Title of research study:

Modified Pre-operative Oral Doses Acetaminophen Versus Intravenous Acetaminophen

Investigator: Cathy R. Lammers, MD

Why am I being invited to take part in a research study?

We invite you to take part in a research study because your child is scheduled for a tonsillectomy and adenoidectomy.

What should I know about a research study?

(Experimental Subject's Bill of Rights)

- Someone will explain this research study to you, including:
  - The nature and purpose of the research study.
  - The procedures to be followed.
  - Any drug or device to be used.
  - Any common or important discomforts and risks.
  - Any benefits you might expect.
- Whether or not you take part is up to you.
- You can choose without force, fraud, deceit, duress, coercion, or undue influence.
- You can choose not to take part.
- You can agree to take part now and later change your mind.
- Whatever you decide it will not be held against you.
- You can ask all the questions you want before you decide.
- If you agree to take part, you will be given a signed and dated copy of this document**.**

Who can I talk to?

If you have questions, concerns, or complaints, or think the research has hurt you, talk to the research team. During business hours, contact:

Ana Arias, Department of Anesthesiology 916-703-5456

Ahmed Bayoumi, Department of Otolaryngology 916-734-2863

For non-emergency issues you can call the UCDMC Hospital Operator (916-734-2011), tell the Operator you are participating in a research study and you wish to talk to the anesthesiologist on- call or the otolaryngologist on-call (24 hours a day/ 7 days a week). In the case of an emergency, dial 911 from any phone.

This research has been reviewed and approved by an Institutional Review Board ("IRB"). Information to help you understand research is on-line at http://www.research.ucdavis.edu/policiescompliance/irb-admin/.You may talk to a IRB staff member at (916) 703-9151, hs-irbadmin@ucdavis.edu, or 2921 Stockton Blvd, Suite 1400, Room 1429, Sacramento, CA 95817 for any of the following:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research subject.
- You want to get information or provide input about this research.

Why is this research being done?

The purpose of the study is to compare pain control between two forms of acetaminophen, and to possibly save money for future patients who have to undergo the same surgery as your child.

Acetaminophen, otherwise known as Tylenol or Ofirmev, has been used by medical providers to help treat moderate to severe surgical pain in children. It is used with various medications including opioids or narcotics to treat pain after surgery. Opioids/narcotics are strong morphine-like medicines that can have multiple side effects that can be very serious in children after tonsillectomies and adenoidectomies (for example: slower breathing rates, sedation, and obstruction).

Because of this, there is interest in the use of acetaminophen to manage surgical pain. Other studies have shown that if acetaminophen is given to a child, then the child will need less of these stronger pain medications to be comfortable after surgery. Acetaminophen comes in various forms including an inexpensive oral form (Tylenol) and a more expensive intravenous (IV) form (Ofirmev).

We think that one loading oral dose of acetaminophen given before surgery can provide better pain control (as measured by less need for morphine-like medicine) compared to one dose of intravenous acetaminophen for pediatric tonsillectomy and adenoidectomy patients.

How long will the research last?

We expect that your child will be in this research study beginning approximately 1 hour before surgery and continuing for approximately 24 hours after surgery.

How many people will be studied?

We expect about 80 children will be in this research study at the UC Davis Children's Hospital.

What happens if I say yes, I want to be in this research?

All patients will receive acetaminophen. The treatment your child gets will be chosen by chance, like flipping a coin. Neither you nor the study doctor will choose what treatment your child gets. Your child will have a 50:50 chance of being given each treatment.

Group 1 will take the acetaminophen by mouth in one dose before surgery. Group 2 will receive their acetaminophen in the operating room before surgery through the IV. After the surgery, both groups will receive acetaminophen in the same way, by mouth. The pharmacists who have prepared the medications for us will know which group you have been assigned to and whether the acetaminophen was given by mouth or by IV. Your doctors, however, will not know which route the acetaminophen was given. To make sure no one other than the pharmacist knows which group you are in, there will be placebo doses. A placebo dose by mouth is plain flavored syrup made to look just like the liquid acetaminophen. A placebo will also be used to look like the IV acetaminophen. Your child will definitely receive acetaminophen but in group 1 it will be by mouth and in group 2 it will be through the IV.

Every patient in both groups will take medicine (acetaminophen or placebo) by mouth prior to surgery.

As part of the study, one set of acetaminophen blood levels will be drawn while your child is still under anesthesia and another set will be drawn 3 hours after the IV drug was given. Your child will be awake for the second draw but in most cases this can be done by pulling the blood sample back through the IV without a needle poke.

Your child will be shown the Wong Baker Faces scale to obtain pain scores. He/she will be given pain medicines in recovery room and in their hospital room per our usual practices at UC Davis Children's Hospital.

What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible for attending your scheduled surgery at the UC Davis children surgery center.

What happens if I do not want to be in this research?

You may decide not to take part in the research and it will not be held against you

If you decide not to have your child participate in this study, his/her surgery will go on as planned.

What happens if I say yes, but I change my mind later?

You can leave the research at any time and it will not be held against you.

Is there any way being in this study could be bad for me?

Participating in this study exposes your child to minimal additional risk. The surgery and anesthesia that your child is undergoing may have other risks, which your physicians will explain to you separately.

