RUTGERS
New Jersey Medical School

SUBJECT CONSENT TO TAKE PART IN A RESEARCH STUDY

TITLE OF STUDY: A multi-center, randomized, double-blind, pilot study on the effect of intravenous multidose acetaminophen on readiness for discharge in patients undergoing laparoscopic cholecystectomy under general anesthesia

Principal Investigator: Michal Gajewski, DO
Co-Investigator: Daniel Rodriguez-Correa, MD (Spanish speaking)

This consent form is part of an informed consent process for a research study and it will provide information that will help you to decide whether you wish to volunteer for this research study. It will help you to understand what the study is about and what will happen in the course of the Study.

If you have questions at any time during the research study, you should feel free to ask them and should expect to be given answers that you completely understand.

After all of your questions have been answered, if you still wish to take part in the study, you will be asked to sign this informed consent form.

You are not giving up any of your legal rights by volunteering for this research study or by signing this consent form.

Who is conducting this research study?
Dr. Michal Gajewski is the Principal Investigator of this research study. A Principal Investigator has the overall responsibility for the conduct of the study. However, there are often other individuals who are part of the research team.

Dr. Gajewski or Dr. Daniel Rodriguez-Correa may be reached at:
Rutgers/NJMS
Department of Anesthesiology MSB E 538
185 South Orange Ave.
Newark, New Jersey 07103
973 972-5007

The study doctor, Dr. Gajewski, or another member of the study team will also be asked to sign this informed consent. You will be given a copy of the signed consent form to keep.

Why is this study being done?
This study is being done as the study doctors wish to study ways to improve recovery after surgery. Injury including surgical injury causes inflammation and pain. Inflammation is the

body's attempt to protect itself and start the healing process. Although mainly a healing response, inflammation can have side effects which delay recovery. The investigators wish to determine the effect of intravenous acetaminophen on post- operative surgical pain. An increase in pain after surgery can cause distress for patients. The narcotic medications which we give to patients to reduce pain have their own side effects. Acetaminophen has been used for reduction of pain. The study doctors would like to see if receiving acetaminophen prior to, during and after surgery can provide:

- a lower level of pain
- a decrease in pain medication
- fewer episodes of nausea and or vomiting
- a shorter hospital stay

Why have you been asked to take part in this study?
You have been asked to participate in this study because you are scheduled to undergoing a laparascopic removal of your gallbladder under general anesthesia.

Who may take part in this study? And who may not?

You *may* take part in this study if:

1. You are 18 years and older.
2. You are not pregnant or nursing
3. You are willing and able to consent
4. You have an American Society of Anesthesiologists (ASA) rating of 1, 2, or 3 as determined by your anesthesiologist*
5. You surgery is not an emergency

You *may not* take part in this study if:

1. You have an allergy or suspected allergy to acetaminophen
2. You are a chronic steroid or opioid/narcotic abuser
3. You have been told by a physician that you have hepatitis or liver disease
4. You have a history of alcohol abuse
5. You use on a daily basis any of these over the counter medications that contain Acetaminophen:
   Actifed, Alka Seltzer, Contac, Anacin, Coricidin, Dayquil, Nyquil, Dimetapp, Dristan, Excedrin, Liquiprin, Midol, Panadol, Robitussin, St. Joseph's Aspirin-Free, Sudafed, Sinutab, Theraflu, Tylenol Brand Products, Vanquish, Zicam

6. You use on a daily basis any of these prescribed drugs that contain acetaminophen:
Lortab, Endocet, Oxycodone, Percocet, Tramadol, Vicodin, Hycotab, Fioricet

***** This classification is used by anesthesiologists to evaluate the degree of the patient's physical state based on their preexisting condition. Those patients who are healthy with no past medical history are classified as ASA 1, those with mild systemic disease (such as well controlled hypertension) are ASA 2, while those with severe systemic illness are ASA 3 (i.e. poorly controlled hypertension). This system is not intended to predict operative risk but is more so utilized to classify patients according to a uniform system. Patients with classifications of 4 and

above have illnesses that are a constant threat to life and may react unpredictably when given the study drug. For this reason only classes 1-3 have been included.

How long will the study take and how many subjects will participate?
We will ask 90 patients to participate in the study. The study will be performed at University Hospital in Newark (approximately 45 patients) and a hospital in Brooklyn, New York (approximately 45 patients). The study is expected to take three years. The study will begin the day of surgery and end at the time of your discharge from the hospital.

