Cover Page for ClinicalTrials.gov

Document: Study Protocol and Statistical Analysis

Official Study Title: Cyclobenzaprine for Postoperative Pain in Minimally Invasive Hysterectomy: A Randomized Controlled Trial

Document Date: 04/10/2026

Objective:
The purpose of this study is to evaluate the role cyclobenzaprine plays in post operative pain management in patients who undergo minimally invasive hysterectomy (MIH). Post-operative pain control is a very popular topic, and most notably has been addressed by the ERAS study. Although many studies investigate the roles of NSAIDs, acetaminophen, and narcotics, there is little evidence on multimodal pain control utilizing muscle relaxants, particularly in the gynecologic population. This study will aim to determine if cyclobenzaprine should be included in standard of care multimodal post operative pain management after minimally invasive gynecologic surgery. This pilot study is intended to estimate the effect size and feasibility for a larger RCT.

Background:
Postoperative pain management remains a popular topic and critical component following any surgery. Effective pain control not only improves patient experience but decreases use of opioid analgesia and its subsequent complications, facilitates early mobilization, and reduces postoperative complications. Opioid analgesia, while commonly used, carries significant side effects including nausea, vomiting, constipation, puritis, sedation, and potential dependence. As such, any opportunity to decrease opioid use should be explored.

Multimodal pain medication regimes have been studied in different surgical populations and found to be highly effective. Many of these multimodal regimes utilize a combination of acetaminophen, NSAIDs, anticonvulsants such as gabapentin, and opioids.[1] Adjuncts such as dexamethasone, alpha-2 agonists, local anesthesia, and transverse abdominis plane blocks have demonstrated efficacy.[2,3] In gynecologic surgery, more novel approaches - including peritoneal ropivacaine,[4] intravenous ketamine,[5] and even the use of postoperative virtual reality devices[6] - have been explored. Specifically, the Enhanced Recovery After Surgery (ERAS) protocol was used after MIH, and demonstrated reductions in hospital stay, nausea and vomiting, and postoperative pain.[7]

Muscle relaxants are frequently used postoperatively, yet the data supporting their efficacy is extremely limited across specialties.[8,9] Commonly prescribed centrally acting skeletal muscle relaxants (CASMRs) are baclofen, cyclobenzaprine (commonly known as Flexeril®), methocarbamol (commonly known as Robaxin®), and tizanidine. For many of these, exact mechanisms of action are unknown.

Cyclobenzaprine, widely used at ChristianaCare Health Systems, has been postulated to inhibit serotonergic descending systems in the spinal cord. The chemical structure of cyclobenzaprine is extremely similar to those of tricyclic antidepressants. Immediate release cyclobenzaprine has an onset of approximately 1 hour, with duration of 4-6 hours, and half-life of 18 hours.[9,10,11] Observational data suggests that muscle relaxants have the greatest effect within the first week of use.[12] When taking cyclobenzaprine three times daily, steady state plasma concentrations are achieved within 3-4 days.[13] Many studies have evaluated and demonstrated the safety cyclobenzaprine. This medication has primarily been studied and found efficacious for the alleviation of musculoskeletal related back pain.

There are limited studies that look at the efficacy of cyclobenzaprine in post operative pain control after surgery. For example, the use of cyclobenzaprine as part of a multimodal pain regime showed a 62% decrease in opioid use after lumbar surgery.[14] Furthermore, there is data to suggest cyclobenzaprine has utility in multimodal pain control for patients with higher baseline pain scores who underwent joint arthroplasty.[15] A review of postoperative pain management indicates that muscle relaxants have the most promising effect after abdominal and joint surgeries, demonstrating significantly lower pain scores, longer intervals to request opioids, and/or reduced analgesic consumption overall.[9]

While minimally invasive hysterectomy is one of the most common gynecologic surgeries performed worldwide, current guidelines for postoperative pain management lack evidence and recommendations remain weak.[16] There are multiple reasons a patient may experience pain after MIH: trocar trauma, abdominal wall manipulation for surgical access, insufflation, and positioning. A MIH typically requires placement of three to five trocars, anywhere from 5-12mm, transversing several muscle layers. Often, patients remain in dorsal

lithotomy at steep Trendelenburg for hours, contributing to musculoskeletal pain. Given these factors, and the pharmacologic properties of cyclobenzaprine, it is reasonable to hypothesize that this medication may improve postoperative pain after MIH. In summary, there is a significant gap in evidence supporting the use of cyclobenzaprine in postoperative pain management, despite its frequent use, highlighting the need for further investigation, particularly in the gynecologic field.

