CEDARS-SINAI MEDICAL CENTER

CONSENT FORM FOR RESEARCH

TITLE: **PROSPECTIVE RANDOMIZED CONTROLLED STUDY OF AN ENHANCED RECOVERY PROTOCOL FOR ANORECTAL SURGERY**

PARTICIPATING RESEARCHERS:
KAREN ZAGHIYAN, M.D. PRINCIPAL INVESTIGATOR
PHILLIP FLESHNER, M.D. CO-INVESTIGATOR
AARON PARRISH, M.D. CO-INVESTIGATOR

STUDY CONTACT PHONE NUMBER AT CSMC: (310) 298-0224

AFTER HOURS CONTACT (24 HOURS): (310) 289-9224

1. WHAT IS THE PURPOSE OF THIS RESEARCH STUDY?

The purpose of the study is to evaluate whether being randomized to an aggressive postoperative non-narcotic pain regimen that treats pain from multiple different pathways may decrease postoperative pain levels, decrease constipation, and decrease the dependency on opioid medications after anorectal surgery versus the standard of care for managing pain. This use of a more aggressive pain regimen is considered an enhanced recovery after surgery (ERAS) protocol because it is theorized to improve or “enhance" postoperative recovery by both decreasing the use of narcotics and their detrimental effects as well as increasing the benefit of using additional non-narcotic pain medication.

Although pain is a predictable part of the postoperative experience, inadequate management of pain is common and can have profound implications Most patients who undergo surgical procedures experience acute postoperative pain, but evidence suggests that less than half report adequate postoperative pain relief. Many preoperative, intraoperative, and postoperative interventions and management strategies are available for reducing and managing postoperative pain. Mostly, pain is treated with opioids which are narcotics. medically they are primarily used for pain relief and these are historically considered “safe” drugs as they do not impose an increased risk of bleeding, kidney, or stomach problems. However, many patients taking high dose opioids have a higher risk of constipation. Unrelieved postoperative pain may result in economic and medical implications such as extended lengths of stay, readmissions, and patient dissatisfaction with medical care. With the rising concern over narcotic use, physicians are increasingly seeking alternative ways to help patients manage pain throughout their hospital stay and beyond However, few studies in anorectal surgery have shown that using an aggressive postoperative non-narcotic pain regimen (ERAS) can help reduce postoperative pain and decreased returns to emergency care.

You are being asked to take part in this research study because you are between the ages of 18 and 70 years old and are scheduled to undergo anorectal surgery as part of your standard of care.

The study will enroll up to 88 people in total.

This research study is designed to compare two pain management procedures pre- and post-surgery. The experimental arm ("ERAS") will include the following drugs Gabapentin, Acetaminophen, Ketorolac, and Oxycodone which are all approved by the Food and Drug Administration (FDA) for pain management. The second arm which is standard of care will receive Oxycodone. In addition, acetaminophen and ibuprofen over the counter, will be allowed if needed.

2. WHAT WILL HAPPEN DURING THE STUDY?

This section provides a general overview of what will happen during your participation in this study. Information included below should be considered along with the flowchart of procedures attached as Appendix A.

The flowchart shows a timeline for research-related or standard of care procedures that are involved in your participation in this study. **Research-related procedures** are those performed solely for the research. They would not be performed if you did not take part in the study. **Standard of care (routine)** procedures would be performed both as part of this study and if you do not participate in this study.

Standard of care procedures that will be repeated or done at greater frequency are listed in the flow chart, attached Appendix A.

Overview of study:
This is a randomized, controlled, single center study. It will study the effects (good or bad) of using ERAS versus the usual standard of care.

- "**Randomized**" means that you will be assigned to a study group by chance, like flipping a coin. You will be randomized into one of 2 study groups and will have a one in two chances of being placed in one of the groups.
- **"Controlled"** means that the experimental arm is being compared with the standard care arm. The standard care arm is considered the "control".

This study has 2 study groups:

- **Group 1 -** ERAS: You will be given 1 pre-operative (pre-op) dose of gabapentin. For post-operative pain management, you will be given Standard of Care drugs: Gabapentin, Acetaminophen, Ketorolac, and Oxycodone (as needed).
- **Group 2** - Usual Standard of Care (SOC): You will not be given any preoperative pain medication. After surgery, you will be given Oxycodone (if you need it to help control the pain) and you will be allowed to take SOC oral acetaminophen and ibuprofen, over the counter, if needed.

A computer will randomly assign you to a study group. This is done because no one knows if the results experienced by the participants in one study group are better, the same, or worse than the results experienced by participants in the other. Once you are put in one group, you cannot switch to another group. Neither you nor your doctor can choose the group in which you will be placed.

