as described below.
3) We will measure and record your vital signs (blood pressure, heart rate, and respiratory rate).
4) About 7 milliliters (mL) (about 1.5 teaspoons) of blood will be drawn from a vein in your arm or hand to measure your blood's chemistry (how well your liver and kidneys are working).

5) A urine sample will be collected and tested for the presence of illicit drugs.
6) Procedures for upcoming study visits will be reviewed. You will be scheduled for PK Study Visit 1, which will occur within 2 weeks of the Baseline Screening Visit.

It is important that you notify us if your care provider changes your buprenorphine dose or dosing interval, or if you forget to take one of your doses within 1 week of your scheduled PK study visit. There must be at least 7 days in a row that you are taking your scheduled doses of buprenorphine before you can participate in a PK study visit.

Pharmacokinetics (PK) Study Visits

As a requirement of the study, you will be asked to participate in study visits intended to measure how your body handles buprenorphine during pregnancy and after delivery. These visits will occur at 3 different times during the study: 1) between 8 and 20 weeks of pregnancy; 2) between 21 and 35 weeks of pregnancy; and 3) between 4 to 6 weeks postpartum. There will be a minimum of 12 weeks between PK study visits while you are pregnant.

You will be required to fast, which means you will not eat or drink anything (except for water) after 12:00 AM (midnight) the day of the PK study visit. Please also do **not** drink grapefruit juice within 3 days of the PK study visit, as doing so may interfere with how your body handles buprenorphine. **Do not take your morning buprenorphine dose BEFORE you arrive at the PK study visit.** You must bring your medication in the prescription bottle and take it during the PK study visit.

You are responsible for bringing your own buprenorphine with you to your PK study visit. At NO time will a member of the study team give you buprenorphine. The PK study visit will be rescheduled if you do not bring your buprenorphine with you.

PK study visits will be performed at MWH, MWH Clinical & Translational Research Center (CTRC), or UPMC Montefiore Hospital CTRC by a member of the study team or CTRC staff. Visits should take about 13 hours (if you are taking buprenorphine twice daily), about 9 hours (if you are taking buprenorphine three times daily), or about 7.5 hours (if you are taking buprenorphine four times daily) to complete. The following tests and procedures will occur at each PK study visit:

1) You will arrive for your study visit in the morning based on the length of your study visit (up until 11am).
2) Your vital signs (including temperature) and weight will be measured and recorded.
3) A current list of medications you are taking will be recorded. You will also be asked about any side effects, medical procedures, or illnesses you have had since the last study visit.
4) A catheter (a small plastic tube) will be inserted into one of the veins of your arm or hand for frequent blood draws, and an IV (intravenous, or through a vein) solution of normal saline (salt water) may be started to prevent the line from clotting. You may be asked to reschedule this study visit or withdraw from the study if a suitable vein cannot be found to use.
5) At the first PK study visit only, about 10 mL (about 2 teaspoons) of blood will be collected for a DNA analysis.

a. DNA (deoxyribonucleic acid) is the genetic blueprint in every cell that is unique to every individual.
b. This DNA sample will be used to evaluate some of your genes that, directly or indirectly, are involved with how your body handles and responds to buprenorphine.