Study Design:
This will be a single center randomized control trial with a 1:1 ratio. The patient population are all females undergoing minimally invasive hysterectomy at ChristianaCare Hospitals. In accordance with ChristianaCare Health Systems policies, this study will be registered with ClinicalTrials.gov prior to enrollment of the first patient.

Potential patients will be identified during office appointments at the MIGS ChristianaCare locations, as well as through chart review. All patients who are planning to undergo minimally invasive hysterectomy will be identified.

Patients will be included if they are English speaking, above 18 years of age, and have no contraindications to any of the standard post operative medications or study medication, cyclobenzaprine. Patients under 18 years of age, who undergo other procedures, are pregnant or breastfeeding, have non-gyn related operations at the same time of surgery, and any contraindications to the standard or study medications, will be excluded. Mini laparotomy, less than 5cm, for specimen extraction alone will not be excluded. The full list of inclusions and exclusions is below.

The goal is to enroll 36 patients in a pilot study. Please see below for study calculations.

Patients will provide voluntary informed consent in-person, while in the office during the initial visit or pre-operative visit, or in the preoperative area prior to the procedure, prior to prescribing medication, by qualified personnel. A patient will only be consented in the preoperative area if they went through the consent form verbally over the phone prior to the day of the procedure and had time to address any questions. This practice routinely prescribes post-operative medications prior to the day of surgery. The eligible and consented patients will be randomized to either the experimental or control group at the time of prescribing post-operative medications by qualified personnel. Qualified personnel will be designated on the Delegation of Authorities document.

For randomization, the study will utilize REDCap randomization module in a block distribution. Randomization will be stratified using race and ethnicity collected from the enrollment form. Participant allocation will be concealed until the participant has been both enrolled and provided informed consent. Prior to enrollment, the participating clinicians and study staff will not have access to group assignments. REDCap is a web-based, centralized system that reduces selection bias and ensures allocation concealment.

This study will be open-label, not blinded to either party. Blinding the clinicians is not feasible, as they must monitor participants for potential side effects and drug interactions. The patients cannot be blinded either, as they will receive an additional medication (cyclobenzaprine) as this study does not have funding for placebo medications. Furthermore, participants deserve transparency regarding their treatment and autonomy when providing informed consent. As such, a placebo pill will also not be required, even if it is financially feasible. To minimize bias, all data will be reported electronically, which decreases reporting bias, and the data will be statistically analyzed by a third party not involved in data collection.

Preoperatively, all patients will receive the standard acetaminophen 975mg once. They will not receive gabapentin, as per this practice's current standard of care. Furthermore, gabapentin, cyclobenzaprine, and oxycodone can all be potentially sedating medications. As such, we are aiming to minimize sedation by removing the one-time gabapentin per the ERAS protocol.

The **control** group will receive standard post operative pain management medications:

- Ketorolac 15mg IV once prior to discharge postoperatively
- Acetaminophen 1000mg q6h x 7 days (quantity = 40)
- Ibuprofen 600mg q6h x 7 days (quantity = 40)
- Oxycodone 5mg q6h PRN x 3 days (quantity = 10)

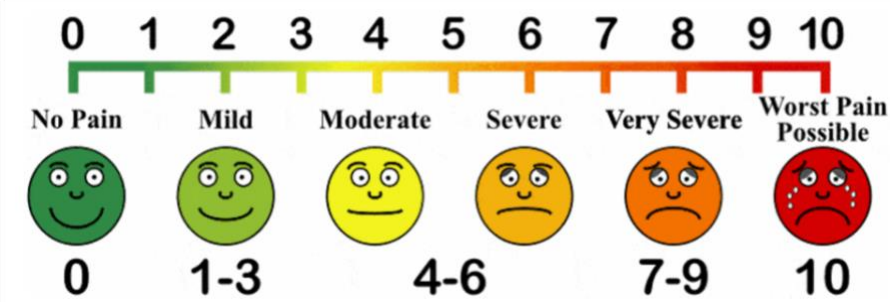
The **experimental** (cyclobenzaprine) group will receive standard post operative pain management medications plus cyclobenzaprine:

