Protocol Title	Intraoperative Sublingual sufentanil for acute pain in the Ambulatory Surgery Center
Principal Investigator/Faculty Advisor	Name: Aaron Berg
	Department: Anesthesiology
	Telephone Number: 612-624-9990
	Email Address: bergx831@umn.edu
Student Investigator	Name:
	Current Academic Status (Student, Fellow, Resident):
	Department:
	Telephone Number:
	Institutional Email Address:
Scientific Assessment	HRPP facilitated scientific assessment
IND/IDE # (if applicable)	N/A
IND/IDE Holder	N/A
Investigational Drug Services # (if applicable)	N/A
Version Number/Date:	0.4 11/20/2020

PROTOCOL COVER PAGE

ANCILLARY REVIEWS

Which ancillary reviews do I need and when do I need them? Refer to HRP-309 for more information about these ancillary reviews.			
Select yes or no	**Does your study…**	*If yes…*	***Impact on IRB Review***
☐ **Yes** ☒ **No**	Include Gillette resources, staff or locations	*Gillette Scientific review and Gillette Research Administration approval is required. Contact: research@gillettechildrens.com*	**Required prior to IRB submission**
☒ **Yes** ☐ **No**	Involve Epic, or Fairview patients, staff, locations, or resources?	*The Fairview ancillary review will be assigned to your study by IRB staff Contact:* ancillaryreview@Fairview.org	**Approval must be received prior to IRB committee/ designated review.** **Consider seeking approval prior to IRB submission.**
☐ **Yes** ☒ **No**	Include evaluation of drugs, devices, biologics, tobacco, or dietary supplements or data subject to FDA inspection?	*The regulatory ancillary review will be assigned to your study by IRB staff Contact: medreg@umn.edu* *See: https://policy.umn.edu/research/indide*	
☒ **Yes** ☐ **No**	Require Scientific Review? Not sure? See guidance on next page.	*Documentation of scientific merit must be provided. Contact: hrpp@umn.edu*	
☐ **Yes** ☒ **No**	Relate to cancer patients, cancer treatments, cancer screening/prevention, or tobacco?	*Complete the CPRC application process. Contact: ccprc@umn.edu*	
☐ **Yes** ☒ **No**	Include the use of radiation? (x-ray imaging, radiopharmaceuticals, external beam or brachytherapy)	*Complete the AURPC Human Use Application and follow instructions on the form for submission to the AURPC committee. Contact: barmstro@umn.edu*	**Approval from these committees must be received prior to IRB approval;** **These groups each have their own application process.**
☐ **Yes** ☒ **No**	Use the Center for Magnetic Resonance Research (CMRR) as a study location?	*Complete the CMRR pre-IRB ancillary review Contact: ande2445@umn.edu*	
☐ **Yes** ☒ **No**	Include the use of recombinant or synthetic nucleic acids, toxins, or infectious agents?	*Complete the IBC application via eprotocol.umn.edu Contact:*	
☐ **Yes** ☒ **No**	Include the use of human fetal tissue, human embryos, or embryonic stem cells?	*Contact OBAO for submission instructions and guidance*	

☒ **Yes** ☐ **No**	Include PHI or are you requesting a HIPAA waiver?	*If yes, HIPCO will conduct a review of this protocol.* *Contact: privacy@umn.edu*	
☐ **Yes** ☒ **No**	Use data from the Information Exchange (IE)?	*The Information Exchange ancillary review will be assigned to your study by IRB staff* *Contact: ics@umn.edu*	**Approval must be received prior to IRB approval.** **These groups do not have a separate application process but additional information from the study team may be required.**
☐ **Yes** ☒ **No**	Use the Biorepository and Laboratory Services to collect tissue for research?	*The BLS ancillary review will be assigned to your study by IRB staff.* *Contact: cdrifka@umn.edu*	
☐ **Yes** ☒ **No**	Have a PI or study team member with a conflict of interest?	*The CoI ancillary review will be assigned to your study by IRB staff* *Contact: becca002@umn.edu*	
☒ **Yes** ☐ **No**	Need to be registered on clinicaltrials.gov?	*If you select "No" in ETHOS, the clinicaltrials.gov ancillary review will be assigned to your study by IRB staff* *Contact: kmmccorm@umn.edu*	
☒ **Yes** ☐ **No**	Require registration in OnCore?	*If you select "No" or "I Don't Know" in ETHOS, the OnCore ancillary review will be assigned to your study by IRB staff* *Contact: oncore@umn.edu*	**Does not affect IRB approval.**