Either of these different approaches could help your condition but could also cause side effects. This study will allow the researchers to learn whether the different approaches are better, the same, or worse than the current standard of care.

If you are assigned to the control group, you will be followed as you receive the care generally followed for individuals with your condition. Standard (routine) care for controls will involve:
Postoperative pain control:

- Oxycodone oral 5 mg as needed every 6 hours (#30, refill #0)
- You will be allowed to take oral acetaminophen and ibuprofen over the counter if needed

When you arrive for your clinically scheduled surgery,

Your medical history will be reviewed at the time you are scheduled for your surgical procedure. Information about your medical history will be collected, as well as pre-and post- medications you received will also be collected from your medical record. In addition, other information collected from your medical records will include information, size of your wound, estimated blood loss, type of anesthesia you received, pain score, and Nausea score. In addition, you will be evaluated for complications related to the surgery or the research, if any develop.

In addition, you will be asked to complete questionnaires pre and post-surgery. Preoperative baseline pain will be measured in the preoperative care unit Preoperative baseline nausea will be measured in the preoperative care unit; preoperative urinary function will be assessed using validated instrument (International Prostate Symptom Score (I-PSS). You will also be asked to report pain and nausea at the 1-week postop period by filling out a pain and nausea daily log for the first postoperative week period. You will also be asked to report pain at defecation for 1 week after surgery. You will also be asked to report urinary function by filling out a questionnaire 1 week after surgery.

How long will you be in the study?

We think you will be in the study for about 1 month. At the 1-month postoperative visit, any additional adverse events or complications, urgent care, emergency department visits or hospital admissions will be collected.

3. WHAT ARE THE POSSIBLE RISKS?

Risks of common medical procedures performed solely for research purposes are described in a table attached to the end of this consent form as Appendix B. Side effects and risks of standard of care procedures are not described in this consent form.

This section describes the possible risks and/or discomforts we anticipate you could experience that are related to the study procedures.

Risks associated with Randomization

The study will choose which treatment you will receive. Usually, your treatment is based on what your doctor thinks is most medically beneficial. In this study, both arms are using medication treatments that are routinely given before and after surgery. However, in this research study, you will be randomly selected for one of two arms. Both arms have risks related to the use of the standard of care medications being used to help lessen the pain. Each of the standard of care medications has its own list of side effects that will be reviewed with you by your study doctor. It is possible that if you are randomized to Group 1 (ERAS), you may experience additional side effects related to the use of these standard medications.

Unknown Risks
There may be other side effects or risks that we cannot predict. Many side effects may go away shortly after the study medication or procedure is stopped. However, in some cases they can be: serious, long-lasting, permanent, and/or fatal.

4. ARE THERE BENEFITS IN TAKING PART IN THE STUDY?

If you agree to take part in this research study, there may or may not be direct medical benefit to you. The possible benefits of taking part in the research study, if you are randomized to ERAS, is that you may experience a decrease in your pain level after surgery, a decrease in constipation, and a decrease in potential dependency on opioid medications. However, no benefit is guaranteed. It is possible that your condition may remain unchanged or even get worse.

We hope the information learned from this research study can show that the use of ERAS may be a better way to manage pain after anorectal surgery compared to the current standard of care..

5. WHY WOULD MY PARTICIPATION BE STOPPED?

Your participation in this study may be stopped at any time by the researcher or the sponsor without your consent for any reason, including:

- The study is stopped or suspended;
- Funding for the study is reduced, stopped or withdrawn;
- If it is in your best interest;
- You do not consent to continue in the study after being told of changes in the research that may affect you;
- You do not follow the study procedures.
- Drug allergy
- Evidence of AKI, Bleeding, or other adverse events from the drugs.
- If you have significant postoperative pain in the control group that is not adequately controlled with opioids and require additional pain medications.
- If you require an additional procedure during the study period.

6. ARE THERE ANY OTHER OPTIONS?

Your participation is voluntary so you have the right to decline to participate or to withdraw from this research study at any time without any penalty or loss of benefits to which you would be entitled outside of the study. Choosing not to participate will not affect the care you receive at Cedars-Sinai Health System.

If you decide not to take part in this study, you have other choices. For example:

- you may choose to be treated following the usual clinical approach which is your treating surgeon will be prescribing you Oxycodone for post-operative pain management after surgery. Additionally, you would be allowed to take oral acetaminophen and ibuprofen over the counter if needed.
- you may choose to take part in a different study at CSMC or elsewhere, if one is available
- you could decide not to be treated.

