Study Title:

ID: 15-18354 Programmed Intermittent Bolus Dosing Versus Continuous Epidural Infusion for Epidural Analgesia in Abdominal Surgery.

NCT Number: NCT03307174

Document Approval Date: 7.30.2018

Study Application (Version 1.12)

1.0 General Information

***Enter the full title of your study:**

A prospective, randomized analysis of epidural anesthesia using programmed intermittent epidural boluses versus continuous epidural infusion in patients undergoing abdominal surgery.

***Enter the study number or study alias**

PCEA with PIEB versus CEI
* This field allows you to enter an abbreviated version of the Study Title to quickly identify this study.

2.0 Add Department(s)

2.1 List the departments associated with this study. The Principal Investigator's department should be Primary.:

Primary Dept?	Department Name
○	**UCSF** - *742524* - Colorectal Surg. MB
◆	**UCSF** - *127037* - M_Anesthesia
○	**UCSF** - *707137* - CANCER CENTER GYN ONCOLOGY
○	**UCSF** - *707131* - CANCER CENTER URO SURGERY
○	**UCSF** - *707143* - CANCER CTR GI SURGICAL ONCOLGY

3.0 List the key study personnel: (Note: external and affiliated collaborators who are not in the UCSF directory can be identified later in the Qualifications of Key Study Personnel section at the end of the form)

3.1 *Please add a Principal Investigator for the study:

Behrends, Matthias, MD

Select if applicable

☐ Department Chair ☐ Resident

☐ Fellow

If the Principal Investigator is a Fellow, the name of the Faculty Advisor must be supplied below.

3.2 If applicable, please select the Research Staff personnel:

A) Additional Investigators

Aleshi, Pedram
Other Investigator
Chen, Lee-Lynn

Other Investigator
Haight, Matthew J
Other Investigator
Latronica, Mark
Other Investigator
Naidu, Ramana K
Co-Principal Investigator
Sarin, Ankit, MD, MHA
Other Investigator
Siegmueller, Claas
Other Investigator
Su, Po-Yi Paul
Co-Principal Investigator

B) Research Support Staff

Clelland, Elle N
Study Coordinator
Delgado, Adrian C
Study Coordinator
Ladd, Michael J
Study Coordinator

3.3 *Please add a Study Contact:

Su, Po-Yi Paul

The Study Contact(s) will receive all important system notifications along with the Principal Investigator. (e.g. The project contact(s) are typically either the Study Coordinator or the Principal Investigator themselves).

3.4 If applicable, please add a Faculty Advisor/Mentor:

3.5 If applicable, please select the Designated Department Approval(s):

Gropper, Michael Allan, MD, PhD
Department Chair

Add the name of the individual authorized to approve and sign off on this protocol from your Department (e.g. the Department Chair or Dean).

4.0 Initial Screening Questions - Updated 2015

(Note: You must answer every question on this page to proceed.)

4.1 * PROJECT SUMMARY: (REQUIRED) Give a brief overview of this project (250 words or less). Tell us what this study is about, who is being studied, and what it aims to achieve. If you have an NIH Abstract, paste it here: Click on the orange question mark to the right for more detailed instructions.

Epidurals are an effective means for providing neuraxial anesthesia and analgesia. Prior studies in labor epidurals have demonstrated that a programmed intermittent bolus application of local anesthesia can improve pain control thus reducing the amount of local anesthetic required as well as improve patient

satisfaction when compared to continuous epidural infusions. The effects of programmed intermittent bolus of epidurals compared to continuous epidural infusions in a surgical setting have yet to be elucidated. Our goal is to evaluate the use of programmed intermittent bolus compared to continuous epidural infusion in a surgical patient population. We plan to enroll patients already undergoing surgery under the enhanced recovery after surgery (ERAS) pathways. ERAS pathway surgeries include colorectal, gynecologic, surgical oncology to name a few. The primary endpoints of the study will be the total local anesthetic consumption and total opioid consumption as surragate markers for the quality of epidural anesthesia. Secondary endpoints are pain scores and functional measurements, patient satisfaction, and incidence of hypotension .

4.2 * HUD DEVICE: (REQUIRED) Does this application involve a Humanitarian Use Device (HUD):

- (•) No
- ( ) Yes, and it includes a research component
- ( ) Yes, and it involves clinical care ONLY

4.3 * TYPE OF RESEARCH: (Click the Help link for definitions and guidance): (REQUIRED)

- (•) Biomedical research
- ( ) Social, behavioral, educational, and/or public policy research
- ( ) Hybrid - includes aspects of BOTH types of research (check this option if your research is mainly social /behavioral but also involves specimen collection or blood draws to look at biological measures)

4.4 * SUBJECT CONTACT: (REQUIRED) Does this study involve ANY contact or interactions with participants:

- (•) Yes (including phone, email or web contact)
- ( ) No (limited to medical records review, biological specimen analysis, and/or data analysis)

4.5 * RADIATION EXPOSURE: Does your protocol involve any radiation exposure to patients/subjects EITHER from standard care OR for research purposes (e.g., x-rays, CT-scans, DEXA, CT-guided biopsy, radiation therapy, or nuclear medicine including PET, MUGA or bone scans): (REQUIRED)

- ( ) Yes (•) No

4.6 * RISK LEVEL: (REQUIRED) What is your estimation of the risk level, including all screening procedures and study activities (Help Text updated 9/13):

- ( ) Minimal risk
- (•) Greater than minimal risk

4.7 * REVIEW LEVEL: (REQUIRED) Requested review level (Click on the orange question mark to the right for definitions and guidance):

- (•) Full Committee
- ( ) Expedited
- ( ) Exempt

4.11 * CLINICAL TRIAL: (REQUIRED) Is this a clinical trial? According to The World Health Organization (WHO) and the International Committee of Medical Journal Editors (ICMJE) a clinical trial is:

- **Any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes.**

ICMJE requires registration of a clinical trial in a public database (such as ClinicalTrials.gov) prior to enrollment, for eventual publication of results in member biomedical journals. Guidance: Public Law

110-85 requires that all investigators who perform an *applicable clinical trial* must ensure that the trial is registered on a government web site called ClinicalTrials.gov. The FDA requires registration for "applicable clinical trials," defined as follows:

- **For any trials of drugs and biologics: controlled clinical investigations, other than Phase 1 investigations, of a product subject to FDA regulation.**
- **For trials of biomedical devices: controlled trials with health outcomes of devices subject to FDA regulation, other than small feasibility studies, and pediatric post-market surveillance.**

For additional information on the ClinicalTrials.gov registration process at UCSF and the definition of a clinical trial for purposes of registration, visit the ClinicalTrials.gov section of the UCSF Clinical Research Resource HUB.

(•) Yes ( ) No

Clinical Trial Registration

"NCT" number for this trial:

Pending

If you don't yet have the NCT#, type 'Pending.'

4.12 * CLINICAL TRIAL PHASE (REQUIRED) Check the applicable phase(s) (Help Text updated 9/13):

- [ ] Phase I
- [ ] Phase II
- [ ] Phase III
- [x] Phase IV

4.13 * INVESTIGATOR-INITIATED: (REQUIRED) Is this an investigator-initiated study:

(•) Yes ( ) No

4.14 SCIENTIFIC REVIEW: If this study has undergone scientific or scholarly review, please indicate which entity performed the review (check all that apply):

- [ ] Cancer Center Protocol Review Committee (PRC) (Full approval is required prior to final CHR approval for cancer-related protocols.)
- [ ] CTSI Clinical Research Services (CRS) Advisory Committee
- [ ] CTSI Consultation Services
- [ ] Departmental scientific review
- [ ] Other:

4.15 * STEM CELLS: (REQUIRED) Does this study involve human stem cells (including iPS cells and adult stem cells), gametes or embryos:

(•) No
( ) Yes, and requires CHR and GESCR review
( ) Yes, and requires GESCR review, but NOT CHR review

4.16 * FINANCIAL INTERESTS: (REQUIRED) Does the Principal Investigator and/or one or more of the key study personnel have financial interests related to this study:

( ) Yes (•) No

5.0 Funding

5.1 * FEDERAL FUNDING: (REQUIRED) Is this study currently supported in whole or in part by Federal funding, *even by a subcontract*, OR has it received ANY Federal funding in the past:

○ Yes ◉ No

5.2 * DoD INVOLVEMENT: Is this project linked in any way to the Department of Defense (DoD): (REQUIRED)

○ Yes ◉ No

5.3 SPONSORS: Identify all sponsors and provide the funding details. If funding comes from a Subcontract, please list only the Prime Sponsor:

External Sponsors:

NOTE: It is no longer necessary to add the A or the P Number. iRIS now allows you to link the proposal to the study (see below)!