REVISION HISTORY

Revision #	Version Date	Summary of Changes	Consent Change?
1	0.2 4/22/20	Scientific Review clarifications	No
2	0.3 6/3/20	Added enrollment length in section 5.3 and pregnancy test stipulation to section 5.2 and consent changes per 4/29/20 modifications. Additionally added e-consent process to 21.0	Yes
3	0.4 11/20/20	Added to exclusion criteria	No

Table of Contents

ABBREVIATIONS/DEFINITIONS

- ASA class: American Society of Anesthesiologists Classification
- ASC: Ambulatory surgery center
- BMI: Body mass index
- BP: Blood pressure
- HR: Heart rate
- NRS: Numerical rating scale
- OBAS: Overall Benefit of Analgesia Survey
- PACU: post anesthesia care unit
- PONV: post-op nausea/vomiting
- SST: sublingual sufentanil tablet

1.0 Objectives

1.1 Purpose: *The purpose of this study is to determine if a single dose of sublingual sufentanil given 15-30 minutes prior to wake up is efficacious at reducing initial PACU pain scores.*

2.0 Background

2.1 Significance of Research Question/Purpose: *This study will help to determine the appropriate timing for the use of sublingual sufentanil in an ambulatory surgery practice.*

2.2 Preliminary Data: *N/A*

2.3 Existing Literature: *This is a follow up study to a prospective randomized trial giving sublingual sufentanil immediately upon a pain score of 4 in the recovery room, which showed that when used as an immediate rescue SST performed similar to IV fentanyl (STUDY00007956). SST is an opioid medication with unique properties as the route of administration differs from traditional opioids used in the peri-operative setting. Of note, sublingual medications are frequently given in this setting without complications however. The half-life of SST is 164 minutes with an estimated onset of 15-30 minutes. These qualities are consistent with standard of care as opioid medications used intraoperatively have shorter and longer half-lives. Intraoperative dosing of opioids is dynamic and the dose of this sublingual sufentanil tablet does not diverge from standard dosages. This study intends to further help determine its perioperative place. Previous studies have demonstrated the superiority of SST to placebo when used for abdominal surgery. Additional open label studies have demonstrated that SST has no change in mental status when given in an emergency room setting and has a safe adverse event profile when used in various inpatient surgical procedures.*

3.0 Study Endpoints/Events/Outcomes

3.1 Primary Endpoint/Event/Outcome:
Initial NRS pain score upon arrival to PACU (11 point 0-10 scale; 0 being no pain, 10 being maximum imaginable pain).

Superiority
H_0: no significant difference in initial NRS pain score
H_A: decreased mean initial NRS pain score of 2 points or greater for Group 1 (≥2 chosen as evidence suggests this is a clinically significant decrease)

Secondary Endpoint(s)/Event(s)/Outcome(s):

Length of time in PACU (recording both Phase 1, Phase 2, and total duration measured in minutes; as is standardly recorded for every case).

Superiority

H_0: no significant difference in recovery room duration

H_A: decreased recovery room duration for the SST group

Additional outcomes: Opioid use in recovery room (medication type and dose, these will also be converted to milligram morphine equivalents for overall summation and comparison), NRS pain score upon discharge from PACU, reduction in pain from initial to discharge pain scores, PONV (defined as treated) and any other adverse events, OBAS score, and anesthesia wake-up time (duration in minutes from procedure closure to removal of endotracheal tube or laryngeal mask airway).