What will you be asked to do if you take part in this research study?
If you decide to participate

Prior to Surgery
Screening visit, this visit encompasses discussing the study, answering questions you may have, and signing the consent. A brief medical history will be taken by one of the members of the study team. A pain scale called the Visual Acuity Scale will be explained to you. One member of the study team will draw 15mL or 3 teaspoons of blood from the intravenous line that the nurse inserts for fluid replacement. (All patients must have this line inserted prior to being brought to the Operating Room) This blood will be sent to a laboratory for analysis of inflammation markers. You will be randomized to either receive acetaminophen or a placebo (sugar water). Randomization is the same as flipping a coin. Half the study subjects will get the acetaminophen and half will get the sugar water. Your doctors will not know which you will receive only the research pharmacist will know. The medication will be given to you through the intravenous line. .

During Surgery
Prior to the surgical incision but while you are comfortably asleep the second blood draw 15mL or 3 teaspoons will be drawn for inflammation markers. While you are sleep, if 4 hours has elapsed since your first dose of the study drug, you will be given a second dose.

Following Surgery
You will go to the PACU where all patients go to recover from anesthesia. While you are there a member of the study team will assess you at 15 minutes intervals. We will ask you to move your legs and arms. We will ask you your pain score. We will ask you if you know where you are and what day it is. **If you require pain medication, it will be given to you**. We will record your pain score, the amount of pain medication you receive, and whether you have any nausea or vomiting. Sixty minutes after your arrival in the PACU we will draw the **third** sample of blood for inflammation markers. We will document the time you leave the PACU and the time you are discharged from the hospital. If 4 hours has elapsed since your last dose of the study medication you will receive another dose. This will be repeated if you stay in the hospital longer. You will not receive more than 4 doses of the study medication. . You will also be asked to complete a 3 question survey. This will not take longer than 3-4 minutes. Once you are discharged you have completed the study.

What are the risks and/or discomforts you might experience if you take part in this study?

There are potential side effects for any medication. The most serious side effect of intravenous acetaminophen is acute liver failure. This could happen in people who receive doses that exceed the recommended daily dose limit**. That is why we ask you to be very careful in telling us about the medicines you take:**
both those prescribed by a doctor and those that you buy over the counter at the store.

Another rare occurrence is a serious skin disorder. You will be watched carefully for any skin rashes or signs of hypersensitivity to this drug. If these signs are observed the medication will be discontinued immediately.

When your blood is drawn, there may be a bruise, or bleeding, or infection, at the place where your blood is drawn. However, infection is rare.

Are there any benefits for you if you choose to take part in this research study?
The benefits of taking part in this **study may be:**

Less pain after surgery
Decrease in pain medication after surgery
Fewer episodes of nausea and vomiting
Shorter hospital stay

However, it is possible that you might receive no direct personal benefit from taking part in this study.

What are your alternatives if you don't want to take part in this study?
If you chose not to enter the study then your surgery will go forward as planned. The anesthesiologist will evaluate you in accordance with his or her customary practice.

How will you know if new information is learned that may affect whether you are willing to stay in this research study?
During the course of the study, you will be updated about any new information that may affect whether you are willing to continue taking part in the study. If new information is learned that may affect you after the study or your follow-up is completed, you will be contacted.

Will there be any cost to you to take part in this study?
There will be no cost to you if you chose to participate in the study.

Will you be paid to take part in this study?
You will not be paid for your participation in this research study.

How will information about you be kept private or confidential?
All efforts will be made to keep your personal information in your research record confidential, but total confidentiality cannot be guaranteed. All paper data records will be locked in the Anesthesia research office. All electronic data will be stored in a password protected computer. Only members of the study team will have access to the data.

A description of this clinical trial will be available on ClinicalTrials.gov, as required by U.S. law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

What will happen if you are injured during this study?
Subjects in this study will be exposed to certain risks of personal injury in addition to those associated with standard forms of treatment, please see the paragraph on risks (page 5). In addition, it is possible that during the course of this study, new adverse effects of intravenous acetaminophen that result in personal injury may be discovered. The University will make appropriate referrals for medical and/or dental treatment for subjects who sustain personal injuries or illnesses as a direct consequence of participation in the research. The subject's health insurance carrier or other third-party payer will be billed for the cost of this treatment; provided that the University shall not submit to federally funded programs, e.g., Medicare, Medicaid or CHAMPUS, for reimbursement first if submission to such programs is prohibited by law. No financial compensation will be provided by the University and no other type of assistance is available from the University.

While you are in the study, you and/or your health care provider will still have to pay for the costs of your regular medical care that are not part of the study(such as laparoscopic cholecystectomy and costs associated with your hospital stay).

What will happen if you do not wish to take part in the study or if you later decide not to stay in the study?
Participation in this study is voluntary. You may choose not to participate or you may change your mind at any time.