6) At the second and third PK visits only, about 7 mL of blood will be collected to measure your blood's chemistry (how well your liver and kidneys are working),
7) At all three PK visits, 7mL of blood will be collected to measure your body's level of certain hormones, your exposure to tobacco, and how much buprenorphine and its breakdown products are in your blood.
8) You will be asked to empty your bladder just before taking your morning dose of buprenorphine. We will collect all of your urine throughout the study visit day, and you will be asked again to empty your bladder before you are discharged home. Urine samples will be used to test for the presence of alcohol and illegal drugs and how buprenorphine is broken down and eliminated by your kidneys.
    a. You will be withdrawn from the study if cocaine or heroin is detected in your urine sample.
9) You will be asked questions about how you feel (your cravings) and physiological testing will be performed. Physiological testing will involve measuring your blood pressure, heart rate, how much your body sweats before and after taking your medication, and the diameter of your pupils.
    a. A small device that attaches to your finger like an oxygen sensor will be used to measure how much your body sweats. This is a painless procedure.
    b. A hand-held device called a pupillometer will be used to measure your pupils. You will look into the pupillometer while it scans an image of your pupils. This is a painless procedure.
    c. If taking buprenorphine twice daily, then these activities will be performed 10 times during the study visit: before taking your morning dose and about 30 minutes, 1 hour, 1.5 hours, 2 hours, 4 hours, 6 hours, 8 hours, 10 hours, and 12 hours after dosing.
    d. If taking buprenorphine three times daily, then these activities will be performed 10 times during the study visit: before taking your morning dose and about 30 minutes, 1 hour, 1.5 hours, 2 hours, 4 hours, 5 hours, 6 hours, 7 hours, and 8 hours after dosing.
    e. If taking buprenorphine four times daily, then these activities will be performed 8 times during the study visit: before taking your morning dose and about 30 minutes, 1 hour, 1.5 hours, 2 hours, 4 hours, 5 hours, and 6 hours after dosing.
10) You will fill your mouth with saliva and swallow it twice just before taking your morning dose of buprenorphine approximately 1 hour after your arrival. You will then place some saliva onto pH paper and the pH of the saliva (how acidic it is) will be recorded. A saliva sample (about 1 to 2 mL) also will be collected and will be tested to see how buprenorphine is broken down in your body.
    a. You will place a swab in your mouth and chew on it for 45 to 60 seconds, after which time we will collect the swab for future testing.
11) You will take your morning dose of buprenorphine approximately 1 hour after your arrival. The time will be based on the length of your study visit that day. You will be asked to hold the medication under your tongue for at least 5 minutes without swallowing to allow it to disintegrate fully. The area under your tongue will be examined at the end of 5 minutes. If any part of the

medication is still present, you will be asked to hold the medication under your tongue for an additional 5 minutes without swallowing.

a. You will not be permitted to eat, drink (except for water), or smoke anything for 2 hours after taking your medication.

12) Blood samples (about 7 mL each) will be collected 12 times for individuals who take buprenorphine twice or three times daily, and 10 times for individuals who take buprenorphine four times daily during the study visit and tested to see how buprenorphine is broken down in your body, your body's level of certain hormones, and your exposure to tobacco.
    a. If taking buprenorphine twice daily, samples will be collected about 10 minutes, 20 minutes, 30 minutes, 1 hour, 1.5 hours, 2 hours, 3 hours, 4 hours, 6 hours, 8 hours, 10 hours, and 12 hours after dosing.
    b. If taking buprenorphine three times daily, samples will be collected about 10 minutes, 20 minutes, 30 minutes, 1 hour, 1.5 hours, 2 hours, 3 hours, 4 hours, 5 hours, 6 hours, 7 hours, and 8 hours after dosing.
    c. If taking buprenorphine four times daily, samples will be collected about 10 minutes, 20 minutes, 30 minutes, 1 hour, 1.5 hours, 2 hours, 3 hours, 4 hours, 5 hours, and 6 hours after dosing.
13) Saliva samples (about 1 to 2 mL each) also will be collected 12 more times for individuals who take buprenorphine twice or three times daily, and 10 more times for individuals who take buprenorphine four times daily during the study visit (on the same schedule as described above in #11 for blood samples) and will be tested to see how buprenorphine is broken down in your body.
    a. You will place a swab in your mouth and chew on it for 45 to 60 seconds, after which time we will collect the swab for future testing.
14) You will receive a meal about 2 to 3 hours after you take your morning dose. You will continue to receive meals for the duration of your study visit, with snacks as requested.
15) You will complete questionnaires about depression, smoking, and alcohol and drug use before the end of the study visit.
16) The catheter will be removed after all samples have been collected, at which time you are free to go home. Discharge times may vary based on the time when the first morning dose was taken.
17) About 98 mL (about 18 teaspoons) of blood will be collected at each PK study, with about an additional 10 mL collected once for DNA.

A member of the study team will contact you the next day to check on your status.

At the Time of Labor and Delivery

The following will be performed if you delivery your baby at MWH:

1) About 7 mL of blood will be collected from a vein in your arm or hand to measure how much buprenorphine is in your blood.
2) After delivery of your baby, about a 3 inch x 3 inch sample of the placenta (after birth) will be collected and stored for testing on how much buprenorphine is present and how well the placenta handles buprenorphine. The placenta is usually discarded at delivery, but we would like to collect a sample for this study. Collection of placental sample is optional.

PERMISSION TO COLLECT, STORE, AND USE PLACENTAL SAMPLE:

I give permission to have a sample of my placenta collected, stored, and used for research purposes.

