Washington University in St. Louis

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INFORMED CONSENT DOCUMENT

Project Title: **A randomized controlled trial to compare hydromorphone vs fentanyl in children undergoing tonsillectomy surgery**

Principal Investigator: **Michael Montana, MD PhD**

Research Team Contact: **Alan Hifko, MD, 314-273-0783**

- 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 and responsibilities 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.

You are invited to take part in a randomized controlled trial to compare hydromorphone vs fentanyl in children undergoing tonsillectomy surgery because you are scheduled for tonsillectomy surgery. This is a research study conducted by Dr. Michael Montana having to do with the management of pain after a tonsillectomy surgery. The purpose of this research study is to compare two pain medications that are regularly given following a tonsillectomy surgery. Those pain medications are called hydromorphone and fentanyl. Both of these drugs are routinely prescribed for pain control during and after a tonsillectomy. We will compare the use and effect of the medication prescribed to you on your pain, specifically, how often and how much of the medication is given to you, measurements of your pain, if the medication affects how you breathe, if you develop an upset stomach, and length of time you spend in the post-surgical recovery room.

You should carefully consider the information in this consent document and discuss it with the research team. You should understand why you might want to participate, or why you might not want to participate. The study is sponsored by the National Institutes of Health. You may choose to participate or not.

If you agree to participate in this study, you will be asked to provide informed consent, and then we will begin to collect personal, medical and health information from your medical record. If you meet all the requirements to participate, you will be randomly assigned to receive one of the two study drugs; either the hydromorphone or fentanyl. This means that the study treatment you receive will be determined purely by chance, like flipping a coin.

Following consent, but before your surgery, we will ask you questions regarding your feelings about your tonsillectomy. You are free to skip any questions that you prefer not to answer.

You will be in the study for approximately 8 days. You will be asked to come to St. Louis Children's Hospital for the procedures in the study. These will include an optional set of 3 blood draws to see how the pain medication, either hydromorphone or fentanyl, is processed through your body over time. These samples would be taken through an additional IV line placed in the surgical suite after anesthesia is given. If you agree, blood samples will be taken at the following time points: 1) within 10 minutes of receiving hydromorphone or fentanyl, 2) within 10 minutes of your arrival in the surgical recovery area, called the PACU, 3) within 10 minutes of your discharge from the PACU.

You may choose to stop participating and withdraw from the study at any time. If you withdraw from the study, the research team may continue to use the information already collected about you.

There are some risks to you if you agree to volunteer for this study. The most serious/most common risks are breach of confidentiality. The risks to you are described in more detail later in this consent document. There is no direct benefit to you but you may help someone else in the future.

All of the above information will be further explained and is listed in more detail in the consent document below.

If you decide to take part in this study, you will be asked to sign at the end of this document, after you have had a chance to review all of the information. Do not sign unless you understand the purpose of the study, what you will be asked to do, and the risks that may be involved. The research team must give you a copy of this signed consent document.

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 for a tonsillectomy surgery.

The purpose of this research study is to compare two pain medications that are regularly given following a tonsillectomy surgery. Those pain medications are called hydromorphone and fentanyl. Both of these drugs are routinely prescribed for pain control during and after a tonsillectomy. We will compare the use and effect of the medication prescribed to you on your pain, specifically, how often and how much of the medication is given to you, measurements of your pain, if the medication affects how you breathe, if you develop an upset stomach, and length of time you spend in the post-surgical recovery room.

Hydromorphone is approved by the U.S. Food and Drug Administration to treat pain. However, the use of hydromorphone has not been approved for use in children and is considered investigational in this study.

Fentanyl is approved by the U.S. Food and Drug Administration to treat pain.

WHAT WILL HAPPEN DURING THIS STUDY?

The consent process is the first part of being in this study. If you provide informed consent and are eligible to continue in the study, we will begin to collect personal, medical and health information from your medical record. If you meet all the requirements to participate, you will be randomly assigned to receive one of the two study drugs; either the hydromorphone or fentanyl. This means that the study treatment you receive will be determined purely by chance, like flipping a coin.

Following consent, but before your surgery, we will ask you questions regarding your feelings about your tonsillectomy. Your parent will also be asked to answer questions about their experiences and feelings about your tonsillectomy. You are free to skip any questions that you prefer not to answer.

During the operation and in the post-operative care unit we will record the analgesic medications you receive, as well as safety mentoring information such as heart rate, blood pressure, and SPO2.

Post-operative pain scores will be measured upon arrival, every 5 minutes for the first 15 minutes, followed by every 15 minutes for the first hour, hourly while in the PACU, as well as at the time of discharge and prior to administration of rescue medication, if rescue medication is needed.
Follow up surveys to assess pain, adverse events, and overall satisfaction will be sent to you by email on post-operative day 3 **(± 1 day)**, and 7 **(± 1 day)**.