4.0 Study Intervention(s)/Investigational Agent(s)

4.1 Description: *15-30 minutes prior to planned emergence from anesthesia patients will either receive 30 mcg of sublingual sufentanil or nothing dispensed by the anesthesia provider who will be the only person who is unblinded. Envelopes will be used for them to discover the randomization group and distributed in order according to a randomization scheme provided by the biostatistician. Upon arrival in the ASC PACU, patient's pain will be assessed. There the patient will receive IV fentanyl for a pain score of 4 or greater (25-50 mcg doses of Fentanyl, up to 100mcg if needed). If 100 mcg of fentanyl is given and pain remains above a 7 then IV hydromorphone will be used (max dose of 1 mg and given in increments of 0.3 mg q 10 minutes prn severe pain). Once the patient is able to tolerate oral medications a dose of 5 mg of oral oxycodone (or 2 mg of oral hydromorphone if allergic to oxycodone) will be given if their pain score is 4 or greater (on the Numerical Rating Scale). This PACU process is all similar to the standard process and medications that would be used in standard care, standardized for study purposes. OBAS and final pain score will be assessed just prior to discharge from the PACU by the PACU nurse doing the discharge. If they request assistance a research coordinator will help ask and record this.*

4.2 Drug/Device Handling: *Sublingual sufentanil will be stored in the OR anesthesia pyxis like other controlled substances.*

4.3 Biosafety: *N/A*

4.4 Stem Cells: *N/A*

4.5 Fetal tissue: *N/A*

5.0 Procedures Involved

5.1 Study Design: *This is a level I randomized prospective outcomes study comparing two groups of patients. Within 15-30 minutes of planned wake-up Group 1 will receive 30 mcg of sublingual sufentanil and group 2 will not receive sublingual sufentanil.*

5.2 Study Procedures: *Patients will be approached on the day of surgery about participating in the trial after being screened for eligibility (inclusion per negative pregnancy test for women of child-bearing age). This will be done as soon as they arrive at the ASC to allow adequate time for them to review the study procedures and consent forms. All questions will be answered and patients will be ensured that they have adequate time to review and understand all study procedures. Patients undergoing orthopedic surgical procedures with general anesthesia will be eligible to participate.*

All patients will have standardized opioid sparing total IV anesthetic with propofol. No opioids will be used on induction and patients will only receive intraoperative opioids if their HR or BP is increased by 20% above baseline. Within 15-30 minutes of wakeup patients will be randomized to receive either 30 mcg of sublingual sufentanil or nothing. There is no need for a placebo as the patient will be under anesthesia. No additional intraoperative opioids will be given after that.

Once in the PACU patients initial pain will be assessed and recorded. There the patient will receive IV fentanyl for a pain score of 4 or greater (25-50 mcg doses of Fentanyl, up to 100 mcg if needed). If 100 mcg of fentanyl is given and pain remains above a 7 then IV hydromorphone will be used (max dose of 1 mg and given in increments of 0.3 mg q 10 minutes prn severe pain). Once the patient is able to tolerate oral medications a dose of 5 mg of oral oxycodone (or 2 mg of oral hydromorphone if allergic to oxycodone) will be given if their pain score is 4 or greater (on the Numerical Rating Scale). This PACU process is all similar to the standard process and medications that would be used in standard care, standardized for study purposes. OBAS and final pain score will be assessed just prior to discharge from the PACU by the PACU nurse doing the discharge. OBAS is a standard survey asking seven questions regarding grade of distress from several possible symptoms and can be done very quickly. This will be recorded on the instruction sheet.

Time until readiness to discharge, opioid use, pain scores and baseline demographics such as surgical procedure, intraoperative opioids, surgical procedure length, ASA class, BMI, weight, age, and sex will be recorded.

Table of Events (research activities, operative day)	
Informed Consent	*Research team, pre-op*
Randomization envelope	*Research team, pre-op*

Group 1/(2) (in)action	*Anesthesia provider, intra-op*
PACU care/Pain scores	*PACU nurse, post-op*
OBAS survey	*PACU nurse or research assistant, post-op*

5.3 Study Duration: *Once ready to discharge from PACU the patient will end study participation after answering questions for the OBAS survey. Participants will be informed that study participation is for their perioperative course until they leave the ambulatory surgery center, an estimated average duration of six hours. It should take 2 months to enroll all patients and another 2 months for full data analysis.*