View Details	Sponsor Name	Sponsor Type	Awardee Institution	Contract Type:	UCSF RAS "P number" or eProposal number	UCSF RAS System Award Number ("A" + 6 digits)
No Sponsor has been added to this IRB Study						

If the funding is coming through UCSF and you don't know the A or P number, you can search the eProposal side for the contract or grant (this does NOT replace adding the sponsor by name above):

Project Status	Proposal Number	Project Title	Principal Investigator
No Projects are Linked to this IRB Study			

Other Funding Sources and Unfunded Research - Gift, Program, or Internal Funding (check all that apply):

- ☐ Funded by gift (specify source below)
- ☐ Funded by UCSF or UC-wide program (specify source below)
- ☐ Specific departmental funding (specify source below)
- ☑ Unfunded (miscellaneous departmental funding)
- ☐ Unfunded student project

6.0 Sites, Programs, Resources, and External IRB Review

6.1 UCSF AND AFFILIATED SITES (check all that apply):

- [ ] UCSF (including Laurel Heights and all the other sites outside the main hospitals)
- [ ] Parnassus
- [x] Mission Bay
- [ ] China Basin
- [ ] Mount Zion
- [ ] Helen Diller Family Comprehensive Cancer Center
- [ ] Langley Porter Psychiatric Institute
- [ ] San Francisco General Hospital (SFGH)
- [ ] SF VA Medical Center (SF VAMC)
- [ ] Blood Centers of the Pacific (BCP)
- [ ] Blood Systems Research Institute (BSRI)
- [ ] Fresno Community Medical Center
- [ ] Gallo
- [ ] Gladstone
- [ ] Jewish Home
- [ ] Institute on Aging (IOA)
- [ ] SF Dept of Public Health (DPH)

6.2 LOCATIONS: At what locations will study visits and activities occur:

UCSF Bakar Cancer Hospital

6.3 OFF-SITE PROCEDURES: Will any study procedures or tests be conducted off-site by non-UCSF personnel:

- ( ) Yes
- (•) No

6.4 RESEARCH PROGRAMS: Check any UCSF research programs this study is associated with:

- [ ] Cancer Center
- [ ] Center for AIDS Prevention Sciences (CAPS)
- [ ] Global Health Sciences
- [ ] Immune Tolerance Network (ITN)
- [ ] Neurosciences Clinical Research Unit (NCRU)
- [ ] Osher Center
- [ ] Positive Health Program

6.5 * CTSI CRS SERVICES: (REQUIRED) Will this study be carried out at one of the UCSF Clinical Research Services (CRS) units or utilize CRS services:

- ( ) Yes
- (•) No

6.6 * MULTI-CENTER TRIAL: (REQUIRED) Is this a multicenter research trial? By multi-center trial, we mean a study where the protocol is developed by an industry sponsor, consortium, a disease-group, etc., who then selects sites across the nation or in different countries to participate in the trial. The local sites do not have any control over the design of the protocol.

- ( ) Yes
- (•) No

6.7 OTHER SITE TYPES: Check all the other types of sites not affiliated with UCSF with which you are cooperating or collaborating on this project: Do NOT check any boxes below if this is a multi-center clinical trial, UCSF is just one of the sites, and neither UCSF nor its affiliates are the coordinating center.

☐ Other UC Campus

☐ Other institution

☐ Other community-based site

☐ Foreign Country

☐ Sovereign Native American nation (e.g. Navajo Nation, Oglala Sioux Tribe, Havasupai, etc.)

6.10 * RELYING ON AN EXTERNAL IRB: Does this application include a request to rely on an a central IRB (other than the NCI CIRB) or an external IRB (UC, commercial, or institutional): (REQUIRED)

○ Yes ◉ No

7.0 Research Plan and Procedures

7.1 This new consolidated section requests information about:

- **Hypothesis**
- **Aims**
- **Study Design**
- **Background and Significance**
- **Preliminary Studies**
- **Procedures**
- **Statistical Methods**
- **References**

Later sections include:

- **Drugs and Devices**
- **Sample Size, Eligibility, and Subjects**
- **Recruitment and Consent**
- **Risks and Benefits**
- **Data and Safety Monitoring Plan**
- **Confidentiality, Privacy and Security**
- **Financial Considerations**
- **Qualifications of Personnel**
- **Other Approval and Registrations**

7.2 HYPOTHESIS: Describe the hypothesis or what the study hopes to prove (Help Text updated 9/13):

Null hypothesis: There is no difference in total local anesthetic and opioids required when comparing patients receiving epidural anesthesia using either programmed intermittent epidural boluses or continuous epidural infusions following abdominal surgery.

7.3 AIMS: List the specific aims:

The aim of this study is to prove the superior efficacy of programmed intermittent bolus administration of epidural medications compared to traditional continuous infusions in providing adequate post-operative analgesia and patient satisfaction in a surgical patient population.

7.4 DESIGN: Briefly describe the study design (e.g., observational, interventional, randomized, placebo-controlled, blinded, cross-over, cross-sectional, longitudinal, pharmacokinetic, etc.):

This is a prospective, randomized controlled study of programmed intermittent bolus administration of local anesthetic in epidural anesthesia compared to traditional continuous infusions for patients undergoing surgery as part of the enhanced recovery after surgery pathway.

As part of the UCSF Enhanced Recovery After Surgery (ERAS) pathway, all patients routinely treated with thoracic/lumbar epidural anesthesia for post-operative analgesia. The planned investigation does not change is approach, but compares solely two different modalities how epidural medications are administered. The study ends when the catheters are removed which is most often on post-operative day two, but can be later in case the patient may still benefit from epidural anesthesia.
During the duration of the treatment with epidural anesthesia, enrolled patients will be randomized to receive either programmed intermittent bolus or continuous epidural administration of the local anesthetic ropivacaine (0.0625%) with fentanyl (2ug/ml). In addition to this maintenance administration of local anesthetic, the patient are also also able to apply additional (demand) boluses of epidural medication by pressing a button. This technique, called patient- controlled epidural anesthesia (PCEA), is routinely used in all patients with epidural catheters and allows patients to receive additional medication in the event they experience discomfort. If the patients have still pain not covered by epidural anesthesia, they have access to additional RN-administered opioid pain medication. The normally used drugs for such treatment are oxycodone p.o. and hydromorphone i.v. However, other opioids could be used in this context and all opioid use would be quantified using a conversion to oral morphine equivalents. The primary outcomes of the study will be the total amount of local anesthetic administered and opioid requirements (oral morphine equivalents). Secondary outcomes arede: numeric pain rating scores (should not be different as patients have access to additional analgesic medication), number of patient attempts to trigger additional PCEA boluses, overall patient satisfaction assessed through validated questionnaires, and incidence of hypotension.

7.5 BACKGROUND AND SIGNIFICANCE: Briefly provide the background and significance of this study (e.g. why is this study needed) (space limit: one half page):

If this is a first in humans study, please summarize the safety data from the animal studies. For pediatric drug or device studies, please identify if this is the first study in pediatric populations.