_____ YES _____ NO _____ INITIALS

3) After delivery of your baby, about a 3 inch sample of the umbilical cord and about 7 mL of the blood inside it (called cord blood) will be collected and stored for testing on how much buprenorphine and its breakdown products are present. The umbilical cord and cord blood are usually discarded at delivery, but we would like to collect it for this study. Collection of the umbilical cord and cord blood samples is optional. Please note: If you intend to store cord blood in a family bank, then that collection will take priority over the collection for this research study. We still will collect cord blood for research purposes if there is enough remaining after your donation to a family bank.

PERMISSION TO COLLECT, STORE, AND USE UMBILICAL CORD AND CORD BLOOD SAMPLES:

I give permission to have samples of my umbilical cord and cord blood collected, stored, and used for research purposes.

_____ YES _____ NO _____ INITIALS

4) After delivery but prior to discharge, a hair sample from the back of your head will be collected and stored for testing on how much buprenorphine and its breakdown products are present. The sample will be collected by a member of the study team using fine scissors to cut, not pull, less than 100 strands as close to your scalp as possible. The strands will come from the back of your head so that longer hair from above will fall and cover it. Hair collection should take less than 5 minutes to complete. Collection of the hair sample is optional.

PERMISSION TO COLLECT, STORE, AND USE HAIR SAMPLE:

I give permission to have a sample of my hair collected, stored, and used for research purposes.

_____ YES _____ NO _____ INITIALS

5) Regardless where you deliver your baby, we will collect information from medical records on your pregnancy, labor, and the status of you and your baby until you are both discharged from the hospital or 120 days after birth, whichever occurs first.

Optional Collection of Postpartum Blood Samples

1) After delivery on the day before you are discharged from the hospital, about 7 mL of blood will be collected to see how much buprenorphine and its breakdown products are in your blood.
2) We also will collect about 7 mL of blood during your routine visits to the MWH buprenorphine clinic each week for the next 4 weeks in a row.
    a. A member of the study team will collect the blood samples, each of which should take about 10 minutes to complete.
    b. Collection of these postpartum blood samples is optional.

PERMISSION TO COLLECT, STORE, AND USE POSTPARTUM BLOOD SAMPLES:

I give permission to have postpartum blood samples collected, stored, and used for research purposes.

_____ YES _____ NO _____ INITIALS

Optional Collection of Breast Milk for a Baby with NAS

If your baby is diagnosed with NAS and is receiving breast milk while in the MWH Neonatal Intensive Care Unit (NICU), then we would like to collect samples of your breast milk in order to determine how long it takes buprenorphine to appear in breast milk. Collection of breast milk samples is optional.

1) On days 3 and 5 of your baby's NICU stay, you will report to MWH and meet with a member of the study team. You will use a breast pump to empty your breast, and we will collect about 5 mL of breast milk each day and then return the rest to you for your baby. This should take less than 30 minutes to complete.
    a. We will collect about 10 mL of breast milk total during days 3 and 5.

PERMISSION TO COLLECT, STORE, AND USE BREAST MILK SAMPLES OBTAINED DURING MY BABY'S STAY IN THE MWH NICU:

I give permission to have breast milk samples collected, stored, and used for research purposes that are obtained during my baby's stay in the MWH NICU.

_____ YES _____ NO _____ INITIALS

Optional Collection of Breast Milk During the Postpartum PK Study Visit

If you are breastfeeding your baby, then we would like to collect samples of your breast milk during the postpartum PK study visit in order to determine how much buprenorphine may be passed to your baby through breast milk. Collection of breast milk samples is optional.

1) In addition to the procedures described above during a PK study visit, you will use a breast pump to empty your breast before your morning dose of buprenorphine, and we will collect about 5 mL of breast milk and then return the rest to you for your baby. You will pump your breast again about every 4 hours after taking your medication, and we will collect about 5 mL of breast milk from each sample and then return the rest to you for your baby. Pumping your breast should take less than 30 minutes to complete.
    a. If taking buprenorphine twice daily, then you will pump 4 times (before taking buprenorphine, and 4 hours, 8 hours, and 12 hours after dosing) and we will collect about 20 mL total.
    b. If taking buprenorphine three times daily, then you will pump 3 times (before taking buprenorphine, and 4 hours and 8 hours after dosing) and we will collect about 15 mL total.
    c. If taking buprenorphine four times daily, then you will pump 3 times (before taking buprenorphine, and 3 and 6 hours after dosing) and we will collect about 15 mL total.

