Washington University in St. Louis

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INFORMED CONSENT DOCUMENT

Project Title: Methadone in Pediatric Anesthesia II

Principal Investigator: Anshuman Sharma

Research Team Contact: Lindsay Juriga, 314-454-7945

- If you are the parent/guardian of a child under the age of 18 who is being invited to participate in this study, the word "you" in this document refers to your child. As the parent/guardian, you will be asked to read and sign this document to give permission for your child to participate.
- If you are under the age of 18 and reading this document, the word "you" in this document refers to you. You will be asked to read and sign this document to indicate your willingness to participate.

This consent form describes the research study and helps you decide if you want to participate. It provides important information about what you will be asked to do during the study, about the risks and benefits of the study, and about your rights as a research participant. By signing this form you are agreeing to participate in this study.

- You should read and understand the information in this document including the procedures, risks and potential benefits.
- If you have questions about anything in this form, you should ask the research team for more information before you agree to participate.
- You may also wish to talk to your family or friends about your participation in this study.
- Do not agree to participate in this study unless the research team has answered your questions and you decide that you want to be part of this study.

WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study. We invite you to participate in this research study because you are scheduled to have spinal surgery and will receive anesthesia including drugs to reduce pain.

Many different drugs are used in anesthesia and surgery including drugs to relieve pain. One commonly used drug is methadone. Methadone works quickly and lasts longer than other pain medications such as morphine. Methadone is approved by the U.S. Food and Drug Administration for treating pain in adults. Previous studies have shown that adults and adolescents are similar in how their bodies handle methadone used for pain during surgery. The purpose of this research study is to determine if administration of the drug methadone during surgery will reduce pain and reduce the amount of pain medications after surgery in adolescents and children. A second purpose of this research study is to understand how well methadone controls pain, how long it last and how long it takes for children and adolescents to metabolize (get rid of) methadone from their bodies.

WHAT WILL HAPPEN DURING THIS STUDY?

If you and one of your parents decide for you to participate in this study your anesthesia will be exactly the same as if you were not in the study. In addition to other pain medication you may also receive a dose of methadone during your surgery. If you do not receive methadone you will receive other pain

medications such as morphine or dilaudid.

This is a randomized study. You will be randomly placed into 1 of 3 groups depending on when you are enrolled to the study.

Study Cohorts: If you are enrolled in one of the Methadone cohorts you will be randomized to receive a dose of methadone in the operating room. The methadone dose will depend on your weight.

Treatment Cohort: If you are enrolled in the methadone treatment cohort 1, you will be randomized to receive intravenous (IV) methadone HCI during your surgery.

Control Cohort: If you are enrolled in the control cohort you will be randomized to receive a standard opioid pain medication, not methadone, by IV during surgery.

This will be the only time you receive methadone for this study.

Before your surgery and every morning for up to 6 days following the procedure (if you are still in the hospital), a member of the research team will ask you questions about your comfort level and any pain that you may experience. A numeric scale and pictures to depict how you are feeling will be used to help assess your comfort level and what you consider acceptable for treating any discomfort. You may be provided with an electronic tablet to answer questions about how you are feeling. Your parents will also be asked to use the tablet to answer questions about your overall wellbeing following your surgery. We also want to know if you experience side effects such as sleepiness, itching and nausea.

To understand how long it takes methadone to disappear from the body, we need to draw blood several times after the methadone is given. We will take a total of about 3 tablespoons of blood over 4 days. We will use the arterial line placed (routine standard of care) after you are asleep in the operating room to draw the blood for the first 24 hours. For the remaining samples, we will continue to collect a blood sample every morning for up to 4 days after your surgery from an IV (intravenous) catheter or collect samples with routine blood draws. Your urine will be collected in a container that is provided for up to four days. Each day the research staff will provide a new container and will collect the container from the previous day.

We will collect information from your medical record such as demographic data, pain medication use and information from your hospital stay.

We would also like for you and your primary caregiver to complete a short questionnaire about your pain and its effects on your family before your surgery. The questionnaire will take approximately 5 minutes.

Will you save my samples or research data to use in future research studies?

As part of this study, we are obtaining blood samples from you. The samples we collect will be saved and labeled with a code and will not contain any personal identifiers, such as your name. If you agree, we would like to use your blood for other research projects going on now and in the future. These future studies may provide additional information that will be helpful in understanding pain. It is unlikely that

what we learn from these studies will have a direct benefit to you. By agreeing to be part of this study you give up any property rights you may have to these samples. There are no plans to provide financial compensation to you for allowing us to store your samples. Your blood samples may be used to develop investigational tests, treatments, drugs, or devices that are not yet approved by the U.S. Food and Drug Administration.