Programmed intermittent bolusing of epidurals have been shown in the labor analgesia setting to have significantly decreased in total local anesthetic consumption as well as significantly higher overall patient satisfaction scores as compared to traditional continuous infusions. Whether these observations apply to post-surgical analgesia settings and post-surgical populations have yet to be elucidated. Addressing the aforementioned question is of clinical importance as this may represent an avenue for the improvement of post-surgical analgesia that is not dependent on the use of opioid based approaches. The planned investigation would be the first study to investigate the use of programmed intermittent bolusing of epidurals in surgical patient populations and in surgical
analgesia.

7.6 PRELIMINARY STUDIES: Briefly summarize any preliminary studies relevant to your proposed research (space limit: one half page):

Prior studies in the use of programmed intermittent epidural bolusing has been in the labor anesthesia literature. Wong et al (2006) showed in a randomized controlled trial that there was significantly less local anesthesia consumption, less requirement for manual rescue bolus, and higher satisfaction scores in the programmed intermittent epidural bolus group compared with the continuous infusion group. Since then numerous other randomized controlled trials were conducted in laboring women and a meta-analysis conducted in 2013 by George et al further supported the observation of less local anesthetic usage and higher maternal satisfaction score in the programmed intermittent bolus group.

7.8 * COMMON RESEARCH ACTIVITIES: Types of research activities that will be carried out. Check all that apply and describe in more detail in the 'Procedures / Methods' section: (REQUIRED)

- [x] Interviews, questionnaires, surveys
- [ ] Educational or cognitive tests
- [ ] Focus groups
- [x] Observation
- [x] Non-invasive imaging or testing (MRI, EEG, pulse oximetry, etc.)
- [ ] Administration of contrast agent
- [ ] Imaging procedures or treatment procedures that involve radiation (x-rays, CT scans, CT-guided biopsies, DEXA scans, MUGA or PET scan)

- [ ] Biopsy conducted solely for research purposes
- [ ] Use of placebo
- [ ] Sham surgical procedure
- [ ] Collection of data from wearable tech such as Fitbit, Apple Watch, Garmin, motion actigraphs, etc.)
- [ ] Fitness tests or other exertion activities
- [ ] Use of mobile health apps or other apps
- [ ] Social media-based research activities
- [ ] None of the above

7.9 * PROCEDURES / METHODS: (REQUIRED)

For clinical research, list all study procedures, tests and treatments required for this study, including when and how often they will be performed. If there are no clinical procedures, describe the research activities.

If some of the activities would occur even if the person were not in the study, as in the case of treatment or tests performed for diagnostic purposes, clearly differentiate between those activities that will be done solely for research purposes and those that are happening as part of routine care.

Examples may include:

- additional scans outside standard clinical diagnosis or monitoring
- additional biopsies to collect tissue for research
- extra clinic visits
- extra lab tests not required for clinical care

If you have a procedure table, attach it to the submission with your other study documents.

All study participants will complete a questionaire that includes their pain history, an anxiety and depession questionaire (Hospital Anxiety and Depression Scale) and the WHO Disability Assessment Schedule 2.0 (WHODAS 2.0). Patients will be block randomized to the programmed intermittent bolus group or continuous infusion group. As part of the existing ERAS pathways, all patients will receive a thoracic/lumbar epidural catheter prior to their scheduled surgical procedure depending on the anticipated surgical incision site. Both groups will receive the same standard concentration of local anesthestic (0.0625% ropivacaine) and opioid (fentanyl 2ug/mL) based epidural mix. A total of 8mL of the epidural mix will be adminstered every hour either as a continuous infusion (8mL/hr) or programmed intermittent epidural bolus (4mL bolus every 30 min) based on the study participant's randomization. The epidural will be started in the OR, prior to the end of the surgical procedure at the discretion of the intraoperative anesthesia provider.
The clinical investigator who enrolled the patient will write the epidural infusion orders. A PACU nurse will be programming the pump following hospital policies. The attending in the acute pain service will be informed about the enrollment of the patient in the study to ensure the pain service has all the information needed to ensure the best pain control to the patient in accordance with the study protocol. The display of the pump will be covered with a removable cover to make sure that the patient will stay blinded about the treatment group. The epidural pumps will subsequently be managed by the acute pain service, not the study investigators. The study protocol allows the reduction of epidural flow rates from 8ml to 6ml/h (from 4ml q30 to 3 ml q30 min in the bolus group) in case of hypotension.

Patients will have the option to administer patient controlled epidural analgesia (PCEA) in addition to the basal rate. For continuous epidural infusion group, they can receive additional 2ml every 15 minutes (lock out period) for a total of 16ml/hr (8ml/hr from continuous infusion and up to 8ml from PCEA). To match the total epidural volume in the programmed intermittent bolus group, they can receive additional 2ml

using a lock out period of 10 minutes. Because 4ml of epidural is bolused every 30 min and a PCEA bolus cannot coincide with the basal bolus doses, the shortend lock out period is necessary to make sure the patient can still receive the same four additional 2ml PCEA boluses as the continuous infusion group.

In addition, patients will be able to receive additional physician manual boluses, IV opioid medications from nursing staff, adjunct medications as per standard UCSF ERAS protocol. Hypotension and itching are some common adverse reactions to epidual analgesia; we will treat and document these episodes as per prexisting UCSF acute pain service epidural protocol.

Outcome measures will be total local anesthetic use (charted by nursing staff each shift as part of routine care), numeric rating scale (charted by nursing staff as part of routine care), total PCEA button presses (recorded on epidural pump), anxiety and functional measures (WHODAS2.0, brief pain inventory, HADS survey) to be measured on post operative day 1 and 2. Incidence of hypotension (charted by nursing staff as part of routine care).

7.10 STANDARD CLINICAL PRACTICE: To what extent, if any, do the planned research procedures differ from the care that people would otherwise receive at this institution or the study site if not being done locally:

The proposed study tries to maintain the care that patients would otherwise receive at UCSF. The differences would be in the use of randomized assignment to programmed intermittent bolus of epidural or continuous epidural infusion. As a measure of the efficacy of the different study arms, additional questionnaires, interviews listed below differ from standard clinical practice.

All other anesthetic interventions, including the placement and use of an epidural catheter, the monitors, safety parameters, availability to pain physicians, supplemental pain medications are consistent with existing standard clinical practice.

7.11 INSTRUMENTS: List all questionnaires, surveys, interview, or focus group guides that will be used for this study:

A brief validated questionnaire (WHO diability assessment schedule 2.0; hospital anxiety and depression score; brief pain inventory) will be adminstered at the time of enrollment into the study. During each 24-hour period that the patient has the epidural in place, an abbreviated brief pain inventory (abbreviated to the inpatient population) will be administered. At the end of the study, prior to discharge, the patients will be handed another questionaire to assess the quality of pain control and patient satisfaction using the expanded brief pain inventory. All the aforementioned surveys are previously published and validated questionnaires.

Attach any unpublished instruments in the 'Other Study Documents' section of the Initial Review Submission Packet form after completing the study application. Published instruments should NOT be attached.

7.12 * BIOSPECIMEN COLLECTION: Are you drawing any blood or collecting other biosamples (e.g. tissue, buccal swabs, urine, saliva, hair, etc.): (REQUIRED)

○ Yes ◉ No

7.25 STATISTICAL METHODS: Briefly summarize the methods and types of analyses that will be performed:

The study is designed as a prospective, randomized, two treatment parallel study.
All patient description as well as outcome variables will compared between groups using appropriate tests, including standard unpaired t-test for continuous variables, chi square tests for categorical variables, and ANOVA for variables with repeated measurements. Post hoc test will be applied if appropriate to assess for statistically significant differences between the two groups.