5.4 Individually Identifiable Health Information: *See attached combined consent/HIPAA form.*

5.5 Use of radiation*: N/A*

5.6 Use of Center for Magnetic Resonance Research*: N/A*

6.0 Data and Specimen Banking

6.1 Storage and Access: *All study data will be stored on excel spreadsheets in Box. Only the PI and members of the research team will have access to the data.*

6.2 Data: *The data from this study will be collected both from Epic and directly from the patient. The data collected includes: demographic data, age, sex, weight, BMI, ASA class, duration of surgery, length of stay in recovery room both phase 1 and 2, amount of opioids given intraoperatively and post-operatively, non-opioid pain medication, pain score (0-10 at arrival in PACU, 30 minutes after arrival, and upon discharge), OBAS score at time to ready to discharge, and any adverse events.*

6.3 Release/Sharing: *De-identified study data will be shared with our biostatistician for assistance with analysis and may be shared with a peer-reviewed journal.*

7.0 Sharing of Results with Participants

7.1 Sharing Results: If participants ask, they will be informed that we plan to publish the study and informed of a potential method for how to search for it, such as searching for the investigator's name, in a number of months.

7.2 Sharing Genetic Results: *N/A*

7.2.1 Disclosure of Results: *N/A*

7.2.2 Returning Results to Participants: N/A

7.2.3 Future analysis of genotypes: N/A

8.0 Study Population

8.1 Inclusion Criteria: *Adult patients aged 18-80 undergoing outpatient ambulatory surgery undergoing general anesthesia for orthopedic surgery.*

Those not able to read will be allowed to participate and the consent process will be followed, including witness signature. Military personnel will be allowed to participate and not be identified and information will not be collected as to a patient's military status. Undervalued and disadvantaged groups will also have the option of participating. This research does not add risk to these groups.

8.2 Exclusion Criteria: *Patients under the age of 18, and over 80. Patients who have allergy or intolerance to the study drugs or derivatives. Patients with chronic pain or a three week or greater history of daily opioid use. Patients undergoing procedures in the prone position.*

Due to cultural concerns over pain tolerance and interpretation observed by the academic pain research community, non-English speaking patients will be excluded. Pregnancy, those with lacking/diminished ability to consent, employees and students of researcher, those in a stressful situation (for example a non-elective procedure), serious health condition for which there are no satisfactory standard treatments, prisoners, those with possible fear of negative consequences for not participating in the research like deportation, and any other dynamic that deemed to increase vulnerability to coercion or exploitation.

8.3 Screening: *Due to dynamic surgical schedules, patients will be screened by looking at the surgical schedule. They arrive several hours before the procedure and will be approached by a member of the clinical care team as they are roomed in the pre-operative area and informed of a potential study they could elect to participate in. If they indicate they are open to hearing more about it they will be asked if a member of the research team can discuss it with them. They will be ensured that they have time to read the consent, discuss and evaluate the study, all questions will be answered and they will be informed that they can decide not to participate for any reason without any consequence.*

9.0 Vulnerable Populations

9.1 Vulnerable Populations:

Population / Group	Identify whether any of the following populations will be targeted, included (not necessarily targeted) or excluded from

	participation in the study.
Children	Excluded from Participation
Pregnant women/fetuses/neonates	Excluded from Participation
Prisoners	Excluded from Participation
Adults lacking capacity to consent and/or adults with diminished capacity to consent, including, but not limited to, those with acute medical conditions, psychiatric disorders, neurologic disorders, developmental disorders, and behavioral disorders	Excluded from Participation
Non-English speakers	Excluded from Participation
Those unable to read (illiterate)	Included/Allowed to Participate
Employees of the researcher	Excluded from Participation
Students of the researcher	Excluded from Participation
Undervalued or disenfranchised social group	Included/Allowed to Participate
Active members of the military (service members), DoD personnel (including civilian employees)	Included/Allowed to Participate
Individual or group that is approached for participation in research during a stressful situation such as emergency room setting, childbirth (labor), etc.	Excluded from Participation
Individual or group that is disadvantaged in the distribution of social goods and services such as income, housing, or healthcare.	Included/Allowed to Participate