- Ketorolac 15mg IV one time prior to discharge postoperatively
- Acetaminophen 1000mg q6h x 7 days (quantity = 40)
- Ibuprofen 600mg q6h x 7 days (quantity = 40)
- Oxycodone 5mg q6h PRN x 3 days (quantity = 10)
- Cyclobenzoprine 5mg q8h x 7 days (quantity = 21)

Study participants will undergo their minimally invasive hysterectomy as per routine by any participating surgeons based on the surgeon's preferences for technique and devices used.

Post-operatively, nursing routinely assesses postoperative pain using the 10-point Visual Analog Scale (VAS, Figure 1). Patients will continue to rate their pain on the VAS scale multiple times throughout their recovery. In total, subjects will rate their pain on post op days 0, 1, 3, 7. This data will be gathered via a secure, online survey via REDCap.

Figure 1:



The REDCap survey will also ask patients if they have any side effects from a multiple-choice list. Common side effects are listed in Table 1.

The survey will also ask if they have been adherent to the ibuprofen/acetaminophen schedule. At each timepoint, the patients will be asked if they are adherent to ibuprofen and acetaminophen (yes/no). On day 7, the patients will be asked to report how many pills of oxycodone and cyclobenzaprine, if applicable, they have left to gauge compliance and narcotic requirement.

The survey will also contain a disclaimer of when to seek medical attention for any post-operative complications that are typically discussed: abnormal bleeding, acute anemia, signs of infection, signs of thrombotic events, etc. Patients will be directed to call the on-call doctor and/or present to the CCHS OBGYN Emergency Room if they experience severe or worrisome side effects.

To maximize compliance with the study, an automated email will be sent to the patients to complete the survey with the link to the REDCap on Days 1, 3, 7. Patients can also be confidentially reminded using portal messages and Doximity texts.

At or after 4 weeks postoperatively, chart review will be done to collect data. Data collected will include patient age, comorbidities, indications for procedure, number of previous abdominal surgeries, size of uterus or specimens removed if reported, any pathology found in specimens, any intraoperative or postoperative

complications, and how many visits or communications the patient had after surgery within 4 weeks postoperatively.

Data will be recorded in a secure database on CCHS servers. De-identified data will be abstracted into a secure spreadsheet by the principal investigator.

Primary Objective:
The primary objective of the study will be to assess pain scores via VAS on Post Op Day 3 compared between the control group vs cyclobenzaprine group. As stated above, VAS pain scores will be collected electronically via REDCap. The survey will be distributed via Doximity text or patient portal message.

Secondary Objectives:
The study is not designed, nor powered, to test any other hypotheses other than the primary outcome. However, the study will collect data on analgesic use over a one-week period. In addition to the primary outcome of pain scores on POD3, pain scores will be collected on post op days 0, 1, and 7. In addition, the study will collect data on and analyze and describe side effects that may be contributed to cyclobenzaprine use. The researchers will also collect data to determine if any of the following variables contribute to changes in pain scores and/or requirements for analgesia: size of uterus, indication for operation, pathology, length of operation, blood loss, complications, and other pelvic surgeries performed. Lastly, we will determine if adding another adjunctive medication for pain changes compliance of post-operative medications and their effectiveness. Analyses of those endpoints will be exploratory.