PERMISSION TO COLLECT, STORE, AND USE BREAST MILK SAMPLES OBTAINED DURING POSTPARTUM PK STUDY VISIT:

I give permission to have breast milk samples collected, stored, and used for research purposes that are obtained during my postpartum PK study visit.

_____ YES _____ NO _____ INITIALS

Optional Collection of a Hair Sample from Your Baby

After birth, your baby will stay in either the MWH nursery or the NICU until discharge. We would like to collect a hair sample from your baby's scalp or body (such as shoulders or back) for testing on how much buprenorphine is present. Collection of the hair sample is optional.

1) The sample will be collected by a member of the study team using fine scissors to cut, not pull, fewer than 100 strands. We will try to cut the strands from an area that is not noticeable. Hair collection should take less than 5 minutes to complete.

PERMISSION TO COLLECT, STORE, AND USE MY BABY'S HAIR SAMPLE:

I give permission to have a sample of my baby's hair collected, stored, and used for research purposes.

_____ YES _____ NO _____ INITIALS

Optional Collection of a Heel Stick Blood Sample from Your Baby

If your baby was diagnosed with NAS and is receiving breast milk while in the MWH NICU, then we would like to collect heel stick blood samples from him/her in order to determine how much buprenorphine is in your baby's blood after breast feeding. Heel sticks, in which a baby's heel is pricked and a small amount of blood then is collected, are routinely used on newborns. For this study, however, collection of heel stick blood samples as described below is optional.

1) On days 3 and 5 of your baby's NICU stay, we will collect about 0.25 mL (about 1/20th of a teaspoon) of blood from a heel stick. Samples will be collected by a member of the study team (or clinical care team if your baby already is scheduled to receive a heel stick as part of routine care) and should take less than 5 minutes to complete.
    a. We will collect about 0.5 mL (about 1/10th of a teaspoon) of blood from heel sticks total during days 3 and 5.

PERMISSION TO COLLECT, STORE, AND USE MY BABY'S HEEL STICK BLOOD SAMPLES OBTAINED DURING MY BABY'S STAY IN THE MWH NICU:

I give permission to have heel stick blood samples from my baby collected, stored, and used for research purposes that are obtained during my baby's stay in the MWH NICU.

_____ YES _____ NO _____ INITIALS

The maximum amount of blood that will be collected from you during this study for full participation (including optional components) is about 353 mL (about 71 teaspoons or about 24 tablespoons).

The maximum amount of heel stick blood that will be collected from your baby is about 0.5 mL (about 1/10th of a teaspoon).

Use and Storage of Biological Samples

Analyses of blood, DNA, urine, saliva, umbilical cord, cord blood, placenta, hair, and breast milk samples will be performed at MWH, UPMC, the University of Pittsburgh, or an OPRC Network laboratory to be determined. Samples will be stored indefinitely in secured freezers, and Dr. Caritis will be responsible for control of the storage areas at MWH, MWRI, and the University of Pittsburgh. Only authorized researchers will have access to the stored samples. Samples will be stored to include assigned code

numbers, and the information linking these code numbers to your identity will be kept in a separate, secure location. De-identified samples (samples that do not indicate your identity) may be made available to investigators from the other OPRC Network sites and to secondary investigators (who are not affiliated with this research study) for future research on pregnancy or other purposes. If you decide to withdraw consent for this study, your de-identified samples will continue to be used for analysis and future research. If you decide that you want your stored samples to be destroyed, please notify Dr. Caritis in writing and we will destroy the samples that are labeled with your study ID.

Results of abnormal standard clinical laboratory tests on your blood samples (such as blood counts, kidney function, and liver function) that are reported to us from the local laboratory will be put in your medical record and provided to you and your care provider by a member of the study team. Genetic tests, study drug measurements, and other research test results will not be reported to you or your care provider, and will not be put in your medical record. These tests are being done entirely for research purposes and are not known to predict clinical outcomes.

What are the risks of participating in this research study?

Although unlikely, it is possible that participation in this study could involve risks to you or your baby that are currently unknown. You will be promptly notified if, during the conduct of this research study, any new information develops that may cause you to change your mind about continuing to participate.

Please note: The risks associated with buprenorphine treatment are not risks of this research study because you are receiving buprenorphine whether or not you choose to participate in this study.

