

## Magee-Womens Hospital of UPMC

Department of Obstetrics, Gynecology, & Reproductive Sciences

### **Summary of Key Information on** the Impact of Pregnancy on Buprenorphine Pharmacokinetics and Pharmacodynamics (Consent for a Minor)

#### **Participation is voluntary**

You are being asked to participate in a research study. Research studies include only people who choose to take part. The study team members will explain the study to you and answer any questions you might have. You should take your time to make your decision.

#### **Study Summary:**

The purpose of this portion of the study is to look at how much buprenorphine is in your child's blood after breastfeeding. Your child is being invited to participate because you (his/her mother) are participating in this study (you have already signed a separate consent form) and you have told the study team that you plan to breastfeed your child at least 50% (one-half) of the time that he/she is fed. If you are participating in the PK study, and have decided that your child will take part in this study, you will bring your child with you to the Postpartum PK Study Visit that occurs between 4-6 weeks after you have given birth. At this time, a member of the study team will collect a heel stick blood sample from your child prior to a feeding and another sample 1 hour after the feeding in order to determine how much buprenorphine is in her/her blood.

If you are breast feeding and have decided that your baby can participate in the other part of this study while he/she is in the hospital, we will obtain 2 heel stick blood samples on three separate occasions when breast milk samples are collected. We will perform a heel stick before and 1 hour after the breast milk feeding.

#### **Risks of being in the study:**

The most common risks associated with drawing blood samples are bruising, bleeding, swelling, and pain at the collection site. There is a minimal risk of breach of confidentiality regarding the collection of medical record information. All research information about your child will be handled in a confidential (private) manner consistent with other hospital medical records.

#### **Benefits of Study Participation:**

Your child will not directly benefit from participation. The knowledge that we gain from his study may help us to learn about how much buprenorphine reaches a baby from breast milk. Therefore, your child's participation can potentially benefit many mothers and their babies in the future.

#### **Alternative Treatments:**

The alternative to this study is not to participate. If you decide not to allow your child to participate in this study, then your child will continue to receive routine pediatric care by his/her health care provider.



## CONSENT FOR A MINOR TO ACT AS A SUBJECT IN A RESEARCH STUDY

**TITLE:** Impact of Pregnancy on Buprenorphine Pharmacokinetics and Pharmacodynamics

**PRINCIPAL INVESTIGATOR:** Steve N. Caritis, MD, Professor  
Magee-Womens Hospital of UPMC  
Department of OB/GYN/RS  
300 Halket Street  
Pittsburgh, PA 15213  
Phone: 412-641-4874  
412-641-1000 (24 Hours)

**SPONSOR:** *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD)

Your child's 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 child's study participation, you may discuss your child's care with another doctor who is not associated with this research study. Your child is not under any obligation to participate in any research study offered by his/her doctor.

### **Introduction**

Your child is invited to take part in this research study. This consent form provides information about the risks and benefits of the study. You are free to choose whether or not your child will take part in the study. A member of the study team is available to answer questions and to provide further explanations. If you agree that your child will 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<sup>®</sup> or Suboxone<sup>®</sup>) 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.

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.



The purpose of this portion of the study will be to look at how much buprenorphine is in your child's blood after breastfeeding.

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

Your child is being invited to participate because you (his/her mother) are participating in this study (you have already signed a separate consent form) and you have told the study team that you are breastfeeding your child at least 50% (one-half) of the time when he/she is fed.

This study will take place at Magee-Womens Hospital (MWH), an OPRC (Obstetric-Fetal Pharmacology Research Center) Network hospital. We will enroll up to 40 babies at MWH.

**What procedures will be performed for research purposes?**

**1. Postpartum PK Study (Part A in the Adult Consent):**

If you are participating in the PK study, and you have decided that your child will take part in this study and once you sign this consent form, you will bring your child with you to the Postpartum PK Study Visit that occurs between 4 to 6 weeks after you have given birth (when your child is about 1 to 1½ months old). This study visit 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. We would like to collect heel stick blood samples from your child in order to determine how much buprenorphine is in his/her blood after receiving breast milk. 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 those in the Postpartum PK study performed at 4-6 weeks after delivery, we will collect heel stick blood samples from your baby just before and 1 hour after a breast feeding. Ideally this should be done with the breastfeeding closest to when you take your morning dose of buprenorphine. This should take less than 5 minutes to complete.

A maximum of 2 heel stick samples will be collected during the postpartum PK study and the total amount of blood that may be collected from your baby is about 0.50 mL (about 1/10<sup>th</sup> of a teaspoon).

**2. Collection of Breast Milk and Heel Stick Samples (Part D in the Adult Consent)**

Whether you are or are not participating in the PK study, your baby may still participate in another optional study while he/she is in the hospital.

For those subjects participating in the collection of breast milk samples (Part D in the adult consent), we will collect 2 infant heel stick samples with each breast milk collection. One heel stick sample will be collected prior to the breast feeding and another one 1 hour after the feeding. A maximum of 6 heel stick samples will be collected (1 sample before a feeding and another one after the feeding on 3 separate occasions). The total amount of blood that may be collected from your baby is about 1.50 mL (about 1/30<sup>th</sup> of a teaspoon).



If your baby participates in both studies described above, a maximum of 8 heel stick samples may be collected. The maximum amount of heel stick blood that may be collected from your baby is about 2.0 mL (less than 1/2 of a teaspoon).

### **Use and Storage of Biological Samples**

Analyses of blood samples will be performed at MWH, Magee-Womens Research Institute (MWRI), 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 child's identity will be kept in a separate, secure location. De-identified samples (samples that do not indicate your child's 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. You will not share in any commercial profit that may result from the future use of your child's de-identified samples.