Variables Collected
- Control or intervention group
- VAS Pain score on days 0, 1, 3, 7
- Any endorsed side effects (multiple choice list) on POD 1, 3, 7
- Patient characteristics
    - Age
    - Comorbidities
    - BMI
    - Number of prior intra-abdominal/pelvic surgeries
- Indication for procedure
- Size of uterus if measured
- Abnormalities on pathology reports
- Length of operation
- Estimated blood loss
- Intra-operative complications
- Number of additional pelvic surgeries performed (ex. LOA, ureterolysis)
- Post op complications within 4 weeks
- Number of communications with team within 4 weeks
- Number of office visits within 4 weeks
- Number of ED visits within 4 weeks
- Number of readmits within 4 weeks
- Compliance and required analgesics
    - Number of oxycodone left after 7 days
    - Number of cyclobenzaprine left after 7 days, if applicable
    - If patient is taking acetaminophen and ibuprofen regularly at each timepoint

Inclusion and Exclusion Criteria:
- Inclusion

    - Age >18yo
    - Female
    - English speaking
    - Undergoing (robotic assisted or classic) total laparoscopic hysterectomy ± unilateral or bilateral salpingectomy ± unilateral or bilateral oophorectomy
        - If other procedures such as lysis of adhesions, excision of endometriosis, or ureterolysis are indicated based on intraoperative evaluation, those patients may still be included
    - Surgery took place at ChristianaCare Hospitals
    - No allergies or contraindications to standard of care post operative pain medications (acetaminophen, NSAIDs, narcotics) or cyclobenzaprine
- Exclusion
    - Age <18yo
    - Male
    - Pregnant, breastfeeding
    - Non-English speaking
    - Primary procedures other than laparoscopic hysterectomy
        - Laparoscopic myomectomy
        - Laparoscopic resection of endometriosis
        - Laparoscopic unilateral or bilateral salpingectomy ± unilateral or bilateral oophorectomy ± unilateral or bilateral cystectomy without hysterectomy
        - Hysteroscopic procedures
        - Bartholin gland marsupialization
        - Operations that are scheduled as or converted to the open approach
    - Procedures with planned or unplanned bladder or bowel surgery
    - Allergies or contraindications to standard post operative pain control medications (acetaminophen, NSAIDs, narcotics), such as kidney or liver damage/failure, bariatric surgery, history of gastric ulcer, etc.
    - Chronic pain issues, whether self-diagnosed or by a physician, currently undergoing management
    - Currently undergoing medication assisted treatment for opioid use disorder
    - Currently using opioids consistently
    - Allergies or contraindications to cyclobenzaprine:
        - Absolute: use of MAO inhibitors within 14 days, recent heart attack, congestive heart failure, heart block or other conduction abnormalities, cardiac arrythmias, hyperthyroidism, history of serotonin syndrome
    - Allergies or contraindications to inactive ingredients in Flexeril, such as lactose
    - Patient's receiving gabapentin at baseline or postoperatively, due to potential sedating effects, or other sedating drugs such as scheduled benzodiazepines and barbiturates

Sample size and Statistical Analysis:
Sample size calculations are based on prior postoperative pain studies. The minimally clinically important difference in pain on the 0–10 VAS is commonly considered 1.0–2.0 points. As such, we assumed a 1.5-point difference. One trial published an SD for VAS pain scores after hysterectomy to be around SD=1.0 (based on graph interpretation).[17] Other published studies on postoperative pain after hysterectomy or abdominal surgery at different time points are typically around SD=1.0-1.5. To be conservative, we will use an SD=1.5 and a MCID (Δ)=1.5. Using the equation n per group = $2 \times (Z_{1-\alpha/2} + Z_{1-\beta})^2 \times \sigma^2 / \Delta^2$, with a power of 80% and α=0.05, the n per group would be 16. With a 10% attrition, the total n would be equal to 36 to evaluate the primary outcome. A full sensitivity table showing sample size requirements due to different plausible SDs and effect sizes is shown below. The chosen n of 36 is powered to evaluate the primary endpoint only. As such, the evaluation of the secondary endpoints will be exploratory and potentially underpowered.

SD (σ)	MCID (Δ)	N per group	Total N	Total N with 10% attrition

1.0	1.0	16	32	35
1.0	1.5	7	14	16
1.0	2.0	4	8	9
1.5	1.0	36	72	80
1.5	1.5	16	32	36
1.5	2.0	9	18	20
2.0	1.0	63	126	139
2.0	1.5	28	56	62
2.0	2.0	16	32	36

Statistical Analysis Plan:
Patients who formally withdraw will be excluded in all analyses. All other randomized participants will be included in the interion-to-treat analysis.