Risks of Collection of Blood Samples

Common: bruising, bleeding, swelling, and pain at the injection site
Other: infection at injection site; blood clot at the injection site; fainting; lightheadedness
The amount of blood to be drawn in this study should not affect your blood count.

Risks of Insertion of IV Line (Catheter)

Common: bruising, bleeding, swelling, and pain at the insertion site
Infrequent: infection at insertion site; blood clot at the insertion site; fainting; lightheadedness

Risks of Collection of Breast Milk Samples

There is minimal risk associated with the collection of breast milk samples.

Risks of Collection of Hair Samples

There is minimal risk associated with the collection of hair samples from you or your baby. Removal should not be noticeable to the appearance since only a small amount will be cut.

Risks of Physiological Testing

There is minimal risk associated with performing the physiological testing.

Risks of Collection of Placental Sample

There is no risk to you or your baby associated with collecting a sample of the placenta.

Risks of Collection of Saliva Samples
There is minimal risk associated with collecting saliva samples.

Risks of Collection of Umbilical Cord and Cord Blood Samples
There is no risk associated with collecting an umbilical cord blood sample since the umbilical cord will be separated from you and your baby.

Risks of Collection of Urine Samples
There is minimal risk associated with collecting urine samples.

Risks of Genetic Testing
Genetic (DNA) testing involves the potential for breach of confidentiality that could impact your insurability, employability, or reproduction plans, or have a negative impact on family relationships, and/or result in paternity suits or stigmatization. Although your genetic information is unique to you, you will share some genetic information with your children and other blood relatives. So, it may be possible that genetic information from them could be used to help identify you. It also may be possible that genetic information from you could be used to help identify them. It is possible that people may develop ways in the future that would allow someone to link your genetic or medical information back to you.

The risk that the tests we do could be used against you is very small. First, the study investigators will be very careful to ensure that only authorized researchers can use study samples, study information (including test results), and your personal information. Second, research information and test results will not be placed in any medical records.

A federal law called the Genetic Information Nondiscrimination Act (GINA) makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law will protect you in the following ways: 1) health insurance companies and group health plans may not request your genetic information that we get from this research, 2) health insurance companies and group health plans may not use your genetic information that we get from this research when making decisions regarding your eligibility or premiums, and 3) 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 new federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance, nor does it protect you against genetic discrimination by all employers.

Risks of Collection of Medical Record Information
There is a minimal risk of breach of confidentiality regarding collection of medical record information. All research information about you will be handled in a confidential (private) manner consistent with other hospital medical records.

Risks of Collection of Vital Signs
There is minimal risk associated with collecting vital signs.

Risks of Answering Study Questions
There is minimal risk from answering the study questions. You do not have to answer any questions that you do not want to answer. You may stop answering questions at any time without affecting your medical care. All of your answers will remain confidential. Please note, however, that if the answers to a questionnaire indicate that you may have a possibility of depression, you will be referred to a hospital social worker according to standard of care practice.

Risks of Collection of Heel Stick Blood Samples
Common: bruising, bleeding, swelling, and pain at the collection site
Other: infection at injection site

Will I benefit from participating in this research study?
You and your baby will not directly benefit from participation. The knowledge that we gain from this study may help us to determine whether different doses or dosing intervals of buprenorphine may be appropriate for pregnant compared to non-pregnant women, and whether dosing should change during different stages of pregnancy. We also may learn about how to reduce the risk of NAS, to determine risk factors for NAS, and about how much buprenorphine reaches a baby. Therefore, your participation can potentially benefit many mothers and their babies in the future.

What treatments or procedures are available if I decide not to take part in this research study?
The alternative to this study is not to participate. If you decide not to participate in this study, then you will continue to receive routine prenatal care and buprenorphine treatment by your care provider. Your decision about taking part in this study will not affect your eligibility for any health plan, any health plan benefits or payments, or any medical care options at any UPMC hospital or doctor's office.

What if I change my mind about participation?
You can change your mind at any time. To formally withdraw your consent for participation in this research study or to withdraw your authorization to allow the research team to review medical records, you should provide a written and dated notice of this decision to Dr. Caritis at the address listed on the first page of this form. Even if you cancel this authorization, the study team may still use and disclose PHI and use the biological samples they already have obtained about you as necessary to maintain the integrity or reliability of the research. However, no new PHI or biological samples will be collected from you after you revoke your authorization. Withdrawing permission for your PHI to be used for the research study will not change the medical care you receive and will not affect your eligibility for any health plan, any health plan benefits or payments, or any medical care options at any UPMC hospital or doctor's office.

