1) Protocol Title

Title: Gabapentin for pain control after osmotic dilator insertion and prior to D&E procedure: a randomized controlled trial

Protocol Version Date: 01/11/2018

2) Objectives

Pain management in the context of abortion is a topic that is both challenging and necessary to research. The Society of Family Planning (SFP 2014) lists it as a top research priority. Most research to date has focused on pain during the abortion procedure. One area that remains under investigated is women's pain experience during the time osmotic dilators are in the cervix prior to the dilation and evacuation procedure. As a result, management of pain during this time period varies greatly and is largely based on anecdotal experience. Adjunctive pain management with non-narcotic medications such as gabapentin may have a place during this time. Gabapentin is unique in that it is both well tolerated with minimal contraindications and low cost with 600 mg doses as low as $0.24. Additionally, widespread dissemination of cell phones and text messaging now gives us the opportunity to communicate with women about their dilator-related pain experience in real-time, potentially improving data quality.

We have planned a randomized, controlled trial of repeated doses of gabapentin compared to placebo for pain management during the time after dilator insertion and prior to D&E the subsequent day. Participants will receive gabapentin 600 mg or placebo prior to dilator insertion. Pain scores will be measured via numeric rating scale (NRS) at baseline and 5 minutes after insertion while the participant is in clinic. Additional pain scores as well as side effect and additional analgesic use will be obtained by text message while the patient is a home at 2 hours, 4 hours, and 8 hours after time of dilator insertion. Final pain score, side effect, and analgesic use assessment will occur upon presentation to the pre-operative are for D&E. We hypothesize that women who receive gabapentin beginning at the time of dilator placement for a D&E procedure will report a smaller increase in pain from baseline at 8 hours after dilator placement compared to women receiving placebo.

3) Background

Osmotic dilators are an essential component of cervical preparation prior to dilation and evacuation (D&E) procedures. To date, research involving osmotic dilators has typically focused on their relationship to ease of D&E completion, either alone or in conjunction with pharmacologic agents such as misoprostol or mifepristone. Those studies that evaluate pain with dilator insertion and during the interval between insertion and the D&E procedure do so as a secondary outcome. [1-4] It is clear that insertion of dilators is more painful than using a medication and there are varied accounts of how this pain changes over time. [2, 3, 5] One recent study evaluating use of intrauterine lidocaine for pain relief during dilator placement found that visual analog scale (VAS) pain scores overall were actually higher during the time after dilator insertion and before D&E than

during the insertion process. [1] As there have been no studies to directly evaluate women's pain during the interval between dilator insertion and D&E, this area remains an under evaluated aspect of women's abortion experience.

Multimodal pain management has become an area of interest across many procedural fields. Though no data exists regarding current pain management strategies for pain after dilator insertion, anecdotal experience includes recommending over-the-counter analgesics (e.g., acetaminophen and ibuprofen) or oral narcotics. Adjunctive analgesic medications have been explored within Obstetrics and Gynecology for pain management, primarily in the context of Cesarean delivery and abdominal hysterectomy. Gabapentin is one such agent which has both analgesic and antiepileptic properties and few contraindications. [6] Use of this agent, as compared to similar drugs such as pregabalin, is appealing due to its low cost. When considering commonly studied perioperative dosing, gabapentin can be purchased for as low as $0.24 per 600 mg dose whereas pregabalin is $14 per 150 mg dose. [7-12] Studies regarding preoperative use of gabapentin in abdominal hysterectomy have demonstrated decreased post-operative narcotic use, decreased nausea and vomiting, and increased patient satisfaction. [8, 13-17] Reports regarding side effects such as sedation are varied. [8, 13-17] Data regarding preoperative gabapentin use and post-operative Cesarean delivery pain is more limited and less consistent. [7, 9, 18, 19] The heterogeneity of gabapentin dosing and overall pain regimen along with study design limitations make these data challenging to generalize to abortion procedures

Ultimately, studies regarding gabapentin for pain relief in abdominal hysterectomy and Cesarean delivery do not serve as good proxies for using gabapentin during abortion care. The pain experience of laparotomy, which is confounded by various regimens of regional and general anesthesia, is different than that of dilator insertion and subsequent D&E. Recent projects by family planning fellows are evaluating the use of gabapentin for medical and surgical abortion in the first trimester. We propose a study to evaluate the effect of gabapentin on the pain experienced between dilator insertion and D&E. I believe this treatment will be beneficial to patients and my findings could be used to create a pain regimen that could encompass both cervical preparation and D&E. Since women will be outside of the healthcare setting for most of their dilator experience, I plan to use short messaging service (SMS; text message) to allow women to communicate pain evaluation and analgesic use in real time.