Individual or group with a serious health condition for which there are no satisfactory standard treatments.	Excluded from Participation
Individual or group with a fear of negative consequences for not participating in the research (e.g. institutionalization, deportation, disclosure of stigmatizing behavior).	Excluded from Participation
Any other circumstance/dynamic that could increase vulnerability to coercion or exploitation that might influence consent to research or decision to continue in research.	Excluded from Participation

9.2 Additional Safeguards: *N/A*

10.0 Local Number of Participants

10.1 Local Number of Participants to be Consented: *Minimum of 50 and maximum of 65*

11.0 Local Recruitment Methods

11.1 Recruitment Process: *Patients will be recruited from the group of adult patients undergoing orthopedic surgery at the University of Minnesota Ambulatory Surgery Center. On the day of surgery as soon as they are checked in, patients will be informed of a research opportunity by a member of the clinical care staff, including the check-in staff, nursing staff, or member of the anesthesiology team, and asked if they are interested in talking with a member of the research team. A research team member will then explain the study and present the consent form. All patients will have sufficient time to review this, ask questions and go over the potential risks of the study with the research team as they arrive several hours prior to the procedure. If they decide to participate they will be consented and provided a copy of the consent form.*

11.2 Identification of Potential Participants: *Patients will be identified by members of the research team by evaluating the surgical schedule. Patients who have opted out of research will not be approached. Patients who agree to participate will sign the combined consent and HIPAA authorization form.*

11.3 Recruitment Materials: *N/A*

11.4 Payment: *No payment will be provided.*

12.0 Withdrawal of Participants

12.1 Withdrawal Circumstances: *Subjects who have consented and later choose not to participate for any reason will be withdrawn and a notation will be made in the study records. The surgeon may choose to withdraw the patient from the study prior to surgery for any medical reason or if they suffer a major life-threatening adverse event.*

12.2 Withdrawal Procedures: *If the patient is withdrawn from study prior to the procedure, for example if they change their mind before induction of anesthesia in the operating room, they will be noted in study records as screen failures. If they undergo the procedure and they decide for any reason they no longer want to be included in the study or are withdrawn by the physician, they will be withdrawn and no further data will be collected. This will also be noted in the study documentation.*

12.3 Termination Procedures: *If the study is terminated for any reason, or there are more than 5% major adverse events the data that is already collected will be stored in a secure location only accessible to research personnel on this study. No further data will be collected if the study is terminated. Existing data may still be sent to the biostatistician in the manner as described in the protocol to help determine if it is sufficient for any conclusions.*

13.0 Risks to Participants

13.1 Foreseeable Risks:

Medication risks include:

- *Life threatening respiratory depression*
- *Addiction, abuse, and misuse*
- *Adrenal insufficiency*
- *Severe hypotension*
- *Gastrointestinal adverse reactions*
- *Seizures*

These risks are the standard risks of using opioids, the standard of care for treating surgical pain. Sublingual sufentanil is already used as an analgesic option at University of MN ASC.

The Department of Anesthesiology has an adverse event and serious adverse event reporting standard operating procedure in place to define, record, report and evaluate adverse events based on the International Conference on Harmonization guidelines.

Adverse event *means any untoward medical occurrence associated with the use of an intervention in humans, whether or not considered intervention-related (21 CFR 312.32 (a)); An adverse event (AE) or suspected adverse reaction is considered "**serious"** if, in the view of either the investigator or sponsor, it results in any of the following outcomes: death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization.*

RATING: *Mild – Events require minimal or no treatment and do not interfere with the participant's daily activities. Moderate – Events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning. Severe – Events interrupt a participant's usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually potentially life-threatening or incapacitating. Of note, the term "severe" does not necessarily equate to "serious".]*

RELATED*: Related – The AE is known to occur with the study intervention, there is a reasonable possibility that the study intervention caused the AE, or there is a temporal relationship between the study intervention and event. Reasonable possibility means that there is evidence to suggest a causal relationship between the study intervention and the AE. Not Related – There is not a reasonable possibility that the administration of the study intervention caused the event, there is no temporal relationship between the study intervention and event onset, or an alternate etiology has been established.* ***(The Principal Investigator will be responsible for determining whether an adverse event (AE) is expected or unexpected. An AE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described for the study intervention.)***

Confidentiality risks:

Participation in research may involve a loss of privacy due to the nature of the questions that are asked during assessment visits and/or data collected. However, records will be handled as confidentially as possible. All participants will be assigned a unique study identifier that will be used to label all of their records only be accessible to specific study staff listed in the Delegation of Authority log. This link will connect the participant's identifying information, such as name, etc., to their assigned ID number. No identifying information will be used in any report or publications that may result from this study. All study records will be kept in a secure database. Paper records will be kept in locked cabinets in locked rooms.