How much will it cost me to participate in this research study?
There will be no cost to you for taking part in this research study, as none of the research procedures that you receive will be billed to you or your insurance company. You and/or your health insurance will be charged, in the standard manner, for services and procedures provided for your routine prenatal care, such as your labor and delivery with associated hospital services, as well as for buprenorphine treatment prescribed by your care giver. Any deductibles or co-payments that are part of your insurance coverage for routine care will apply.

Will I be paid to participate in this research study?
You will be paid at the end of each study visit via WePay (a reloadable debit card). You will receive:

$50 for completing the Baseline Screening Visit	$25 for the optional breast milk samples during the Postpartum PK Study Visit
$250 for completing each of the 3 possible PK Study Visits (maximum of $750)	$15 for each optional blood sample collected from you postpartum, up to 5 samples (maximum of $75)
An additional $250 if you complete all 3 PK Study Visits	$25 for each optional breast milk sample during your baby's stay in the NICU (maximum of $50)
$45 for completing all of the study procedures at the time of labor and delivery	$25 for the optional hair sample from your baby
$25 for the optional hair sample from you	$25 for each optional heel stick sample collected from your baby (maximum of $50)

You will receive a total of $1,345 if you and your baby complete all parts of this study. You also will receive a voucher for free parking for each study visit. Transportation will be provided to those who need travel assistance to attend the PK visits.

Please note: If your total payment for participation in this study is more than $600 in a year, then the amount will be reported to the Internal Revenue Service (IRS) as income.

Some of the research conducted using your and your baby's samples or information could lead to the development of new diagnostic tests, new drugs, or other commercial products. Should this occur, there is no plan to provide you with any part of the profits.

Who will pay if I am injured as a result of taking part in this study?
UPMC and MWH investigators and their associates recognize the importance of your voluntary participation to their research studies. These individuals and their staffs will make reasonable efforts to minimize, control, and treat any injuries that may arise as a result of this research. If you believe that you are injured as the result of the research procedures being performed, please immediately contact Dr. Caritis. Emergency medical treatment for injuries solely and directly relating to your participation in this research will be provided to you by UPMC and MWH. It is possible that UPMC and MWH may bill your insurance company for the costs of this emergency treatment, but none of these costs will be charged directly to you. If your research-related injury requires medical care beyond this emergency treatment, you will be responsible for the costs of this follow-up care, unless otherwise specifically stated in this consent. There is no plan for monetary compensation. You do not, however, waive any legal rights by signing this form.

How will my privacy and confidentiality be protected?
Your privacy is very important to us. Protected Health Information (PHI) is medical record information about a person's health that includes information that would make it possible to figure out whose it is. According to federal law, you have the right to decide who can see your PHI. All information obtained

from this research study that can be identified with you or your baby will remain confidential within the limits of the law.

When choosing to take part in this research study, you are giving us permission to see and use all medical information and personal identifiers from your medical records and from information that you give to a researcher, such as information related to your eligibility for this study; demographic information; medical history; obstetrical history; labor, delivery, and discharge information; and treatments of whatever kind related to or collected for use in this research study. From your baby's medical records, we will get information about your baby's health up to the time that your baby is discharged from the hospital or 120 days after birth, whichever occurs first. If we lose track of you, the study team may collect information from the internet, including social network sites, in order to find your contact information. Identifiable medical record information will be made available to members of the study team for an indefinite period of time.

The information collected for this research study will be held at DM-STAT in a database consisting of information from all of the participants in this study. The information at DM-STAT will include your PHI such as hospitalization dates and the date of delivery (which is your baby's date of birth). In all other cases, we will use a study ID number to identify your study information. Records linking your name to the study ID will be securely stored in a locked file cabinet in the office of the research staff at MWH.

Any research information that identifies you will not be voluntarily released or disclosed without a separate consent, except as specifically required by law. If the investigators learn that you or someone with whom you are involved is in serious danger or potential harm, they will need to inform, as required by Pennsylvania law, the appropriate agencies.

General de-identified information from this research may be published in medical journals, shared with secondary investigators, and placed in a public data set so that health care providers might learn to provide better care to women in the future. By taking part in this study, a copy of this signed consent form will be put into your medical chart at MWH. You are allowed to see any research information that becomes part of your medical record.