We will also offer an optional set of 3 blood draws to see how the pain medication, either hydromorphone or fentanyl, is processed through your body over time. These samples would be taken through an additional IV line placed in the surgical suite after anesthesia is given. If you agree, blood samples will be taken at the following time points: 1) within 10 minutes of you receiving hydromorphone or fentanyl, 2) within 10 minutes of your arrival in the surgical recovery area, called the PACU, 3) within 10 minutes of your discharge from the PACU.

Please place your initials in the blank next to Yes or No for the question below:

You may place an additional IV line during surgery for the purposes of collecting 3 blood samples from me:

_____ Yes **_____ No**
Initials **Initials**

Will you save my research information and/or biospecimens to use in future research studies?

We would like to use the blood and data we are obtaining in this study for studies going on right now as well as studies that are conducted in the future. These studies may provide additional information that will be helpful in understanding pain management, or other diseases or conditions, including research to develop investigational tests, treatments, drugs or devices that are not yet approved by the U.S. Food and Drug Administration. It is unlikely that what we learn from these studies will have a direct benefit to you. There are no plans to provide financial compensation to you should this occur. By allowing us to use your blood and data you give up any property rights you may have in the blood and data.

We will share your blood and data with other researchers. They may be doing research in areas similar to this research or in other unrelated areas. These researchers may be at Washington University, at other research centers and institutions, or industry sponsors of research. We may also share your research data with large data repositories (a repository is a database of information) for broad sharing with the research community. If your individual research data is placed in one of these repositories only qualified researchers, who have received prior approval from individuals that monitor the use of the data, will be able to look at your information.

If you change your mind and do not want us to store and use your blood and data for future research you should contact the research team member identified at the top of this document. The blood and data will no longer be used for research purposes. However, if some research with your blood and data has already been completed, the information from that research may still be used. Also, if the blood and data has been shared with other researchers it might not be possible to withdraw the blood and data to the extent it has been shared.

Please place your initials in the blank next to Yes or No for each of the questions below:

My blood and data may be stored and used for future research as described above.

_____ Yes **_____ No**
Initials **Initials**

My blood and data may be shared with other researchers and used by these researchers for the future research as described above.

_____ Yes **_____ No**
Initials **Initials**

Identifiers may be removed from your private information including blood and data and used for future research or shared with others. If this occurs, we will not ask you for additional consent.

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 300 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 for approximately 8 days for your surgery, recovery time, and follow up surveys. This time commitment may vary from participant to participant.

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.

Some risks described in this consent document, if severe, may cause death.

Risk of IV Placement
There is a chance that you will have some bruising or bleeding at the IV insertion site.

Hydromorphone
Likely / Common
Nausea
Vomiting
Sleepiness

Less Likely / Less Common
Low blood pressure, low heart rate
Low breathing rate

Rare
Very low breathing rate; cessation of breathing.

Fentanyl
Likely / Common
Nausea
Vomiting
Sleepiness

Less Likely / Less Common
Low blood pressure, low heart rate
Low breathing rate

Rare
Very low breathing rate; cessation of breathing.

Women Capable of Becoming Pregnant
If you are a woman capable of becoming pregnant, we will ask you to have a pregnancy test before beginning this study. You must use effective birth control methods and try not to become pregnant

while participating in this study. If you become pregnant, there may be unknown risks to your unborn child, or risks to your unborn child that we did not anticipate. There may be long-term effects of the treatment being studied that could increase the risk of harm to an unborn child. You must tell the doctor if your birth control method fails while you are on the study. If you believe or know you have become pregnant while participating in this research study, please contact the research team member identified at the top of this document as soon as possible. Please discuss with the research team how long you need to wait before becoming pregnant after completing the treatment or procedures on this study.

Breach of Confidentiality
One risk of participating in this study is that confidential information about you may be accidentally disclosed. We will use our best efforts to keep the information about you secure. Please see the section in this consent form titled *"How will you keep my information confidential?"* for more information.

WHAT ARE THE BENEFITS OF THIS STUDY?

You may or may not benefit from being in this study.

However, we hope that, in the future, other people might benefit from this study because knowing the differences in drugs used for pain management could improve the way we manage pain for tonsillectomy patients.

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. Instead of being in this study, you could simply not participate and continue with the care prescribed by your medical team.

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

As part of this study you will receive tests and procedures that are similar to what you would receive during routine clinical care of your condition. Your health plan/insurance company will be billed for some or all of these costs, and you will be responsible for any co-pays and deductibles that are normally required by your health plan/insurance. Not all insurance plans cover the costs associated with being in a study. Even if they do, you may be responsible for more out-of-pocket expenses, such as co-pays and deductibles, when there are more tests and procedures or more expensive tests and procedures involved in the study than if you were to receive routine clinical care outside the study.

If you wish to know whether there are more tests and procedures or more expensive tests and procedures in the study, you should ask your study doctor.

If you wish to know whether your insurance will pay, you should contact them directly, or speak with the study team about obtaining a financial pre-certification prior to enrolling in the study.