7.26 REFERENCES: List only the 5-10 most relevant references (a separate bibliography can be attached

for reference purposes if this study involves novel approaches, agents, or an emerging technology that the IRB may not be familiar with):

Capogna G, Camorcia M, Stirparo S, Farcomeni A. Programmed intermittent epidural bolus versus continuous epidural infusion for labor analgesia: the effects on maternal motor function and labor outcome. A randomized boule-blind study in nulliparous women. Anesth Analg. 2011;113:826-31.

George RB, Allen TK, Habib AS. Intermittent epidural bolus compared with continuous epidural infusion for labor analgesia: a systematic review and meta-analysis. Anesth Analg. 2013;116:133-44.

Hogan Q. Distribution of solution in the epidural space: examination by cryomicrotome section. Reg Anesth Pain Med. 2002;27:150-6.

Kang S, Jeon S, Choe JH, Bang SR, Lee KH. Comparison of analgesic effects of programmed intermittent epidural bolus and continuous epidural infusion after total knee arthroplasty. Korean J Anesthesiol. 2013; 65:S130-1.

Taboada M, Rodriguez J, Bermudez M, Amor M, Ulloa B, Aneiros F, et al. Comparison of continuous infusion versus automated bolus for postoperative patient-controlled analgesia with popliteal sciatic nerve catheters. Anesthesiology. 2009;110:150-4.

Wong CA, Ratliff JT, Sullivan JT, Scavone BM, Toledo P, McCarthy RJ. A randomized comparison of programmed intermittent epidural bolus with continuous epidural infusion for labor analgesia. Anesth Analg. 2006;102:904-9.

Wong CA, McCarthy RJ, Hewlet B. The effect of manipulation of the programmed intermittent bolus time interval and injection volume on total drug use for labor epidural analgesia: a randomized control trial. Anesth Analg. 2011;112:904-11.

8.0 Drugs and Devices

8.1 * DRUGS AND/OR BIOLOGICS: Are you STUDYING any drugs and/or biologics that are either approved or unapproved: (REQUIRED)

(•) Yes ( ) No

8.2 LIST THE DRUGS/AGENTS: List the drugs or biologics that will be studied:

View Details	Drug Name	FDA Approved	A new drug or a new use of approved drug:	IND Number
⊟	**Trade Drug Name:** NAROPIN **Generic Drug Name:** ROPIVACAINE HYDROCHLORIDE MONOHYDRATE **Investigational Drug Name:**	Yes	No	

Trade Drug Name:	NAROPIN
Generic Drug Name:	ROPIVACAINE HYDROCHLORIDE MONOHYDRATE
Investigational Drug Name:	
Identify the name of the manufacturer or source of investigational drug/biologic:	
Is the drug supplied at no cost?	Yes
Is the Drug FDA Approved:	Yes
Is this a new drug or a new use of an already approved drug	No

Is an IND necessary	No
IND Number	
Who holds the IND:	N/A
IND details:	
If FDA Approved and an IND is not required, Please provide a rationale for exemption:	
Are you currently using this IND in another research project?	No
If yes, list the IRB Number(s):	
Will the investigational pharmacy be dispensing?	No
If the source is not a FDA licensed facility, provide details regarding the purity, quality, stability and sterility of the investigational drug /biologic:	

⊟	**Trade Drug Name:** FENTANYL **Generic Drug Name:** FENTANYL CITRATE **Investigational Drug Name:**	Yes	No	

Trade Drug Name:	FENTANYL
Generic Drug Name:	FENTANYL CITRATE
Investigational Drug Name:	
Identify the name of the manufacturer or source of investigational drug/biologic:	
Is the drug supplied at no cost?	Yes
Is the Drug FDA Approved:	Yes
Is this a new drug or a new use of an already approved drug	No
Is an IND necessary	No
IND Number	
Who holds the IND:	N/A
IND details:	
If FDA Approved and an IND is not required, Please provide a rationale for exemption:	
Are you currently using this IND in another research project?	No
If yes, list the IRB Number(s):	
Will the investigational pharmacy be dispensing?	No
If the source is not a FDA licensed facility, provide details regarding the purity, quality, stability and sterility of the investigational drug /biologic:	

8.3 * MEDICAL DEVICES: Are you STUDYING any medical devices, in vitro diagnostics, or assays that are either approved or unapproved:(REQUIRED)

- ○ Yes
- ◉ No

8.6 * EXPANDED ACCESS: Is this an expanded access or compassionate use protocol, meaning the primary purpose is to dignose, monitor or treat a patient's condition, rather than the collection of safety and efficacy data of the experimental agent or device: (REQUIRED)

- ○ Yes
- ◉ No

9.0 Sample Size and Eligibility Criteria

9.1 ENROLLMENT TARGET: How many people will you enroll:

120

If there are multiple participant groups, indicate how many people will be in each group:

9.3 SAMPLE SIZE JUSTIFICATION: Explain how and why the number of people was chosen. For multi-site studies, this is referring to the number that will be enrolled across all sites:

Based on labor analgesia literature, the median local bupivacaine dose per hour of analgesia was 10.5mg /hr with 95% confidence interval of 9.5 - 11.8mg/hr compared with continuous infusion group of 12.3mg /hr with 95% confidence interval of 10.5 - 14.0mg/hr. We expect similar effective size (0.6). With a power of 80% and accepting an alpha error of 0.05, we need 44 patients in each group.

In order to compensate for incomplete data collection, we estimated a total of 120 patients, 60 patients in each group should be enrolled.

9.4 * PARTICIPANT AGE RANGE: Eligible age ranges: (REQUIRED)

- ☐ 0-6 years
- ☐ 7-12 years
- ☐ 13-17 years
- ☑ 18-64 years
- ☑ 65+

9.5 * STUDY POPULATIONS: Data will be collected from or about the following types of people (check all that apply): (REQUIRED)

- ☑ Inpatients
- ☐ Outpatients
- ☐ Family members or caregivers
- ☐ Providers
- ☐ People who have a condition but who are not being seen as patients
- ☐ Healthy volunteers
- ☐ Students
- ☐ Staff of UCSF or affiliated institutions
- ☐ None of the above

9.6 * SPECIAL SUBJECT GROUPS: Check the populations that may be enrolled: (REQUIRED)

- [ ] Children / Minors
- [ ] Subjects unable to consent for themselves
- [ ] Subjects unable to consent for themselves (emergency setting)
- [ ] Subjects with diminished capacity to consent
- [ ] Subjects unable to read, speak or understand English
- [ ] Pregnant women
- [ ] Fetuses
- [ ] Neonates
- [ ] Prisoners
- [ ] Economically or educationally disadvantaged persons
- [x] None of the above

9.7 INCLUSION CRITERIA: Briefly describe the population(s) that will be involved in this study. Include anyone that data will be collected from or about (e.g. patients, healthy controls, caregivers, providers, administrators, students, parents, family members, etc.):

Patients age 18 years of age or older, American Society of Anesthesia physical classification I - III, scheduled for abdominal surgery with epidural anesthesia as part of the perioperative treatment plan. Surgery at UCSF Mission Bay hospital.

9.8 EXCLUSION CRITERIA: List any exclusion criteria (e.g. reasons why someone would not be included in the study):

Age younger than 18 years of age, non-English speaking, contraindication for neuraxial anesthesia (such as, but not limited to coagulopathy, infection at site, allergy to local anesthetic), preexisting neurologic deficits, inability to consent due to cognitive dysfunction, patients with pain numeric rating score > 5 each day for greater than 3 months, daily opioid consumption > 100 oral morphine equivalents for 14 consecutive days prior to surgery, patient refusal.