If you do not want to enter the study or decide to stop participating, your relationship with the study staff will not change, and you may do so without penalty and without loss of benefits to which you are otherwise entitled.

You may also withdraw your consent for the use of data already collected about you, but you must do this in writing to:

Dr. Michal Gajewski or Dr. Daniel Rodriguez-Correa
Rutgers University/New Jersey Medical School
Department of Anesthesiology –MSB E 538
185 South Orange Ave.
Newark, New Jersey 07103

At any time, the study doctor can take you out of this study because it would not be in your best interest to stay in it. Your study doctor can stop treatment even if you are willing to stay in the study. Some circumstances under which your participation may be terminated by the study doctor include:

- *If your surgery is converted to an open procedure*
- *If you have a intraoperative change in you hemodynamic status (blood pressure or heart rate)*
- *If you have an allergic or suspected allergic response to the study medication*
- *If your anesthesiologist is unable to remove your breathing tube prior to your leaving the Operating Room*

If you decide to withdraw from the study for any reason, you may be asked to return for at least one additional visit for safety reasons.

Who can you call if you have any questions?
If you have any questions about taking part in this study or if you feel you may have suffered a research related injury, you can call the study doctor:

Michal Gajewski, DO or Daniel Rodriguez-Correa, MD
Department of Anesthesiology
973 972-5007

If you have any questions about your rights as a research subject, you can call:
Director of Institutional Review Board
(973)-972-3608 Newark
Or the office Human Subject Protection Program
973-972-1149

What are your rights if you decide to take part in this research study?
You have the right to ask questions about any part of the study at any time. You should not sign this form unless you have had a chance to ask questions and have been given answers to all of your questions.

PERMISSION (Authorization) TO USE OR SHARE HEALTH INFORMATION THAT IDENTIFIES YOU FOR A RESEARCH STUDY

Information about you and your health is personal and private, so this information generally cannot be used in research without your written permission. The next few paragraphs tell you about how researchers want to use and share your health information in this research study. Your information will only be used as described here or as allowed or required by law. Ask questions if you do not understand any part of the research or the use of your health information. If you sign this consent form, you agree to let the researchers use your information in the research and share it with others as described below.

What is the purpose of the research and how will my information be used?
You are being invited to take part in this research study which is described at the beginning of this form. The purpose of collecting and using your health information for this study is to help researchers answer the questions that are being asked in the research.

What information about me will be used?
- age, weight, allergies, blood pressure, heart rate
- Medical history or treatment
- Medications including over the counter medications
- A questionnaire regarding your surgical experience

- Operative report (about this surgery)and anesthesia reports

Who may use, share or receive my information?
The research team may use or share your information collected or created for this study with the following people and institutions:

- Rutgers University researchers involved in the study;
- The Rutgers University Institutional Review Board and Compliance Boards
- The Office for Human Research Protections in the U.S. Dept. of Health and Human Services
- US Food and Drug Administration
- Researchers involved at New York Methodist Hospital in Brooklyn, New York.

Those persons or organizations that receive your information may not be required by Federal privacy laws to protect it and may share your information with others without your permission, if permitted by the laws governing them.

Will I be able to review my research record while the research is ongoing?
No. We are not able to share information in the research records with you until the study is over. To ask for this information, please contact the Principal Investigator, the person in charge of this research study.

Do I have to give my permission?
No. You do not have to permit use of your information. But, if you do not give permission, you cannot take part in this research study. (Saying no does not stop you from getting medical care or other benefits you are eligible for outside of this study.)

If I say yes now, can I change my mind and take away my permission later?
Yes. You may change your mind and not allow the continued use of your information (and to stop taking part in the study) at any time. If you take away permission, your information will no longer be used or shared in the study, but we will not be able to take back information that has already been used or shared with others. If you say yes now but change your mind later for use of your information in the research, you must write to the researcher and tell him of your decision:

Dr. Michal Gajewski or Dr. Daniel Rodriguez-Correa
Rutgers University/New Jersey Medical School
Department of Anesthesiology –MSB E 538
185 South Orange Ave.
Newark, New Jersey 07103

How long will my permission last?
Your permission for the use and sharing of your health information will last until the end of the study.

AGREEMENT TO PARTICIPATE

1. Subject consent:

I have read this entire form, or it has been read to me, and I believe that I understand what has been discussed. All of my questions about this form or this study have been answered.

Subject Name:_____

Subject Signature:_____ Date:_____

2. Signature of Investigator/Individual Obtaining Consent:

To the best of my ability, I have explained and discussed the full contents of the study including all of the information contained in this consent form. All questions of the research subject and those of his/her parent or legally authorized representative have been accurately answered.

Investigator/Person Obtaining Consent (printed name):_____

Signature:_____ Date: _____