What is a Certificate of Confidentiality?

To further protect the privacy of you and your baby, the researchers will apply for a Certificate of Confidentiality from the NICHD. This Certificate means that the researchers cannot be forced (for example, by court order) to disclose any information that might identify you to any federal, state, or local court. A Certificate of Confidentiality does not prevent you from voluntarily giving information to others about your participation in this research study. We will not release any information collected as part of the research study regarding use of illicit drugs. However, information gathered and tests done as part of your routine clinical care, including drug use, are not protected by the Certificate of Confidentiality that we will obtain for this research study.

Who will have access to my PHI related to my participation in this research study?

In addition to Dr. Caritis and his research staff, the following individuals may have access to your PHI related to your participation in this research study:

1) Authorized representatives from the sponsor (NICHD) and DM-STAT may look at or copy study records for the purpose of monitoring the accuracy and completeness of the research data and for performing required scientific analyses of the research data. The results of this research study also will be provided to the sponsor.
2) The Office for Human Research Protections (OHRP) may look at your study records to protect your safety and welfare.
    a. Persons who receive your PHI may not be required by federal privacy laws to protect it. Some of these persons may be able to share your information with others without your separate permission. By taking part in this study, you are giving your permission for these persons to collect, use, and share your PHI. If you choose not to let these persons, collect, use, and share your PHI as explained above, then you will not be able to participate in this research study.
    b. While NICHD, DM-STAT, and OHRP understand the importance of maintaining the confidentiality of your PHI, the University of Pittsburgh, UPMC, and MWH cannot guarantee the confidentiality of this information after it has been obtained by them. The investigators involved in the conduct of this research study may receive funding from the sponsor to perform the research procedures and to provide the sponsor with your PHI related to your participation in the study.
3) Authorized representatives of the University of Pittsburgh Research Conduct and Compliance Office may review your PHI for the purpose of monitoring the appropriate conduct of this research study.
4) Authorized representatives of UPMC hospitals or other affiliated health care providers may have access to your PHI related to your participation in this research study for the purpose of: fulfilling orders, made by the investigators, for hospital and health care services associated with research study participation; addressing correct payment for tests and procedures ordered by the investigators; and/or for internal hospital operations (such as quality assurance).

For how long will the investigators be permitted to use and disclose identifiable information related to my participation in this research study?

The link to identifying information will be destroyed seven years after study completion. After that time, study identifiers will be destroyed and your information will be coded and retained anonymously indefinitely. Records of your child will be maintained until the child is 23 years of age. After that time, identifiers will be destroyed and your child's data will be coded and retained anonymously indefinitely.

Can I be removed without my permission from this study?

Dr. Caritis or the study sponsor can withdraw you from this study without your approval. This could happen, for example, if it is determined not to be in your best interest to continue in the study, if you do not follow the study procedures, if cocaine or heroin is detected in your urine sample, or if the study is stopped early by the sponsor.

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VOLUNTARY CONSENT AND PARENTAL PERMISSION

I certify that I have read the above information or it has been read to me. All of the above information has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions about any aspects of this research study during the course of this study, and that such future questions will be answered by the researchers listed on the first page of this consent document. The Human Subject Protection Advocate of the Institutional Review Board (IRB) Office, University of Pittsburgh (1-866-212-2668), will answer any questions that I have about my rights as a research participant.

By signing this form, I agree to participate in this research study and give my authorization for the University of Pittsburgh, UPMC, and Magee-Womens Hospital to allow the individuals listed above to use my medical records and my child's medical records for this research study for an indefinite period of time. If applicable, I also grant permission for blood and/or hair samples to be collected from my child, as described above. A copy of this consent form will be given to me.

_____
Printed Name of Participant

_____ _____ _____
Signature of Participant Date Time

CERTIFICATION OF INFORMED CONSENT

I certify that I have explained the nature and purpose of this research study to the above-named individual(s), and I have discussed the potential benefits and possible risks of study participation. Any questions the individual(s) have about this study have been answered, and a member of the study team will always be available to address future questions, concerns or complaints as they arise. I further certify that no research component of this protocol was begun until after this consent form was signed.

_____ _____
Printed Name of Person Obtaining Consent Role in Research Study

_____ _____ _____
Signature of Person Obtaining Consent Date Time