9.9 * RESEARCH CONDUCTED ON PATIENT CARE WARDS: Do any study activities take place on patient care units: (REQUIRED)

(•) Yes ( ) No

Attach a letter of acknowledgement for the study from the involved patient care manager. If you don't know who the patient care manager is, click here to send an email to the nursing group.

10.0 Recruitment and Consent

10.1 * RECRUITMENT METHODS: What kinds of methods will be used to identify potential participants for recruitment (check all that apply): (REQUIRED)

- [x] Medical records review
- [ ] Recruitment registry
- [ ] Re-contact of participants from the investigators' previous studies
- [ ] Referrals from colleagues (attach the 'Dear Colleague' letter or other recruitment materials you will provide to colleagues)
- [ ] Referrals from the community / word of mouth
- [ ] Advertisements (flyers, brochures, radio or t.v. ads, posting on clinical research sites or social media, presentation of the study at community events/media, etc.)
- [ ] Online recruiting tool such as TrialSpark
- [ ] CTSI Recruitment Services unit
- [x] Other method (describe below)

* Provide details about the other recruitment methods: **(REQUIRED)**

We will plan to screen eligible patients based from their encounters with the anesthesia Prepare appointment as part of their preparation for upcoming surgery. We will recruit them at that time or contact them after they have been identified. Additionally, patients can also be identified by using the surgical scheduling board for specific procedures.

10.2 * SEARCHING OF MEDICAL RECORDS: (REQUIRED)

Whose patients are they:

- [x] Investigators' own patients or patients seen within the same practice
- [ ] Patients not under the care of the investigators

How and by whom will records be accessed and searched (check all that apply):

- [x] Self-search in APeX or other medical records source
- [ ] Self-search using UCSF's Research Cohort Selection Tool
- [ ] CTSI Consultation Service Recruitment Services
- [ ] UCSF Academic Research Services (ARS)
- [ ] University of California Research Exchange (UC ReX)
- [ ] Other method (describe below)

10.3 DETERMINATION OF ELIGIBILITY: How, when, and by whom will eligibility for recruitment be determined:

Eligibility will be determined after patients undergo a pre-operative anesthesia evaluation by a nurse practicioner or anesthesia provider prior to surgery. This appointment varies from a few days to a few weeks before the scheduled operation. Eligible paitents will be identified by anesthesia providers involved in the study.

10.4 INITIATION OF CONTACT: Who initiates contact (check all that apply):

- [x] Investigators/study team
- [ ] UCSF recruitment unit (e.g. CTSI Consultation Services)
- [ ] Potential participant

10.5 * HOW IS CONTACT INITIATED: (check all that apply): (REQUIRED)

- [ ] In person
- [x] Phone
- [ ] Letter / email
- [ ] Website or app
- [ ] Other (explain below)

Attach the telephone recruitment script in the Other Study Documents section of the Initial Review Submission Packet Form. If potential participants will initiate contact, attach the telephone screening script that will be used to provide more information about the study and determine if callers are eligible to participate.

10.6 RECRUITMENT PLAN: Based on the checkboxes you chose above, please provide a narrative describing your recruitment plan. We want to know:

- **Who is conducting the search for potential participants, and how?**
- **How are potential subjects being approached for recruitment? By whom, and when?**

If there will be more than one participant group (e.g. patients, healthy controls, caregivers, family members, providers, etc.), provide details about the recruitment plans for each group. (Recommended length - 100-250 words)

Patients eligible for this study will be informed of the study by an anesthesia provider participating in the study after their initial pre-operative anesthesia evaluation, but prior to day of surgery. Patient who meet the inclusion and non-inclusion criteria will receive a phone call from one of the study investigators explaining the study prior to the day of surgery. The consent form will be offered to them via mail or e-mail prior to the day of surgery to allow ample time to review and consider the patient's participation in the study. On the day of surgery, information about the study will be reiterated by an anesthesia provider and all questions will be ansered prior to randomization.

10.7 * CONSENT METHODS: How will permission to participate (i.e., informed consent) be obtained from each potential participant. If there will be multiple groups and different plans for consenting each, check all that apply. See the orange Help bubble to the right for more detailed guidance. Participants will (check all that apply): (REQUIRED)

- [x] Sign a consent form at the end of the consent discussion (signed consent)
- [ ] Provide online 'eConsent' using DocuSign or another E-Signature system
- [ ] Click through a link in a survey or email after reading about the study and then complete the study online (electronic consent)
- [ ] Be told about the study and be given a handout/information sheet and be asked if they agree to participate (verbal consent)
- [ ] Complete the study activities and turn in materials, as in the case of a completed survey that is placed in a drop box or mailed to the study team (implied consent)
- [ ] Not be able to provide consent and will have a family member consent for them, as in the case of a critically ill or unconscious patient (surrogate consent)
- [ ] Not be able to provide consent (emergency waiver of consent - allowed for minimal risk research or greater than minimal risk research with an approved community consultation plan)
- [ ] Not know about the study, as in the case of chart reviews or observations of public behavior (waiver of consent)
- [ ] Other method (describe below)

Attach your consent form, information sheet, or electronic consent text in the Informed Consent Documents section of the Initial Review Submission Packet Form.

10.8 * CONSENT PROCESS: Describe the process for obtaining informed consent, including details such as who will have the consent discussion and when participants will be asked to sign the consent form in relation to finding out about the study. For online and electronic consent, explain that process in detail: (REQUIRED) If there are multiple groups being consented differently, provide details about the consent process for each group. If you are relying on verbal or implied consent, provide details about how that will happen. We encourage researchers to review UC Irvine's excellent guidance on obtaining informed consent.

Potential patients meeting the inclusion/non-inclusion criterias will be contacted via telephone prior to their day of surgery by a member of the research team. At this time, the research team will introduce themselves, confirm the surgery type and surgery day and any other clarifying information regarding the patient's past medical information as it is relevant to the study. If there are no contraindications for the patient for the study, the patient will be introduced to the study. We will discuss the study's goals, risks and benefits. If the patient agrees to be a participant, the research team will offer to send them a consent via mail or email prior to the date of surgery. A formal written consent will be obtained the day of surgery.

Potential study participatnets will be introduced to the study after their routine pre-operative anesthesia evaluation verbally. They will also be offered a written copy of the consent form via mail or email prior to the day of surgery. This consent form includes the name and contact information of the study investigator. On the day of surgery, an anesthesia attending will review this information, answer any questions, and assure that there is a written consent prior to randomization.

* It is important that the people obtaining consent are qualified to do so. Briefly describe the training and experience these individuals have in obtaining informed consent: **(REQUIRED)**

All study personel involved in the enrollment process have prior experience in enrolling patients for clinical studies. They are either fully trained, board certified anesthesiologists, anesthesia residents involved in the design of this study (P.S), or study coordinators currently enrolling patients in other ongoing clinical studies done by our department.

10.9 * CONSENT COMPREHENSION: Indicate how the study team will assess and enhance the subjects' understanding of study procedures, risks, and benefits prior to signing the consent form (check all that apply): (REQUIRED) Tip: Review the Consent Comprehension - Learning Notes in the Help bubble at the right for specific questions that can be asked to assess comprehension, consider using UCSD's Brief Assessment of Capacity to Consent (UBACC), and review UC Irvine's guidance on Subject Consent Assessment for more detail on how to conduct the assessment.

- [x] The study team will engage the potential participant in a dialogue, using open-ended questions about the nature of the study or the experimental treatment, the risks and benefits of participating, and the voluntary nature of participation
- [ ] Potential participants will be asked or shown a series of questions to assess their understanding of the study purpose, procedures, risks and benefits, as well as the voluntary nature of participation (especially appropriate when the consent process happens online or through a mobile health app)
- [ ] Other method (describe below):

10.13 TIME: What is the estimated time commitment for participants (per visit and in total):

IMPORTANT TIP: Ensure this information is consistent with the information provided in the consent form.