WILL I BE PAID FOR PARTICIPATING?

You will be paid for being in this research study. You will need to provide your social security number

(SSN) in order for us to pay you. You may choose to participate without being paid if you do not wish to provide your social security number (SSN) for this purpose. You may also need to provide your address if a check will be mailed to you. If your social security number is obtained for payment purposes only, it will not be retained for research purposes.

You will receive a $25 Amazon Gift card at the end of your study participation.

WHO IS FUNDING THIS STUDY?

The National Institutes of Health (NIH) is funding this research study. This means that Washington University is receiving payments from the NIH to support the activities that are required to conduct the study. No one on the research team will receive a direct payment or increase in salary from the NIH for conducting 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 at 314-565-8119 and/or the Human Research Protection Office at 1-(800)-438-0445.

Decisions about whether 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?

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. We will keep your participation in this research study confidential to the extent permitted by law.

- Government representatives (including the Office for Human Research Protections) to complete federal or state responsibilities
- The U.S. Food and Drug Administration
- The National Institutes of Health (NIH)
- The sponsor (NIH) may also inspect any part of your medical record for the purposes of auditing the conduct of the study.
- 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 will be available to anyone with access to your health care record, including your health insurance company. This information may also be released as part of a release of information request.
- The last four digits of your social security number may be used in hospital or University systems to track billing information for research procedures.
- Washington University's Institutional Review Board (a committee that oversees the conduct of research involving human participants) and the Human Research Protection Office. The

Institutional Review Board has reviewed and approved this study.

- Any report or article that we write will not include information that can directly identify you. The journals that publish these reports or articles require that we share your information that was collected for this study with others to make sure the results of this study are correct and help develop new ideas for research. Your information will be shared in a way that cannot directly identify you.

To help protect your confidentiality, you will be assigned a study ID number and we will use that ID to manage all your study related information and blood samples. This includes paper documents, electronic documents and blood specimens that we collect from you during your participation. Additionally, the key to the ID code linking code numbers to names will be kept at a separate location, under lock and key, and only the research team will have access to it. We will destroy the link between your ID and your identifiers at the end of the 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.

To further protect your privacy, this research is covered by a Certificate of Confidentiality from the federal government. This means that the researchers can refuse to disclose information that may identify you in any legal or court proceeding or to anyone who is not connected with the research except if:

- there is a law that requires disclosure, such as to report child abuse and neglect, or harm to self or others*;*
- you give permission to disclose your information, including as described in this consent form; or
- it is used for other scientific research allowed by federal law.

You have the right to share your information or involvement in this study with anyone at any time. You may also give the research team permission to disclose your information to a third party or any other person not connected with the research.

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 or as permitted or required by law. 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
- This authorization does not expire.
- 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 https://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 as necessary to maintain the integrity of the research, for example, to account for a participant's withdrawal from the research study or for safety reasons.
      - You will not be allowed to continue to participate in the study.

Can we contact you by email?

We would like to contact you by email for the purposes listed below. Some of these emails may contain health information that identifies you.

- Follow up surveys which will include questions about pain, adverse reactions, and overall satisfaction. Follow up surveys will be sent on post-operative day 3 (± 1 day) and day 7 (± 1 day).

Only the research team will have access to your email communications. We will only communicate by email to send you the information listed above. If you have any questions or need to contact us for an urgent or emergent situation, please contact the research team member identified at the top of this document.

You should be aware that there are risks associated with sending your health information via email.

- There is always a risk that the message could be intercepted or sent to the wrong email address. To avoid sending messages to the wrong email address, the first email we send you will be a test message to ensure we have the correct email address.

- When using any computer you should be careful to protect your username and password. Make sure you log-out before getting up from the computer.
- If you share a home computer with other family members, and do not want them to know you are participating in this study make sure you provide an email address that only you can access.
- Your employer will have access to any email communications sent or received on any electronic devices used for work or through a work server.

Do you agree to allow us to send your health information via email?

_____ Yes **_____ No**
Initials **Initials**

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. Any data that was collected as part of your participation in the study will remain as part of the study records and cannot be removed.

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 https://hrpo.wustl.edu/participants/withdrawing-from-a-study/ 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 investigator might decide to end your participation in this research study earlier than planned. This might happen for no reason or 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: Dr. Montana at 314-565-8119. If you experience a research-related injury, please contact: Dr. Montana at 314-565-8119.

If you have questions, concerns, or complaints about your rights as a research participant, please contact the Human Research Protection Office 1-(800)-438-0445, or email hrpo@wustl.edu. General information about being a research participant can be found on the Human Research Protection Office web site, http://hrpo.wustl.edu. To offer input about your experiences as a research participant 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.

Parent/Guardian Name and Relationship to Participant:

By signing this form you are agreeing to participate in this study and providing permission for your child to participate.

Do not sign this form if today's date is after EXPIRATION DATE: 11/15/22.

_____
(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 they understand 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)