If you decide to withdraw consent for your child to participate in this study, your child's de-identified samples will continue to be used for analysis and future research. If you decide that you want your child's stored samples to be destroyed, please notify Dr. Caritis in writing and we will destroy the samples that are labeled with your child's study ID.

Study drug measurements and other research test results will not be reported to you, your child, or his/her care provider, and will not be put in your child's 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 your child 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 having your child continue to participate.

#### *Risks of Collection of Heel Stick Blood Samples*

*Common:* bruising, bleeding, swelling, and pain at the collection site

*Other:* infection at injection site

#### *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 your child will be handled in a confidential (private) manner consistent with other hospital medical records.

### **Will my child benefit from participating in this research study?**

Your child will not directly benefit from participation. The knowledge that we gain from this study may help us to learn about how much buprenorphine reaches a baby from breast milk. Therefore, your child's participation can potentially benefit many mothers and their babies in the future.



**What treatments or procedures are available if I decide not to allow my child to take part in this research study?**

The alternative to this study is not to participate. If you decide not to allow your child to participate in this study, then your child will continue to receive routine pediatric care by his/her care provider. Your decision about your child taking part in this study will not affect your child's 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 my child's participation?**

You can change your mind at any time. To formally withdraw your consent for your child's participation in this research study or to withdraw your authorization to allow the research team to use your child's PHI (Protected Health Information), 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 your child as necessary to maintain the integrity or reliability of the research. However, no new PHI or biological samples will be collected from your child after you revoke your authorization. Withdrawing permission for your child's PHI to be used for the research study will not change the medical care your child receives and will not affect your child's 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 allow my child to participate in this research study?**

There will be no cost to you or your child for allowing your child to take part in this research study, as the research procedures that your child receives will not be billed to you or your/your child's insurance company. You and/or your/your child's health insurance will be charged, in the standard manner, for services and procedures provided for his/her routine pediatric care. Any deductibles or co-payments that are part of your/your child's insurance coverage for routine care will apply.

**Will I be paid to allow my child to participate in this research study?**

- You will be paid \$25 for each set (before and after the feeding) of heel stick samples collected from your baby (maximum of 4 sets of samples or \$100) via a reloadable debit card:

Please note: If the total payment for your/your child's 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. This means you have to pay taxes on all research study income when it reaches \$600 in one year.

Some of the research conducted using your child'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 or your child with any part of the profits.

**Who will pay if my child is injured as a result of taking part in this study?**

UPMC and MWH investigators and their associates recognize the importance of your child's 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



your child is 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 child's participation in this research will be provided to your child by UPMC and MWH. It is possible that UPMC and MWH may bill you/your child's insurance company for the costs of this emergency treatment, but none of these costs will be charged directly to you/your child. If your child's research-related injury requires medical care beyond this emergency treatment, you/your child 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/your child do not, however, waive any legal rights by signing this form.

### **How will my child's privacy and confidentiality be protected?**

Your child's 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 who's it is. According to federal law, you have the right to decide who can see your child's PHI. All information obtained from this research study that can be identified with your child will remain confidential within the limits of the law.

When choosing to take part in this research study, you are giving us permission to use your child's PHI (specifically, his/her name) that you give to a researcher. This 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 MWH in a secure location and will include information from all of the participants in this study. The information at MWH will include your child's PHI such as date of birth. In all other cases, we will use a study ID number to identify your child's study information. Records linking your child's 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 your child will not be voluntarily released or disclosed without a separate consent, except as specifically required by law. If the investigators learn that your child 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 and their children in the future. By taking part in this study, a copy of this signed consent form will be put into your child's medical chart at MWH. You are allowed to see any research information that becomes part of your child's medical record until he/she reaches the age of 18 years old.

### **What is a Certificate of Confidentiality?**

To further protect the privacy of your child, 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 your child to any federal, state, or local court. A



Certificate of Confidentiality does not prevent you from voluntarily giving information to others about your child's participation in this research study.

**Who will have access to my child's PHI related to his/her participation in this research study?**

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

- 1) Authorized representatives from the sponsor (NICHD) 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 child's study records to protect his/her safety and welfare.
  - a. Persons who receive your child's PHI may not be required by federal privacy laws to protect it. Some of these persons may be able to share your child's 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 child's PHI. If you choose not to let these persons, collect, use, and share your child's PHI as explained above, then your child will not be able to participate in this research study.
  - b. While NICHD and OHRP understand the importance of maintaining the confidentiality of your child's 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 child's PHI related to his/her participation in the study.
- 3) Authorized representatives of the University of Pittsburgh Research Conduct and Compliance Office may review your child's 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 child's PHI related to his/her 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 child's participation in this research study?**

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 my child be removed without my permission from this study?**

Dr. Caritis or the study sponsor can withdraw your child from this study without your approval. This could happen, for example, if the study is stopped early by the sponsor.



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**PARENTAL PERMISSION**

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 aspect of this research study during the course of this study, and that such future questions will be answered by a qualified individual or by the investigator(s) listed on the first page of this consent document at the telephone number(s) given. I understand that I may always request that my questions, concerns or complaints be addressed by a listed investigator.

I understand that I may contact the Human Subjects Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668) to discuss problems, concerns, and questions; obtain information; offer input; or discuss situations in the event that the research team is unavailable. A copy of this consent form will be given to me.

\_\_\_\_\_  
Printed Name of Child-Subject

I understand that, as a minor (age less than 18 years), the above-named child is not permitted to participate in this research study without my consent. Therefore, by signing this form, I give my permission for his/her participation in this research study.

\_\_\_\_\_  
Printed Name of Parent/Guardian

\_\_\_\_\_  
Relationship to Participant (Child)

\_\_\_\_\_  
Signature of Parent/Guardian

\_\_\_\_\_  
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