An initial phone call to the patient to introduce the study to the patient will take approximately 10 minutes. We will offer the informed consent form to eligible patients via mail or e-mail prior to the day of surgery. On the day of surgery, additional time may be allotted if needed to answer any additional questions from the patient. Epidural placement will follow pre-established ERAS protocol as per institution guidelines and should not distrupt the current work flow of the perioperative setting. Follow up with regards to pain scores, hypotension, amount of adjunct analgesics will be obtained via chart biopsy. Patient satisfcation will be obtained at the time of discontinuation of the epidural, which should take approximal 5 minutes. Total face-time will be approximately 15 minutes. Epidurals are removed typically on the morning of post-operative day 2, however some may be removed earlier or later pending clinical scenario.

11.0 Waiver of Consent/Authorization for Recruitment Purposes

This section is required when medical records may be reviewed to determine eligibility for recruitment.

11.1 * PRACTICABILITY OF OBTAINING CONSENT PRIOR TO ACCESS: Study personnel need to access protected health information (PHI) during the recruitment process and it is not practicable to obtain informed consent until potential subjects have been identified: (REQUIRED)

- (•) Yes

If **no**, a waiver of consent/authorization is NOT needed.

11.2 * RISK TO PRIVACY: A waiver for screening of health records to identify potential subjects poses no more than minimal risk to privacy for participants:

- (•) Yes

If **no**, a waiver of authorization can NOT be granted.

11.3 * RIGHTS/WELFARE: Screening health records prior to obtaining consent will not adversely affect subjects' rights and welfare:

(•) Yes

If **no**, a waiver of authorization can NOT be granted.

11.4 * IDENTIFIERS: Check all the identifiers that will be collected prior to obtaining informed consent:

- [x] Names
- [x] Dates
- [x] Postal addresses
- [x] Phone numbers
- [x] Fax numbers
- [x] Email addresses
- [ ] Social Security Numbers*
- [x] Medical record numbers
- [ ] Health plan numbers
- [ ] Account numbers
- [ ] License or certificate numbers
- [ ] Vehicle ID numbers
- [ ] Device identifiers or serial numbers
- [ ] Web URLs
- [ ] IP address numbers
- [ ] Biometric identifiers
- [ ] Facial photos or other identifiable images
- [ ] Any other unique identifier
- [ ] None

Note: HIPAA rules require that you collect the minimum necessary.

11.5 * HEALTH INFORMATION: Describe any health information that will be collected prior to obtaining informed consent:

All study investigators have access to the surgery schedule at the UCSF Mission Bay. Patient that are potential research participants (scheduled for surgeries with pre-existing ERAS pathways) will be identified. Research members will then collect the patient's name, medical record number, date of surgery. The patient's medical record will then be reviewed to screen for inclusion and exclusion criteria. If the patient is a potential candidate for enrollment, based on our inclusion/noninclusion criteria, will will retrieve the contact information to contact the patient.

Note: HIPAA requires that you collect the minimum necessary.

11.6 * DATA RETENTION/DESTRUCTION PLAN: Describe your plan to destroy any identifiable data collected to determine eligibility for recruitment. This should be done at the earliest opportunity. If you plan to retain identifiable recruitment data, provide the justification for doing so:

All identifying information will be destroyed at the earliest opportunity upon completion of the study.

12.0 Risks and Benefits

12.1 RESEARCH-RELATED RISKS: Check if your study involves any of these specific research-related risks

to participants that may need to be disclosed in the consent form:

- [x] For interventional studies, risk that the regimen may be more harmful or less effective than other available interventions
- [ ] Risks associated with radiation exposure for imaging studies specifically for research purposes
- [ ] Risks associated with the administration of contrast agent for imaging studies
- [ ] Risks associated with withholding of treatment or discontinuation of current treatment (e.g., washout period is required by the study protocol)
- [ ] For randomized, placebo-controlled trials, possible temporary or permanent health consequences from the deprivation of effective therapies during the placebo administration period
- [ ] For studies involving a sham surgical procedure, the risk that participants may experience increased morbidity without the possibility of benefit
- [ ] Risks associated with modification or extension of a surgical procedure primarily for research purposes (e.g. risks associated with prolonging anesthesia, time in the operating room, etc.)
- [ ] Risk of pain or physical discomfort caused by the research intervention
- [ ] Possible personal discomfort due to sensitive topics (stress, embarassment, trauma)

* For any boxes checked above, describe how you will minimize these risks and discomforts, e.g., adding or increasing the frequency of monitoring, additional screening to identify and exclude people with diminished kidney or liver function, or modification of procedures such as changing imaging studies to avoid giving contrast agent to people who are more likely to suffer side effects from it, etc.: **(REQUIRED)**

Participants in the study have the risk that their study intervention (local anesthesic administration by bolus application or continuous infusion) results in inferior pain control. To ameliorate this risk we are firstly offering all patients the ability to obtain addtional (demand) bolus administrations of local anesthetic and fentanyl through their epidural catheter. Secondly, all patients will have additional analgesics ordered in case they require additional pain control. We expect that all patients will be offered excellent pain control. For this reason, we did not choose pain scores as primary endpoint (we don't expect any differences here), but the need to administer additional analgesics.

12.2 RISKS: Describe any anticipated risks and discomforts not listed above:

There are risks associated with the placement and use of epidural anesthesia. However, this study will only performed in patients who have already consented to the current standard of care in the ERAS pathways. ERAS pathways routinely includes the use of epidural anesthesia. Patients in this study will be seen daily by the study investigators as well as the acute pain service at Mission Bay. They will routinely be asked for side effects of regional anesthesia such as hypotension, itching and the catheter site will be inspected. In case of hypotension with a mean arterial blood pressure <60 mmHg, nursing orders to contact the primary service and the acute pain service for appropriate clinical response remain in place.

12.3 MINIMIZING RISKS: Describe the steps you have taken to minimize the risks/discomforts to subjects. Examples include:

- **designing the study to make use of procedures involving less risk when appropriate**
- **minimizing study procedures by taking advantage of clinical procedures conducted on the study participants**
- **mitigating risks by planning special monitoring or conducting supportive interventions for the study**
- **having a plan for evaluation and possible referral of subjects who report suicidal ideation**

There will be no interference with the care of the patient. The treatment of enrolled patients is not different from patients who do not participate in the study. We have already been using the programmed intermittent bolus function successfully in these patients, but it always happened at the descretion of the ordering anesthesia provider.
All procedures will be performed by or under direct supervision of an anesthesiology attending as per current institutional protocol. Medication changes to the epidural solution will be handled by physicians only as per current institutional protocol.

Patient data remains confidential and de-identified. Only encrypted computers will be used for data collection and management.

12.4 RESOURCES: Describe the resources in place to conduct this study in a way that assures protection of the rights and welfare of participants: These resources typically include appropriately trained and qualified personnel (in terms availability, number, expertise and experience), funding, space, equipment, and time to devote to study activities. Depending on the nature of the research study, investigators should consider the proximity or availability of critical resources that may be essential to the safety and welfare of participants, such as

- **the proximity of an emergency facility for care of participant injury**
- **availability of psychological support after participation**
- **resources for participant communication, such as language translation services**

The treatment of study patients does not deviate from our current clinical practice. The additional riks to the wellfare of the patients should be minimal.
The use of a study coordinator facilitates patient enrollment and should minimize delays in the clinical care of the patients. All procedures the patients are undergoing are part of their regular medical care. The only additional study interventions are the programming of the pump, the follow visits and the follow up interview.
To protect the patient's privacy and medical information, all study documentation will be secured in a locked file cabinet. Data will be collected using RedCap. Only encrypted computer will be used.

12.5 * BENEFITS: (REQUIRED) Note: These are the benefits that the IRB will consider during their review. They are not necessarily appropriate to include in the consent form.