The researcher will discuss these options and their risks and benefits with you.

7. WILL MY INFORMATION BE KEPT CONFIDENTIAL?

We will do our best to make sure that the personal information collected as part of this study is kept private. However, we cannot guarantee total privacy. A copy of your research consent and authorization forms may be filed in your electronic medical record at CSMC. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other identifiable personal information will not be used. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include: accrediting agencies, government and regulatory groups (such as Food and Drug Administration (FDA), Office for Human Research Protections (OHRP), etc.), safety monitors, companies that sponsor the study, and authorized representatives of the sponsor.

You will be asked to sign a separate "Authorization Form" that outlines with whom your information may be shared for the purposes of this research and under what circumstances.

A description of this clinical trial will be available on http://www.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.

8. WHAT IF I BECOME ILL OR INJURED BECAUSE OF TAKING PART IN THIS STUDY?

Contact your researcher at once if you feel that you are ill or have been injured because of taking part in this study. If it is a medical emergency, call 911 or go to an emergency room. Promptly notify your researcher of your situation at the phone number listed on page 1 of this consent form.

Who pays for my research related illness or injury?
Cedars-Sinai has no plans to pay for costs associated with the treatment of research-related injury or illness. We will make every effort to seek reimbursement from your health plan. However, you will be responsible for any deductibles and co-payments required under your health plan and for any claims ultimately denied by your health plan. Financial assistance may be available under Cedars-Sinai's Charity Care Policy and Procedure. If you feel that you have had a research-related injury and need financial assistance, please contact the IRB Office at 310-423-3783.

9. FINANCIAL CONSIDERATIONS

Costs of Participation

Please review the attached Appendix A flowchart for a listing of items, drugs and services that will be billed to you and/or your insurance and those that will be covered by the study sponsor.

Only items, drugs and services that are reasonable and necessary for your medical care throughout the study will be billed to your insurance. You remain responsible for all deductibles, co-pays, and balances under your health benefit plan. If your insurance company does not pay, you will be billed for those charges. You should check with your health benefit plan if you have questions or concerns about your insurance coverage.

Compensation for Participating
You will not be paid for taking part in this research study.

Financial Interest in the Research
The PI and institution have no potential financial conflict of interest with respect to this study.

10. WHAT IF I HAVE QUESTIONS OR PROBLEMS?

Please contact one of the investigators listed on the first page of this form for questions or concerns about the research.

If you have questions, problems, or concerns that you want to discuss with someone who is not associated with this study, or want to offer suggestions or feedback, please contact:

Cedars-Sinai Human Research Protection Program (HRPP) Phone: (310) 423-3783
Email: ResearchConcerns@cshs.org

The Cedars-Sinai HRPP has been established to protect the rights and welfare of research participants. You may also contact the Cedars-Sinai HRPP if you want to offer input or obtain information regarding the study.

11. CONSENT PROVISIONS

If you sign this form below, it means that:

(1) You have taken the time to carefully read and understand the information presented in this informed consent form; you should discuss it with others, and if appropriate seek a second opinion to make an informed decision;
(2) The information concerning the research study and its involved procedures has been fully explained to you and your questions have been answered to your satisfaction;
(3) You have received and understand all of the information you desire regarding your participation in the research study;
(4) You have considered the potential risks, any anticipated benefits and alternatives (and their relative risks and benefits) of participation;
(5) You are voluntarily agreeing to participate in this research study;
(6) You understand that by consenting to participate in the research, you are not giving up any of your legal rights;
(7) You understand that you have the right to be informed of significant new findings related to this research study which may affect your willingness to continue participating in this study; and
(8) You have been provided with a copy of the "Experimental Subject's Bill of Rights", if applicable to this research study, and have been provided with an opportunity to ask questions regarding the Bill of Rights.

We will give you a copy of this signed and dated consent form and a signed copy of the Experimental Subject's Bill of Rights.

SIGNATURE BY THE PARTICIPANT:

_____	_____	_____
Name of Participant (Print)	Signature of Participant	Date of Signature

SIGNATURE BY THE INVESTIGATOR:

I have personally explained the research to the participant in non-technical terms, answered all questions, and attest that he/she freely consents to participate. The participant has been provided with the Experimental Subject's Bill of Rights.

_____
Name of Investigator (Print)

_____	_____
Signature of the Investigator Who Obtained Consent	Date of Signature

CEDARS-SINAI MEDICAL CENTER

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

In accordance with California Health and Safety Code 24172, any person who is required to consent to participate as a subject in a research study involving a medical experiment or who is requested to consent on behalf of another has the right to:

1. Be informed of the nature and purpose of the experiment.

2. Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized.