13.2 Reproduction Risks: *N/A*

13.3 Risks to Others: *N/A*

14.0 Potential Benefits to Participants

Potential Benefits: *There may be no direct benefit to participants. However, potential benefits include reduced pain and shortened recovery room stay.*

15.0 Statistical Considerations

15.1 Data Analysis Plan: *We plan to collect our data using excel which will be maintained in the box. When the study is completed and ready for statistical analysis the data will be shared with our staff statistician.*

15.2 Power Analysis: *We based our power analysis off a previous prospective randomized controlled trial which showed average initial pain scores of patients who had orthopedic surgery to be 6.63 (SD=2.13). In order to detect a mean difference of 2 in the pain scores between groups with a two-sample t-test assuming equal variances, we need 50 total participants (25 per group) to achieve 90% power.*

15.3 Statistical Analysis: This study data will be de-identified and shared with our staff biostatistician to be analyzed. The statistician will be provided the protocol so they are able to analyze for primary and secondary objectives.

Continuous data will be summarized with mean (standard deviation) or median (interquartile range) and categorical data will be summarize by count (percent). Normality will be evaluated with both the Shapiro-Wilk test and graphical evaluation. Univariate comparisons between groups will use t-tests or Mann-Whitney U-tests, as appropriate for normality, to compare continuous variables and chi-squared or Fisher's exact tests to compare categorical variables between groups. Linear regression models will be explored to adjust for variables that are imbalanced after randomization or other covariates that may be clinically relevant.

15.4 Data Integrity: *All patients will be assigned a unique patient identifier. Research assistants will have experience with similar trials and data collection.*

16.0 Health Information and Privacy Compliance

16.1 Select which of the following is applicable to your research:

☐ My research does not require access to individual health information.

☒ I am requesting that all research participants sign a HIPCO approved HIPAA Disclosure Authorization to participate in the research (either the standalone form or the combined consent and HIPAA Authorization).

☐ I am requesting the IRB to approve a Waiver or an alteration of research participant authorization to participate in the research.

Appropriate Use for Research:

16.2 Identify the source of Private Health Information you will be using for your research (Check all that apply)

☐ I will use the Informatics Consulting Services (ICS) available through CTSI (also referred to as the University's Information Exchange (IE) or data shelter) to pull records for me

☒ I will collect information directly from research participants.

☐ I will use University services to access and retrieve records from the Bone Marrow Transplant (BMPT) database, also known as the HSCT (Hematopoietic Stem Cell Transplant) database.

☒ I will pull records directly from EPIC.

☐ I will retrieve record directly from axiUm / MiPACS

☐ I will receive data from the Center for Medicare/Medicaid Services

☐ I will receive a limited data set from another institution

☐ Other. Describe:

16.3 Explain how you will ensure that only records of patients who have agreed to have their information used for research will be reviewed: *Only records from patients that have signed a combined consent and HIPAA Authorization form will be reviewed. Patients who have research opt-out indicated in chart will not be approached.*

16.4 Approximate number of records required for review: *65*

16.5 Please describe how you will communicate with research participants during the course of this research. Check all applicable boxes

☐ This research involves record review only. There will be no communication with research participants.

☒ Communication with research participants will take place in the course of treatment, through MyChart, or other similar forms of communication used with patients receiving treatment.

☐ Communication with research participants will take place outside of treatment settings. If this box is selected, please describe the type of communication and how it will be received by participants.

16.6 Explain how the research team has legitimate access to patients/potential participants: *Team consists of those providing anesthetic care to the patients and department of anesthesiology research assistants.*

16.7 Location(s) of storage, sharing and analysis of research data, including any links to research data (check all that apply).