Primary Analysis: The primary analysis will follow the intention-to-treat principle and include all randomized subjects who have consented to participate in the trial, regardless of adherence, deviations, or completeness of outcome data.

The primary outcome, the VAS score on POD3, will be compared between the control and cyclobenzaprine. The primary analysis will be completed using analysis of covariance (ANCOVA) to estimate the adjusted mean difference between groups. The VAS score on POD 3 will be the outcome, and the cyclobenzaprine group will be the primary predictor. Covariates include the VAS score on POD 0 (baseline pain), age, BMI, and number of prior pelvic/abdominal surgeries (grouped into 4 categories: 0, 1, 2, 3 or more). In sensitivity analyses, we may additionally adjust for operative time, estimated blood loss, indication for surgery (categorical), and weight of uterus. Results will be reported as adjusted mean difference with 95% confidence intervals and two-sided p-values; $\alpha = 0.05$.

Secondary Analysis: Secondary objectives include VAS pain scores on POD 0, 1, 7. As each participant provides multiple pain scores, a linear mixed-effects model will be used to analyze the data. The fixed effects will be for treatment, time, and treatment × time interaction. The intergroup difference at POD3 from this model will be reported as a sensitivity analysis.

This survey will also collect reported side effects on POD 1, 3, and 7. The incidence of side effects reported on the REDCap survey will be analyzed using chi-square or Fisher's exact tests. Safety data (adverse effects) will be reviewed periodically by investigators with this information.

Compliance and requirement of narcotics will be determined by remaining oxycodone on POD 7. Total oxycodone remaining will be reported in number of pills left on POD 7 and converted to morphine milligram equivalents (MME). If the number of pills taken or total MME is not normally distributed, we will use negative binomial or zero-inflated regression models for analysis. When appropriate, pill counts will be summarized using medians and interquartile ranges and compared between groups using the Wilcoxon rank-sum test.

Further compliance of postoperative medications will be determined by self-reported binary indication of regular acetaminophen and ibuprofen use (yes/no) on POD 1, 3, and 7. This will be compared between groups with chi-square or Fisher's exact tests and modeled with logistic regression to estimate odds ratios and 95% confidence intervals.

A per-protocol analysis will be conducted as a secondary sensitivity analysis to evaluate the effect of treatment with cyclobenzaprine among participants with adequate adherence and without major protocol violations. Participants will be excluded from the per-protocol population if they were found to be ineligible after randomization, fail to complete the REDCap Survey at the designated time points, were prescribed

contraindicated medication leading to discontinuation of cyclobenzaprine if applicable, fail to receive the cyclobenzaprine medication if applicable, or underwent a protocol-discordant surgical procedure as listed in the inclusion and exclusion criteria. The per-protocol analysis will repeat the primary ANCOVA model with only eligible participants. Results will be compared to those from the intention-to-treat analysis. All per-protocol exclusions will be documented.

Based on the settings used in the REDCap surveys, missing data is not anticipated. In the event of missing data, it will be evaluated for patterns and multiple imputation will be performed if the proportion of missing data exceeds 5%. Sensitivity analyses will be conducted to compare results from complete-case and imputed datasets.

This study is powered to evaluate the pain scores on POD 3 between groups. All secondary analyses may be underpowered and are considered exploratory. No formal interim efficacy analysis is planned given the pilot nature of the study. Analyses will be performed using R. Statistical significance will be defined as $p < 0.05$ (two-tailed).

Protocol deviations, whether intentional or unintentional, will be defined as major or minor. Major deviations are those that affect subject safety, rights, or data integrity; these include enrollment of an ineligible subject, failure to obtain informed consent, overdose, incorrect dispensing of cyclobenzaprine to wrong patient). Minor deviations include minor documentation lapses, scheduling deviations, or one missed REDCap survey reminder. Deviations will be documented by the investigator who discovers the deviation. Documentation will include participant ID, date/time of deviation, brief description, major vs minor, and any corrective actions taken. All deviations will be reported immediately to the PI and the IRB in accordance with ChristianaCare policy. The PI will review all deviation logs at least weekly. If patterns arise that suggest a systemic issue, enrollment will be paused to implement corrective actions before resuming.