I agree to have my blood stored: Yes _____ No _____
initials initials

You will also be asked to have blood collected and used for genetic testing. The purpose is to obtain DNA (the blue print for a person's genetic makeup) to help us learn about the genes (the part of DNA that tells your body how to make proteins) associated with pain. We will look at the genes which may affect how long methadone lasts. Only personnel involved with this research project will have access to the DNA samples. You will not be told the results of the gene tests because they are experimental, and because we don't know of any conclusive links between these genes and the risk of disease or any adverse events from drug therapy. If you agree, we will take approximately one teaspoon of blood either from your arterial line or from an IV at the same time as other blood sample collections. We will store your DNA for at least ten (10) years. Your DNA will be given a code number and contain no personal identifiers. Your DNA samples may be used to develop investigational tests, treatments, drugs, or devices that are not yet approved by the U.S. Food and Drug Administration.

I agree to have my DNA stored: Yes _____ No _____
initials initials

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 75 people will take part in this study conducted by investigators at Washington University.

HOW LONG WILL I BE IN THIS STUDY?

If you agree to take part in this study, your involvement will last six days or until discharged from the hospital, whichever comes first.

WHAT ARE THE RISKS OF THIS STUDY?

You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study.

Methadone:
The risks listed below can also happen with other pain medications.
Likely: Some people can get sick to their stomach (nausea) or throw up (vomit) after methadone.
Less likely: Methadone can possibly decrease your breathing rate, or cause sleepiness when several doses are given. However these have not been a problem with the single dose we will give you, which has been used safely before.
Rare: Serious decreases in breathing rate or heart rate can happen in patients given many, very high doses for several days when first starting methadone. You will receive only one dose.

Completing the questionnaires or assessments may cause emotional discomfort, boredom, or fatigue. You have the right, however, to refuse to answer any question for any reason.

All the information you give us will be given a code number. A master list linking the code number and your identity will be kept separate from the research data. Only the PI and people helping him/her will be able to see the list. We will protect your information, but there is a chance somebody might see it.

Risk to the Unborn Child:
Because the drugs in this study may affect an unborn baby, you should not become pregnant while in this study. If you are a female capable of becoming pregnant, you must have a negative pregnancy test before beginning participation. This will be done as standard care. In addition, you must not be breastfeeding a baby during this study.

Breach of Confidentiality:
Medical records are considered confidential and records are kept in a secured area accessible only to the research team involved in the conduct of the study. You will not be identified by name in any publication or presentation of the results of this study unless prior written consent is obtained. Although we will make every effort possible to maintain confidentiality, there is however, a slight risk of breach of confidentiality.

WHAT ARE THE BENEFITS OF THIS STUDY?
We don't know if you will benefit from being in this study.

However, we hope that in the future, other people might benefit from this study because we will have a better understanding of how methadone works in children and adolescents, which may improve the treatment of pain.

WHAT OTHER TREATMENT OPTIONS ARE THERE?
Before you decide whether or not to be in this study, your doctor will discuss the other options that are available to you. If you do not want to participate in this study, the choice of pain medicine used for your surgery will be made by your anesthesiologist.

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?
You will not have any additional costs for being in this research study.

You and/or your medical/hospital insurance provider will remain responsible for your regular medical care expenses.

WILL I BE PAID FOR PARTICIPATING?
You will not be paid for being in this research study.

WHO IS FUNDING THIS STUDY?
There is no funding for this study.

WHAT IF I AM INJURED AS A RESULT OF THIS STUDY?

Washington University investigators and staff will try to reduce, control, and treat any complications from this research. If you feel you are injured because of the study, please contact the investigator Dr. Sharma at 314-454-4229 and/or the Human Research Protection Office at 1-(800)-438-0445.

Decisions about payment for medical treatment for injuries relating to your participation in research will be made by Washington University**.** If you need to seek medical care for a research-related injury, please notify the investigator as soon as possible.

HOW WILL YOU KEEP MY INFORMATION CONFIDENTIAL?

We will keep your participation in this research study confidential to the extent permitted by law. However, it is possible that other people such as those indicated below may become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you.

- Government representatives, (including the Office for Human Research Protections) to complete federal or state responsibilities
- The U.S. Food and Drug Administration
- Hospital or University representatives, to complete Hospital or University responsibilities
- Information about your participation in this study may be documented in your health care records and be available to your health care providers who are not part of the research team.
- Washington University's Institutional Review Board (a committee that oversees the conduct of research involving human participants.) The Institutional Review Board has reviewed and approved this study.

To help protect your confidentiality, we will have all paper documents locked office/filing cabinet of a member of the study team. We will keep all electronic documents on secured servers that are password protected and have various state of the art firewall protections with frequent upgrades of these protections. There is not an intention to transport the data; the only access point will be that of our secure research drives and servers. Of note, access to these electronic research files is restricted to only members of the study team. Your blood samples will be housed within the Department of Anesthesiology's. If we write a report or article about this study or share the study data set with others, we will do so in such a way that you cannot be directly identified.

This consent form or similar documentation that you are participating in a research study will be included in your clinical medical record. Anyone with access to your medical record, including your health insurance company will be able to see that you are participating in a research study.