3. Be given a description of any attendant discomforts and risks to the subject reasonably to be expected from the experiment.

4. Be given an explanation of any benefits to the subject reasonably to be expected from the experiment, if applicable.

5. Be given a disclosure of any appropriate alternative procedures, drugs or devices that might be advantageous to the subject, and their relative risks and benefits.

6. Be informed of the avenues of medical treatment, if any, available to the subject after the experiment if complications should arise.

7. Be given an opportunity to ask any questions concerning the experiment or the procedure involved.

8. Be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation in the medical experiment without prejudice.

9. Be given a copy of any signed and dated written consent form used in relation to the experiment.

10. Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence on the subject's decision.

_____ _____

Signature of Experimental Subject **Date**

Distribution instruction for researchers:

The signed (i) Consent form, (ii) Authorization for Use and Disclosure of Identifiable Health Information and (iii) "Experimental Subject's Bill of Rights" (the latter required if the research study involves medical interventions) should be distributed to:

1) Medical Chart
2) Research Participant
3) Pharmacy (if a drug study)
4) Principal Investigator's research records (original)

APPENDIX A: FLOWCHART OF PROCEDURES – Medicare Coverage Analysis (MCA) Review

Procedures	Screening Visit	Procedure	Post-op Visit (7 days)	Post-op Visit (30 Days)
Informed Consent	R	-	-	-
Medical record review and data collection: demographics and medical history	R		-	
Physical Exam	S		S	S
Randomization to study groups (Arm 1 OR Arm 2)	R			
Arm 1-Perianal and bilateral pudendal block using bupivacaine, epinephrine and dexamethasone OR		S		
Arm 2-Perianal and bilateral pudendal block using bupivacaine and epinephrine		S		
Anorectal Surgery		S		
Pre-operative and post-operative administration of oral gabapentin, acetaminophen, oral Ketorolac=-Arm 1		S	S	S
Post-operative administration of acetaminophen and ibuprofen over the counter as needed = Arm 2			S	S
Intraoperative: IV Ketorolac, IV Fentanyl (ARM 1)		S		
Intraoperative: IV Fentanyl (ARM 2)		S		
Post-op: Oxycodone pain medication (as needed) and daily MiraLAX, daily milk of magnesia and mineral oil (as needed) both arms			S	S

Pre-op questionnaire: VAS pain scale, baseline nausea, urinary function		R		
Data collection: surgical characteristics		R		
PACU Questionnaire: Pain (VAS) score, nausea score		R		
Post-op Questionnaire: Pain (VAS) score, nausea score, ability to void prior to discharge, pain at defecation questionnaire, first defection			R	
Data collection: PACU IV fluids administered, total narcotic (morphine equivalents) administered		R		
Adverse events		R	R	R
Compliance with medication review[1]			R	R

LEGEND

R = Research item/procedure done only for research purposes and covered by the study

S = Standard of care item/procedure that is part of regular care and billed to the patient/insurance

Footnotes:

1. Any new prescriptions prescribed in the 2-week postoperative period will be recorded, any refills on prescription medications will be recorded.

APPENDIX B: Detailed Description of Common Medical Procedures Performed for Research Purposes and Associated Risks

The procedures listed below are often performed as part of routine care for a person with your condition. They are being repeated, or performed more frequently as part of this research. However, the risks associated with each procedure should be comparable to what you would experience even if you were undergoing the procedure outside this research study.

Study Procedure	Related Risks
Physical Exam: Includes height, weight, vital signs (heart rate and blood pressure)	There are no physical risks associated with these procedures.
Concomitant Medications: You will be asked about your previous and current medications that you take.	There are no physical risks associated with these procedures.
Medical History Review: You will be asked about your medical and surgical history with attention to current and past surgical procedures.	There are no physical risks associated with this procedure.
Questionnaires: You will be asked to complete questionnaires, prior to surgery (pre-op) and after surgery (post-op). We will ask questions to evaluate your pain, nausea, and urinary function. We think it should take about 5 minutes to complete the questionnaire. Questionnaires will ask you to respond to questions about urinary incontinence for example, have you had the sensation of not emptying your bladder? Or have you had a weak urinary stream?	If you feel uncomfortable or embarrassed answering any question, you may skip it. The questionnaire will be labeled with a unique study number that will link your identity so that only the research team can recognize you.
Demographic Information: You will be asked about your age, gender, race, ethnicity	There are no physical risks associated with these procedures.