Possible immediate and/or direct benefits to participants and society at large (check all that apply):

- [x] Positive health outcome (e.g. improvement of condition, relief of pain, increased mobility, etc.)
- [ ] Closer follow-up than standard care may lead to improved outcomes or patient engagement
- [ ] Health and lifestyle changes may occur as a result of participation
- [x] Knowledge may be gained about their health and health conditions
- [ ] Feeling of contribution to knowledge in the health or social sciences field
- [ ] The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children
- [ ] Other benefit (describe below)
- [ ] None

12.6 RISK TO BENEFIT RATIO: Explain why the risks to subjects are reasonable in relation to anticipated benefits, if any, to the participant or society:

The treatment of study patients does not deviate from our current clinical practice. The additional riks to the wellfare of the patients should be minimal.

13.0 Data and Safety Monitoring Plan

13.2 * DATA AND SAFETY MONITORING PLAN: (REQUIRED)

All greater than minimal risk studies are required to provide a plan. Lack of an adequate plan is one of the most common reasons why IRB approval is delayed.

Instructions:

Describe the plan for monitoring data quality and participant safety. Key areas that should be included in the plan are:

- An explanation of the plan to monitor data collection, study progress, and safety
- A description of who will perform the monitoring and at what frequency (e.g., the PI only, a contract research organization, a Data and Safety Monitoring Board or Data Monitoring Committee, etc.)
- The type of data and events that will be reviewed (e.g., adverse events, breaches of confidentiality, unanticipated problems involving risk to participants or others, unblinded efficacy data, etc.)
- Procedures and timeline for communicating monitoring results to the UCSF IRB, the study sponsor, and other appropriate entities
- Assurance that the research team will adhere to the **UCSF IRB reporting requirements**

As appropriate:

- A plan for conducting and reporting interim analysis
- Clearly defined stopping rules
- Clearly defined rules for withdrawing participants from study interventions

Patients will be monitored as per routine nursing care as well as followed by the acute pain service for the management of the epidural catheter. Any adverse events occuring in a study participant will be managed by the acute pain service and be brought immediately to the principal investigator for review. Given that epidural is routinely performed for the ERAS pathway, we consider this a low-risk study.

Serious or unexpected adverse events will be reported to the CHR within 10 working days in accordance with CHR guidelines.
We are also planning on perfoming an interims analysis after 44 patients have completed the study to investigate whether there are any differences in outcomes as well as adverse events reported between study groups.

13.3 * DATA AND SAFETY MONITORING BOARD (DSMB): Will a Data and Safety Monitoring Board (DSMB) be established: (REQUIRED)

- ○ Yes
- ◉ No

Guidelines

A Data and Safety Monitoring Board (DSMB) or Data Monitoring Committee (DMC) is a formal, independent committee that is specifically established to conduct interim monitoring, oversight and analysis of study information and data to assure the continuing safety, efficacy, appropriateness, relevance, and integrity of the study.

The UCSF IRB reserves the right to request a DSMB/DMC for any study. However, the following are factors that the IRB will consider when making this determination:

- There is a significant likelihood of a serious adverse event to subjects
- The study is conducted at multiple sites and the level of risk is greater than minimal
- The study generates data that are blinded or randomized
- The study involves a large number of patients randomized to one of two or more interventions

- A study for which the performance of an interim analysis is crucial for the protection of the subjects
- First use in humans
- First use in children
- The study involves gene transfer, stem cell therapy, or other novel interventions for which long-term outcome data are not known or available

14.0 Confidentiality, Privacy, and Data Security

14.1 PROTECTING PRIVACY: Indicate how subject privacy will be protected:

- [x] Conduct conversations about the research in a private room
- [x] Ask the subject how they wish to be communicated with – what phone numbers can be called, can messages be left, can they receive mail about the study at home, etc.
- [ ] Take special measures to ensure that data collected about sensitive issues do not get added to their medical records or shared with others without the subject's permission
- [ ] Other methods (describe below)

14.2 SENSITIVE DATA: Do any of the instruments ask about illegal or stigmatized behavior:

○ Yes ◉ No

14.3 CONSEQUENCES OF A LOSS OF PRIVACY OR CONFIDENTIALITY: Could a breach of privacy or confidentiality result in any significant consequences to participants, such as criminal or civil liability, loss of state or federal benefits, or be damaging to the participant's financial standing, employability, or reputation:

○ Yes ◉ No

14.4 EXTRA CONFIDENTIALITY MEASURES: Explain any extra steps that will be taken to assure confidentiality and protect identifiable information from improper use and disclosure, if any:

All patient identifiers will be decoupled from the remainder of the data as soon as possible to minimize loss of confidentiality through the study.

14.5 * REPORTABILITY: Do you anticipate that this study may collect information that State or Federal law requires to be reported to other officials, such as elder abuse, child abuse, or threat to self or others: (REQUIRED)

○ Yes ◉ No

14.6 CERTIFICATE OF CONFIDENTIALITY: Will this study obain a Certificate of Confidentiality:

○ Yes ◉ No

14.7 SHARING OF RESEARCH RESULTS: Will there be any sharing of EXPERIMENTAL research test results with subjects or their care providers:

○ Yes ◉ No

14.8 * IDENTIFIERS: Will personal identifiers be included in research records: (REQUIRED)

(•) Yes ( ) No

Check all the identifiers that may be included:

- [x] Names
- [x] Dates
- [ ] Postal addresses
- [x] Phone numbers
- [ ] Fax numbers
- [x] Email addresses
- [ ] Social Security Numbers*
- [x] Medical record numbers
- [ ] Health plan numbers
- [ ] Account numbers
- [ ] License or certificate numbers
- [ ] Vehicle ID numbers
- [ ] Device identifiers or serial numbers
- [ ] Web URLs
- [ ] IP address numbers
- [ ] Biometric identifiers
- [ ] Facial photos or other identifiable images
- [ ] Any other unique identifier

* Could study records include *ANY* photos or images (even 'unidentifiable' ones): **(REQUIRED)**

( ) Yes (•) No

14.9 DATA DISCLOSURE: Will identifiable information be shared with outside groups:

( ) Yes (•) No

14.11 * DATA COLLECTION AND STORAGE: (check all that apply): (REQUIRED)

Collection methods:

- [x] Paper-based (surveys, logs, diaries, etc.)
- [x] Electronic case report forms (CRFs), such as OnCore or another clinical trial management portal
- [ ] Web-based online surveys or computer-assisted interview tool
- [ ] Mobile applications (mobile or tablet-based)
- [ ] Wearable devices
- [ ] Audio/video recordings
- [ ] Other:

* Data will be collected/stored in systems owned by (check all that apply): **(REQUIRED)**

- [x] UCSF
- [ ] SF VAMC
- [ ] Amazon (Amazon Cloud)
- [ ] Other academic institution
- [ ] 3rd party vendor (business entity)
- [ ] Other (explain below)

14.12 DATA SECURITY: Indicate how data are kept secure and protected from improper use and

disclosure (check all that apply): NOTE: Whenever possible, do not store subject identifiers on laptops, PDAs, or other portable devices. If you collect subject identifiers on portable devices, you MUST encrypt the devices.