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.

Are there additional protections for my health information?

Protected Health Information (PHI) is health information that identifies you. PHI is protected by federal law under HIPAA (the Health Insurance Portability and Accountability Act). To take part in this

research, you must give the research team permission to use and disclose (share) your PHI for the study as explained in this consent form. The research team will follow state and federal laws and may share your health information with the agencies and people listed under the previous section titled, "How will you keep my information confidential?".

Once your health information is shared with someone outside of the research team, it may no longer be protected by HIPAA.

The research team will only use and share your information as talked about in this form. When possible, the research team will make sure information cannot be linked to you (de-identified). Once information is de-identified, it may be used and shared for other purposes not discussed in this consent form. If you have questions or concerns about your privacy and the use of your PHI, please contact the University's Privacy Officer at 866-747-4975.

Although you will not be allowed to see the study information, you may be given access to your health care records by contacting your health care provider.

If you decide not to sign this form, it will not affect

- your treatment or the care given by your health provider.
- your insurance payment or enrollment in any health plans.
- any benefits to which you are entitled.

However, it will not be possible for you to take part in the study.

If you sign this form:

- You authorize the use of your PHI for this research
- Your signature and this form will not expire as long as you wish to participate.
- You may later change your mind and not let the research team use or share your information (you may revoke your authorization).
    - To revoke your authorization, complete the withdrawal letter, found in the Participant section of the Human Research Protection Office website at http://hrpo.wustl.edu/participants//withdrawing-from-a-study/ or you may request that the Investigator send you a copy of the letter.
        - **If you revoke your authorization:**
            - The research team may only use and share information already collected for the study.
            - Your information may still be used and shared if necessary for safety reasons.
            - You will not be allowed to continue to participate in the study.

IS BEING IN THIS STUDY VOLUNTARY?

Taking part in this research study is completely voluntary. You may choose not to take part at all. If you decide to be in this study, you may stop participating at any time. If you decide not to be in this study, or if you stop participating at any time, you won't be penalized or lose any benefits for which you otherwise qualify.

What if I decide to withdraw from the study?

You may withdraw by telling the study team you are no longer interested in participating in the study or

you may send in a withdrawal letter. A sample withdrawal letter can be found at http://hrpo.wustl.edu/participants/ under Withdrawing from a Research Study.

Will I receive new information about the study while participating?
If we obtain any new information during this study that might affect your willingness to continue participating in the study, we'll promptly provide you with that information.

Can someone else end my participation in this study?
Under certain circumstances, the researchers might decide to end your participation in this research study earlier than planned. This might happen because in our judgment it would not be safe for you to continue.

WHAT IF I HAVE QUESTIONS?
We encourage you to ask questions. If you have any questions about the research study itself, please contact: Lindsay Juriga, 314-454-7945**.** If you experience a research-related injury, please contact: Dr. Sharma at 314-454-4229.

If you have questions, concerns, or complaints about your rights as a research participant, please contact the Human Research Protection Office, 660 South Euclid Avenue, Campus Box 8089, St. Louis, MO 63110, 1-(800)-438-0445, or email hrpo@wusm.wustl.edu. General information about being a research participant can be found by clicking "Participants" on the Human Research Protection Office web site, http://hrpo.wustl.edu. To offer input about your experiences as a research subject or to speak to someone other than the research staff, call the Human Research Protection Office at the number above.

This consent form is not a contract. It is a written explanation of what will happen during the study if you decide to participate. You are not waiving any legal rights by agreeing to participate in this study. As a participant you have rights and responsibilities as described in this document and including:

- To be given enough time before signing below to weigh the risks and potential benefits and decide if you want to participate without any pressure from the research team or others.
- To understand all of the information included in the document, have your questions answered, and receive an explanation of anything you do not understand.
- To follow the procedures described in this document and the instructions of the research team to the best of your ability unless you choose to stop your participation in the research study.
- To give the research team accurate and complete information.
- To tell the research team promptly about any problems you have related to your participation, or if you are unable to continue and wish to stop participating in the research study.

Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a signed and dated copy of this form.

Do not sign this form if today's date is after EXPIRATION DATE: 01/30/18.

_____ _____
(Signature of Participant) (Date)

_____
(Participant's name – printed)

Parent/Guardian Name and Relationship to Participant:

Do not sign this form if today's date is after EXPIRATION DATE: 01/30/18.

_____
(Child's name – printed)

_____ _____
(Signature of Parent/Guardian) (Date)

_____ _____
(Name of Parent/Guardian- printed) (Relationship to participant – printed)

Statement of Person Who Obtained Consent

The information in this document has been discussed with the participant or, where appropriate, with the participant's legally authorized representative. The participant has indicated that he or she understands the risks, benefits, and procedures involved with participation in this research study.

_____ _____
(Signature of Person who Obtained Consent) (Date)

_____
(Name of Person who Obtained Consent - printed)