Risks and Benefits

This study does not involve investigational drug use, as cyclobenzaprine and oxycodone are both FDA-approved and prescribed at standard doses.

There is potential risk of additional or compounded side effects from cyclobenzaprine administration. The common side effects include dry mouth, dizziness, confusion, and somnolence. Rare side effects that are unique to cyclobenzaprine include mydriasis, dyspepsia, and urinary retention. The FDA labels for various cyclobenzaprine compilations do not report addiction as a side effect. The FDA has come up with a new Adverse Event reporting system. Of 18,289,374 adverse events reported, only 2,425 were linked to cyclobenzaprine, 179 of which were potential drug abuse.[18] The study states that the postulated euphoric events that lead to addiction or abuse were caused by long term use and at doses over 20mg.[18]

A comprehensive list of side effects for cyclobenzaprine and oxycodone are listed in Table 1. Risks of side effects from cyclobenzaprine will be minimized as the lowest dose, 5mg, is being utilized. Studies found that taken three times daily, 5mg of cyclobenzaprine is as effect as 10mg, with a decrease in side effects.[19]

Furthermore, there will be strict exclusion criteria for patients at higher risk of experiencing side effects, such as use of MAO inhibitors within 14 days, recent heart attack, congestive heart failure, heart block or other conduction abnormalities, cardiac arrythmias, hyperthyroidism, and a history of serotonin syndrome. Whilst obtaining informed consent, patients will be made aware of the potential interactions with diphenhydramine and other CNS depressants. There is a theoretical risk of using cyclobenzaprine in conjunction with SSRIs, SNRIs, or TCAs given cyclobenzaprine's similarity in structure to TCAs. A single case report of serotonin syndrome in a patient who ingested 50-60mg of cyclobenzaprine, alcohol, and fluoxetine.[20]

A study by Chen et al. found that there was not a statistical change in hazard ratio for injury in patients taking oxycodone and cyclobenzaprine concomminantly.[21] Moreover, a study on the concomitant use of muscle relaxants and chronic opioids utilized cyclobenzaprine as a reference point, as their pooled databases

documented over 440,000 patients who were prescribed cyclobenzaprine, followed by tizanidine at 160,000 patients.[22] This illustrates the broad use of this medication. This study also found that of patients on opioids and cyclobenzaprine, 28% of patients were on SSRIs, 15.8% were on SNRIs, 10.5% were on TCAs, 16.7% were on other antidepressants, and 43.4% were on benzodiazepines, which illustrates the common practice of utilizing these medications together.[22] Lastly, this study determined that there is increased risk of opioid overdose in chronic opioid users who take baclofen (weighted HR 2.48) and carisoprodol (HR 1.70) relative to cyclobenzaprine. Alternatively, methocarbamol, tizanidine, and chlorzoxazone/orphenadrine have similar weighted hazard ratios to cyclobenzaprine. Only metaxalone had a decreased hazard ratio at 0.61, however the price of this medication is approximately five times that of cyclobenzaprine.[22] Although this study is relevant, it is important to note that all patients included in the study were on chronic opioids, over 90 days, compared to the short course proposed in this study.

All patients will be advised against drinking alcohol, using benzodiazepines or barbiturates, or using any recreational drugs that could interact with cyclobenzaprine or opioids.

Patients will be able to report side effects on the study survey. Survey data of side effects will be reviewed by an investigator at least twice weekly to ensure close monitoring for adverse effects. If any serious or life-threatening adverse effects are reported, patients will be directed to call the on-call doctor and/or present to the CCHS OBGYN Emergency Room. If side effects are severe, the patient will be withdrawn from the study immediately. Serious adverse events or unanticipated problems will be reported to the IRB in accordance with ChristianaCare policy.

Potential benefits on the patient level include improved postoperative pain management and decreased opioid utilization. There is also significant potential benefit for the medical community, as there is a clear lack of evidence on muscle relaxant use for postoperative pain control.