Acetaminophen is available over the counter and is considered to be safe for use in children, with few side effects. However, as with all drugs, side effects have been reported and include nausea, rash, and headache. Children who received intravenous acetaminophen have also reported to have had side effects of nausea, vomiting, itching and agitation. Other rare side effects following intravenous acetaminophen that have been reported in clinical studies include decreased blood count, abdominal pain, diarrhea, injection site pain, peripheral swelling, fever, elevated liver enzymes, increased blood volume, muscle spasms, pain in legs or arms, headache, loss of or altered sleep, decreased urine output, fluid in or around the lungs, swelling around the eyes, rash, and high or low blood pressure. Very rare but severe reactions include liver injury or toxicity, kidney damage, allergic reactions and death. This has been rarely reported when acetaminophen has been given within the recommended dose.

The blood draws that will be part of this study will be obtained from existing IV sites. If the IV cannot be drawn, a single venipuncture (needle poke) will be performed while your child is still under anesthesia. For the second acetaminophen blood level, which is drawn when your child is awake, we will most likely be able to draw it back from the existing IV without a needle poke. If his/her IV no longer works, you have the option to have the blood drawn with a small needle or decline this test and still remain in the study.

<u>Abnormal Test Results</u>

It is unlikely that there will be any abnormal results from the blood draws. We have designed the study to make this risk small. However, if a lab result for the blood level of study drug/ acetaminophen is abnormal then we will notify the ENT physician that will be taking care of your child while he/she is at the hospital. We will also notify your child's bedside nurse. If the blood level is high then we will hold the next dose of acetaminophen. You will be made aware of this and a different pain medicine will be used if needed.

If there are any other abnormal test results that are discovered, you will be informed about these results and recommend you contact your private medical provider for follow-up. Please be advised that as researchers, we are not trained to diagnose or treat all medical conditions. You or your insurance company will be responsible for payment of any treatment of medical conditions.

Will being in this study help me in any way?

We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits include better pain control.

What happens to the information collected for the research?

Efforts will be made to limit use or disclosure of your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete confidentiality. Organizations that may inspect and copy your information include the IRB and other University of California representatives responsible for the management or oversight of this study.

During your participation in this research, data will be collected about you. The de-identified data and any specimens, such as blood or tissue that are taken from you for this study, they will become the property of the University of California. The specimens may be used in this research, may be used in other research, and may be shared with other organizations. The specimens could lead to discoveries or inventions that may be of value to the University of California or to other organizations. Under state law you do not have any right to money or other compensation stemming from products that may be developed from the specimens.

If you agree to share the biological specimen(s) collected from you, please initial here. _____

The sponsor, monitors, auditors, the IRB, the Food and Drug Administration will be granted direct access to your research records to conduct and oversee the study. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

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.

If we access protected health information (e.g., your medical record), you will be asked to sign a separate form to give your permission.

Federal law provides additional protections of your medical records and related health information. These are described in the UC Davis Health System Notice of Privacy Practices (http://www.ucdmc.ucdavis.edu/compliance/pdf/notice.pdf) and in an attached document.

Can I be removed from the research without my OK?

The person in charge of the research study or the sponsor can remove you from the research study without your approval. Possible reasons for removal include:

- It is in your child's best interest to be removed
- Your child experiences a study – related injury
- Your child needs an additional or different medication/treatment
- You or your child do not comply with the study plan
- Administrative and/or medical reasons

We will tell you about any new information that may affect your health, welfare, or choice to stay in the research.

What else do I need to know?

You or your health plan will be billed for the costs of routine medical care you receive during the study. These costs may include operating room fees, pharmacy charges, treatments, hospitalization, scans, etc. You will be expected to pay for the usual deductibles and co-payments, and for any routine care that is not covered.

Only the costs of research or experimental procedures will be paid by the study**.** This includes the cost of the acetaminophen and the cost of processing blood work for acetaminophen levels.

For more information about possible costs, please contact the research team. The research team can follow UC Davis Uninsured Non-Emergency Estimate Policy (Policy ID 1883) to work with their department and Decision Support Services to get you a cost estimate.

It is important that you promptly tell the person in charge of the research if you believe that you have been injured because of taking part in this study. If you are injured as a result of being in this study, the University of California will provide necessary medical treatment. Depending on the circumstances, the costs of the treatment may be covered by University or the study sponsor or may be billed to your insurance company just like other medical costs. The University and the study sponsor do not normally provide any other form of compensation for injury. For more information about compensation, you may call the IRB Administration at (916) 703-9151 or email at HS-IRBAdmin@ucdavis.edu.

You will not be compensated for taking part in this study.

Signature Block for Children

Your signature documents your permission for the named child to take part in this research.

Printed name of child

Signature of parent or individual legally authorized to consent to the child's general medical care

Date

❑ Parent
❑ Individual legally authorized to consent to the child's general medical care (See note below)

Printed name of parent or individual legally authorized to consent to the child's general medical care

❑ I allow the research team to leave me research – related voicemail messages.

Assent

❑ Obtained
❑ Not obtained because the capability of the child is so limited that the child cannot reasonably be consulted.
❑ Waived by the IRB because the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the child and is available only in the context of the research.

Signature of person obtaining consent and assent

Date

Printed name of person obtaining consent

My signature below documents that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the subject, and that consent was freely given by the subject.

Signature of witness to consent process	Date

Printed name of person witnessing consent process

For IRB Use

APPROVED by the Institutional Review Board at the University of California, Davis	
Protocol	Approved
948256	08/02/2017

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