- [ ] Data are stored securely in My Research
- [ ] Data are coded; data key is destroyed at end of study
- [ ] Data are coded; data key is kept separately and securely
- [x] Data are kept in a locked file cabinet
- [ ] Data are kept in a locked office or suite
- [x] Electronic data are protected with a password
- [x] Data are stored on a secure network
- [x] Data are collected/stored using REDCap or REDCap Survey
- [ ] Data are securely stored in OnCore

14.13 * DATA SECURITY: Confirm below that you will keep data confidential: (REQUIRED) I will keep any data sets that include identifiers secure and protected from improper use and disclosure by using methods such as:

- **Physical Security – Keeping data in locked file cabinets, locked offices, locked suites, and physically securing computers and servers.**
- **Electronic Security – Following UCSF minimum security standards for electronic information resources, which includes (but is not limited to): not storing identifiers on portable devices like laptops or flash drives if they are unencrypted, encrypting portable devices, and storing data in password-protected files and on secure networks.**

- (•) Yes

14.15 * HIPAA APPLICABILITY: Study data will be: (REQUIRED)

- [ ] Derived from the Integrated Data Repository (IDR) or The Health Record Data Service (THREDS) at SFGH
- [x] Derived from a medical record (e.g. APeX, OnCore, etc. Identify source below)
- [ ] Added to the hospital or clinical medical record
- [ ] Created or collected as part of health care
- [x] Obtained from the subject, including interviews, questionnaires
- [ ] Obtained ONLY from a foreign country or countries
- [ ] Obtained ONLY from records open to the public
- [ ] Obtained from existing research records
- [ ] None of the above

In addition to signing a consent form, each subject will have to sign the UCSF Research Subject Authorization Form (HIPAA Form).
NEW REQUIREMENT - This form should be uploaded in the Other Study Documents section of the Initial Review Submission Packet Form. Failure to have the signed HIPAA Authorization is one of the most common findings from QIU Routine Site Visits and can result in a Serious Noncompliance determination. Please call the IRB office at 415-476-1814 if you have questions about HIPAA research requirements.

14.16 * HIPAA - PERMISSION TO ACCESS SENSITIVE DATA: Does the research require access to any of the following types of health information from the medical record: (check all that apply) (REQUIRED)

- [ ] Drug or alcohol abuse, diagnosis or treatment
- [ ] HIV/AIDS testing information
- [ ] Genetic testing information
- [ ] Mental health diagnosis or treatment
- [x] None of the above

Important note: Ensure that participants DO NOT initial any of the lines in Section C of the HIPAA authorization form during the consent process.

15.0 Financial Considerations

15.1 * PAYMENT: Will subjects be paid for participation, reimbursed for time or expenses, or receive any other kind of compensation: (REQUIRED)

○ Yes ◉ No

15.4 COSTS TO SUBJECTS: Will subjects or their insurance be charged for any study activities:

○ Yes ◉ No

16.0 Qualifications of Key Study Personnel

16.1 NOTE: This information is required and your application will be considered incomplete without it. If this study involves invasive or risky procedures, or procedures requiring special training or certification, please identify who will be conducting these procedures and provide details about their qualifications and training. Also identify each person who will be involved in the consent process. Click the orange question mark for more information and examples.

Under qualifications, please include:

- **Academic Title**
- **Institutional Affiliation (UCSF, SFGH, VAMC, etc.)**
- **Department**
- **Certifications**

November, 2015 - NEW Definition of Key Study Personnel and CITI Training Requirements:

UCSF Key Study Personnel include the Principal Investigator, other investigators and research personnel who are directly involved in conducting research with study participants or who are directly involved in using study participants' identifiable private information during the course of the research. Key Personnel also include faculty mentors/advisors who provide direct oversight to Postdoctoral Fellows, Residents and Clinical Fellows serving as PI on the IRB application. **The IRB requires that all Key Study Personnel complete Human Subjects Protection Training through CITI prior to approval of a new study, or a modification in which KSP are being added. More information on the CITI training requirement can be found on our website.**

		Description of Study Responsibilities - Briefly describe what will each person be doing on the study. If there	

KSP Name	are procedures requiring special expertise or certification, identify who will be carrying these out. Also identify who will be obtaining informed consent.	Qualifications, Licensure, and Training
Behrends, Matthias, MD	Briefly describe what will each person be doing on the study. If there are procedures requiring special expertise or certification, identify who will be carrying these out. Also identify who will be obtaining informed consent. patient enrollment, data collection, data analysis, patient follow up	board certified anesthesiologist, PI status, CITI trained
Chen, Lee-Lynn	Briefly describe what will each person be doing on the study. If there are procedures requiring special expertise or certification, identify who will be carrying these out. Also identify who will be obtaining informed consent. patient enrollment, data collection, patient follow up	board certified anesthesiologist, PI status, CITI trained
Naidu, Ramana K	Briefly describe what will each person be doing on the study. If there are procedures requiring special expertise or certification, identify who will be carrying these out. Also identify who will be obtaining informed consent. patient enrollment, data collection, data analysis, patient follow up	board certified anesthesiologist, PI status, CITI trained
Su, Po-Yi Paul	Briefly describe what will each person be doing on the study. If there are procedures requiring special expertise or certification, identify who will be carrying	anesthesia resident, CITI trained

	these out. Also identify who will be obtaining informed consent. patient enrollment, data collection, data analysis, patient follow up	
Aleshi, Pedram	Briefly describe what will each person be doing on the study. If there are procedures requiring special expertise or certification, identify who will be carrying these out. Also identify who will be obtaining informed consent. patient enrollment, data collection, patient follow up	board certified anesthesiologist, PI status, CITI trained
Siegmueller, Claas	Briefly describe what will each person be doing on the study. If there are procedures requiring special expertise or certification, identify who will be carrying these out. Also identify who will be obtaining informed consent. patient enrollment, data collection, patient follow up	board certified anesthesiologist, PI status, CITI trained
Haight, Matthew J	Briefly describe what will each person be doing on the study. If there are procedures requiring special expertise or certification, identify who will be carrying these out. Also identify who will be obtaining informed consent. patient enrollment, data collection, patient follow up	board certified anesthesiologist,
Delgado, Adrian C	Briefly describe what will each person be doing on the study. If there are procedures requiring special expertise or certification, identify who will be carrying	UCSF research coordinator, CITI trained

	these out. Also identify who will be obtaining informed consent. patient enrollment, data collection, patient follow up	
Latronica, Mark	Briefly describe what will each person be doing on the study. If there are procedures requiring special expertise or certification, identify who will be carrying these out. Also identify who will be obtaining informed consent. Patient enrollment, data collection, patient follow up	board certified anesthesiologist, PI status, CITI trained
Ladd, Michael J	Briefly describe what will each person be doing on the study. If there are procedures requiring special expertise or certification, identify who will be carrying these out. Also identify who will be obtaining informed consent. patient enrollment, data collection, patient follow up	UCSF research coordinator, CITI trained
Clelland, Elle N	Briefly describe what will each person be doing on the study. If there are procedures requiring special expertise or certification, identify who will be carrying these out. Also identify who will be obtaining informed consent. patient enrollment, data collection, patient follow up	UCSF research coordinator, CITI trained

17.0 Other Approvals and Registrations

17.1 * ADMINISTRATION OF RECOMBINANT DNA: Does this study involve administration of vaccines produced using recombinant DNA technologies to human subjects (Help Link added Aug '15): (REQUIRED)

○ Yes ◉ No

17.2 * **HUMAN GENE TRANSFER: Does this study involve human gene transfer (NOTE: Requires NIH Recombinant DNA Advisory Committee (RAC) review prior to CHR approval): (REQUIRED)**

○ Yes ◉ No

17.4 OTHER APPROVALS: Indicate if this study involves other regulated materials and requires approval and/or authorization from the following regulatory committees:

☐ Institutional Biological Safety Committee (IBC)

Specify BUA #:

☐ Institutional Animal Care and Use Committee (IACUC)

Specify IACUC #:

☐ Controlled Substances

18.0 End of Study Application

18.1 **End of Study Application Form** **To continue working on the Study Application: Click on the section you need to edit in the left-hand menu. Remember to save through the entire Study Application after making changes. If you are done working on the Study Application: Click Save and Continue. If this is a new study, you will automatically enter the Initial Review Submission Packet form, where you can attach consent forms or other study documents. Review the Initial Review Submission Checklist for a list of required attachments. Answer all questions and attach all required documents to speed up your approval.**