☐ In the data shelter of the Information Exchange (IE)
☐ Store ☐ Analyze ☐ Share

☐ In the Bone Marrow Transplant (BMT) database, also known as the HSCT (Hematopoietic Stem Cell Transplant) Database
☐ Store ☐ Analyze ☐ Share

☐ In REDCap (recap.ahc.umn.edu)
☐ Store ☐ Analyze ☐ Share

☐ In Qualtrics (qualtrics.umn.edu)
☐ Store ☐ Analyze ☐ Share

☒ In OnCore (oncore.umn.edu)
☒ Store ☐ Analyze ☐ Share

☒ In the University's Box Secure Storage (box.umn.edu)
☒ Store ☒ Analyze ☒ Share

☐ In an AHC-IS supported server. Provide folder path, location of server and IT Support Contact:
☐ Store ☐ Analyze ☐ Share

☐ In an AHC-IS supported desktop or laptop.
Provide UMN device numbers of all devices:
☐ Store ☐ Analyze ☐ Share

☐ Other:

Indicate if data will be collected, downloaded, accessed, shared or stored using a server, desktop, laptop, external drive or mobile device (including a tablet computer such as an iPad or a smartform (iPhone or Android devices) that you have not already identified in the preceding questions

☐I will use a server not previously listed to collect/download research data

☐I will use a desktop or laptop not previously listed

☐I will use an external hard drive or USB drive ("flash" or "thumb" drives) not previously listed

☐I will use a mobile device such as an tablet or smartphone not previously listed

16.8 Consultants. Vendors. Third Parties: *N/A*

16.9 Links to identifiable data: *All data will be identified with an identification code unique to the participant. Study staff will keep the mapping of identification code to the identity of the participant on an Xcel spreadsheet in Box, protected by two-levels of password protection stored separately from the data. Any internal data reports will use only these codes and will not use any identifiable information. Any external data reports, abstracts, publications, presentations, etc. will present de-*

identified, grouped, and/or aggregate data. Any reports to the University of Minnesota IRB (such as Adverse Event reporting and annual renewal reports) will be kept confidential; they will not include participant-identifiable information; only the participant's identification code will be used.

16.10 Sharing of Data with Research Team Members: *Only IRB-approved members of the study team will have access to the data. Data will be shared through UMN Box.*

16.11 Storage and Disposal of Paper Documents: *All paper documents and consent forms will be stored in a locked cabinet in the anesthesia research office in B573 Mayo. All paper documents will be destroyed after completion of the study in accordance with U of M policy.*

17.0 Confidentiality

17.1 Data Security: *All study data will be stored electronically in Box and only the PI and members of the research team will have access to the data.*

18.0 Provisions to Monitor the Data to Ensure the Safety of Participants

18.1 Data Integrity Monitoring: *The PI, co-investigators, research supervisor and research assistants will all have access to the study data stored in the University's Box storage system. All the research assistants have experience collecting pain scores and other relevant study information. The PI of the study will periodically review the study data to ensure accuracy and completeness of study data.*

18.2 Data Safety Monitoring: *The Department of Anesthesiology has a Data and Safety Monitoring Committee consisting of several staff anesthesiologists which include persons who are board certified as pain specialists. If there are patterns of adverse events, the board will meet as needed and provide recommendations. The data will be reviewed on a regular basis (weekly) by the PI and research staff. Chi-square or Fisher's exact tests (performed in R or SAS) will be used to test for differences in adverse event rates between treatment and control groups for Data Safety monitoring reports.*

19.0 Provisions to Protect the Privacy Interests of Participants

19.1 Protecting Privacy: *Patients will be able to decline research involvement when member of care team mentions it. The study consent form will describe in detail any intrusive, uncomfortable, or unfamiliar questions, procedures, or interactions with researchers or study personnel that the participant will be asked to complete. Furthermore, the study consent form will communicate that it is the participant's right to opt-out of any study procedures or the study as a whole or withdraw from the study at any time and this information will be reiterated and revisited periodically throughout*

the study in advance of intrusive, uncomfortable, or unfamiliar questions procedures or interactions. Participants will not be compelled or pressured to provide information or specimens or study data that they do not wish to provide.