Table 1. Risks of Oxycodone and Cyclobenzaprine, Compiled from FDA Labels and StatPearls

	Oxycodone – exclusive side effects	Side effects shared by oxycodone and cyclobenzaprine	Cyclobenzaprine – exclusive side effects
Most Common	Asthenia Constipation Nausea Pruritus Sweating Vomiting	Dry mouth Drowsiness Confusion Fatigue	
Other	Bradycardia Hypotension Photosensitivity Rash Anorexia Glossitis Increased cerebrospinal pressure Cough Respiratory depression Dependence	Headache Fatigue Palpitations Diarrhea Sedation Hallucinations Irritability Abdominal pain Seizures	Mydriasis Urinary retention Dyspepsia

FDA Investigational New Drug (IND) Exemption Justification

This randomized controlled trial is evaluating the effect of cyclobenzaprine, an FDA-approved muscle relaxant, on postoperative pain control following minimally invasive hysterectomy for benign indications. This study is investigator-initiated. In the United States, cyclobenzaprine is lawfully marketed (NDA 17-821/S-045, specific to

Flexeril®). In this study, the proposed use of 5mg three times daily is within the approved oral dosing range (5–10 mg).

This study is solely designed to improve medical knowledge about postoperative pain management. It is not intended to support any new indications of the drug or a significant labeling change. The study will not be designed to change any advertising claim or for commercial promotion. This trial will not involve a new route of administration or higher dose of cyclobenzaprine. In addition, cyclobenzaprine will not be given to a patient population that would significantly increase the risk to subjects beyond that encountered in routine medical practice. As stated in earlier in this proposal, any patients with known contraindications to cyclobenzaprine will be excluded from the trial.

As such, this study meets all criteria under 21 CFR 312.2(b) for exemption from IND requirements. The protocol will adhere to all applicable human subjects protections including being under review from the IRB and utilizing a uniform informed consent process (21 CFR parts 50 and 56).

Informed Consent:
Voluntary informed consent is required for this study. There are inherent risks for any medication, including ones already routinely used for postoperative care by this practice. This research poses minimal additional risk to individual patients, limited to the risks of cyclobenzaprine. As such, the risk imposed by this study is limited to the intervention group. Please see the attached Informed Consent form. All persons who are able to obtain Informed Consent will be listed on the Delegation Log.

Patients will provide voluntary informed consent in person, either during the initial or preoperative office visit, or in the preoperative area. This will be done prior to any medication being prescribed by authorized personnel. Consent in the preoperative area will only occur if the patient has previously reviewed the consent form verbally over the phone and had an opportunity to ask questions. Eligible, enrolled, and consented patients will be randomized to either the experimental or control group at the time postoperative medications are prescribed by qualified personnel, or at the earliest opportunity, no later than in the perioperative setting. Patients may refuse or withdraw consent at any time without affecting their care.

Confidentiality and Security:
Voluntary informed consent will be requested from all eligible subjects and required for participation. In order to facilitate data collection, medical record numbers and record ID numbers will be recorded on the informed consent forms to link identifiers. Informed consent will be obtained electronically. All electronic and web-based study documents, including identifiers, will be stored in REDCap. PHI collected will include name, date of birth, race, ethnicity, email, and medical record number. Access to REDCap will be limited to the principal investigator, supervisor, and sub-investigators. Extracted, deidentified data and any analyses from REDCap will be saved in an excel document on the ChristianaCare server or a secure flash drive. There is no plan to share this data outside of ChristianaCare. Any identifiers collected will remain in REDCap and informed consent copies be stored on the ChristianaCare shared drive. These documents will not be shared outside of ChristianaCare. When data collection is complete, all identifiers except for the study ID number will be redacted from the data set to further protect confidentiality. All informed consents and identified data will later be deleted or destroyed in a manner compliant with CCHS data security.

Data Safety Monitoring
Due to this being a low-risk, short duration pilot study, using an FDA-approved medication; a formal Data Safety Monitoring Board is not required. Safety will be monitored by investigators.

Withdrawal Procedure:

Participants may withdraw from the study at any time without penalty. Data collected prior to withdrawal will be retained unless the participant requests removal.

Subject Compensation:
Participants will not be compensated for participating in this study.

Funding:
There is no additional funding for this project.

Conflicts of Interest:
There are no conflicts of interest amongst any participating clinician.

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