19.2 Access to Participants*: They will have signed the consent and HIPAA form during consent process giving permission. Participants have been fully informed of the ways in which their data will/may be used during the informed consent process. The research team has been trained in conducting these conversations and the participants are also assessed for their understanding of consent prior to signing the consent form or initiating any study procedures.*

20.0 Compensation for Research-Related Injury

20.1 Compensation for Research-Related Injury: *In the event that this research activity results in an injury, treatment will be available, including first aid, emergency treatment, and follow-up care as needed. Care for such injuries will be billed in the ordinary manner, to the patient and/or insurance company.*

20.2 Contract Language: *N/A*

21.0 Consent Process

21.1 Consent Process (when consent will be obtained): *Patients will be identified in the pre-operative time period by the research team on the day of surgery. As soon as they enter the pre-operative room, an anesthesiologist will mention the study and ask permission for them or a research staff member to discuss it further if they are interested. If an anesthesiologist is not available when they are roomed, check-in or nursing staff will mention the study and ask the patient if a research member can discuss it with them further. If they are interested they will meet a research staff member and be presented with a combined Health and Insurance Portability and Accountability Act (HIPAA) and study consent form, with the REDCap e-consent process being preferentially used. The patient will review the form with a member of the research team. They will be reminded that participation is completely voluntary, and that they may stop participation at any time without question or penalty. The research team will answer any questions that they may have about the study, and the teach-back method will be utilized to ensure comprehension. If the patient decides to participate, they will be asked to sign the consent and HIPAA form. One copy will be saved for study records, and the subject will be provided with a copy of the forms.*

21.2 Waiver or Alteration of Consent Process (when consent will not be obtained): *N/A*

21.3 Waiver of Written/Signed Documentation of Consent (when written/signed consent will not be obtained): *N/A*

21.4 Non-English Speaking Participants: *N/A*

21.5 Participants Who Are Not Yet Adults (infants, children, teenagers under 18 years of age): *N/A*

21.6 Cognitively Impaired Adults, or adults with fluctuating or diminished capacity to consent: *N/A*

21.7 Adults Unable to Consent:

- Permission: *N/A*
- Assent: *N/A*
- Dissent: *N/A*

22.0 Setting

22.1 Research Sites: *M Health Fairview ASC.*

22.2 International Research: *N/A*

23.0 Multi-Site Research

23.1 Study-Wide Number of Participants: *N/A*

23.2 Study-Wide Recruitment Methods: *N/A*

23.3 Study-Wide Recruitment Materials: *N/A*

23.4 Communication Among Sites: *N/A*

23.5 Communication to Sites: *N/A*

24.0 Coordinating Center Research

24.1 Role: *N/A*

24.2 Responsibilities: *N/A*

24.3 Oversight: *N/A*

24.4 Collection and Management of Data: *N/A*

25.0 Resources Available

25.1 Resources Available: *A research supervisor and research assistants are available to aid in consent and data acquisition. All research team members will be familiar with the study protocol and have experience working with similar studies as well as CITI and HIPAA training completed and up-to-date. All procedures will be performed in the clinical facilities at the M Health Fairview Clinics and Surgery Center. We do not anticipate this issue, but if research activity may disrupt normal work flow, the patient will not be approached. A delegation of authority log will also be maintained to track which personnel are responsible for specific duties.*

This center performs approximately 40 orthopedic surgical procedures under general anesthesia weekly. We plan to conduct this study over 2

months. Enrollment and data collection will be completed at this time. Statistical Analysis will take approximately two months to complete.

26.0 References

1. Hutchins JL et al. An Open-Label study of sufentanil sublingual tablet 30 mcg in patients with postoperative pain. Pain Med 2017
2. Minkowitz HS et al. Sufentanil sublingual tablet 30 mcg for the management of pain following abdominal surgery: A randomized, placebo-controlled phase-3 study. Pain Pract. 2017;17:848-858.
3. Kendrick DB et al. The minimum clinically significant difference in patient-assigned numeric scores for pain, Am. J. Emerg. Med. 2005;828-832.