4) Inclusion and Exclusion Criteria

Patients undergoing preoperative evaluation for abortion at the UCDMC family planning clinic will be the population for subject recruitment.

Women presenting for dilator insertion on the day prior to their scheduled D&E procedure with gestational age 15 weeks 0 days to 23 weeks 5 days at time of preoperative appointment will be eligible for inclusion. Eligible participants will be able to read and write in English. Women age 18 or greater may be included. Due to possible sedative effects if randomized to gabapentin, women will require a ride from the clinic to be included. Participants must have a text messaging enabled phone and be willing to send and receive text messages about their experience during the study time period.

Exclusion criteria include current gabapentin or pregabalin use, allergy to gabapentin. Ibuprofen, acetaminophen or codeine, self-reported renal disease, and self-reported active narcotic use. Patients who are currently incarcerated will also be excluded. Adults who are unable to consent are not traditionally encountered due to the nature of abortion care (with abortion as a voluntary procedure), however they will also be excluded in the unlikely event this situation arises.

Eligible women will be approached by Family Planning physicians and/or research staff about the study. Women will be counseled that study participation will not impact their clinical care. Those who are interested will be given adequate time to review the study consent form and to address any questions with a study investigator. Written consent will be obtained only after consent for clinical care is completed. There will be no advertising or external recruitment for this study.

5) Study Timelines

Participant's involvement in the study will extend from recruitment during preoperative visit in clinic, through their overnight experience with cervical dilators in place, and end after their final interview in the preoperative area in the main operating room prior to their abortion procedure.

Based on our current volume, we estimate that we will complete enrollment of 121 women in 12 months (goal of February 2017 – January 2018). Between August 2015 and June 2016, the clinical Family Planning fellow completed 228 D&E from 15 weeks 0 days to 23 weeks 6 days gestational age (on date of procedure) at the UC Davis Medical Center. Completion of the primary analysis will occur by March 2018.

6) Study Endpoints

The primary study endpoint is enrollment of 121 total participants. The study will be reviewed at least monthly to monitor for adverse events that would indicate safety issues and thus a safety-related endpoint. Adverse events will include both

medical concerns and patient privacy concerns given text message contact at home.

7) Procedures Involved

Recruitment will occur in the Division of Family Planning pre-operative clinic held once to twice weekly in the Lawrence J. Ellison Ambulatory Care Center of the UC Davis Department of Obstetrics and Gynecology. This clinic is specifically for patients seeking abortion procedures. Family Planning physicians and/or research assistants will obtain informed consent from eligible women that opt to participate (all family planning attendings and fellows will be trained as study personnel). An institutional HIPAA Authorization form will also be obtained to allow access to participant's medical record for information related to the study. Study information will include demographic traits and information from dilator placement.

The current standard of care at our institution is for women to present for pre-operative evaluation and osmotic dilator placement on the day prior to scheduled D&E. Cervical anesthesia with Xylocaine 1% 20 mL is standardly administered immediately prior to dilator insertion. All providers follow standard guidelines on the number of dilators to place based on gestational age. Xylocaine is the cervical anesthetic standardly used at our institution as well as in other reported pain studies. [20-23] Although bupivacaine has a longer duration of action than xylocaine (2-4 hours and 1-2 hours, respectively), the increased duration does not cover the entire osmotic dilator experience. [24] Additionally, bupivacaine is not commonly used in cervical anesthesia-related abortion literature or clinical practice, limiting generalizability. Only Dilapan-S® hygroscopic cervical dilators are used in our practice. Misoprostol is not used in conjunction with dilators. Mifepristone is only used in the context of suboptimal dilator placement or gestational age of 22 weeks or more. After dilator placement, women standardly receive prescriptions for acetaminophen 300 mg/codeine 30 mg and ibuprofen 800 mg which can be used as needed for pain management during the time between dilator placement and D&E. At UC Davis Medical Center (UCDMC), D&E procedures are completed in the main operating rooms on the day following dilator placement with the aid of deep sedation. **There will be no deviation from the above standard practice for participants in this study.**

Study methodology for this randomized double-blind placebo-controlled trial will proceed as follows:

1. Eligible women at 15 weeks 0 days – 23 weeks 5 days gestational age at time of preoperative appointment will be approached regarding the study prior to dilator placement. Consent will be obtained.
2. Relevant baseline demographics (age, race, ethnicity, education level, gravidity, detailed parity, reported history of anxiety, depression, drug abuse, chronic pain, recent narcotic pain medication use, and reason for pregnancy termination) will be collected. These are standard questions asked of **all** patients during their preoperative abortion evaluation.

3. Participant will be asked to provide pain level on 11-point (0-10) NRS immediately before study drug ingestion as the baseline pain score. Baseline symptoms (sedation and dizziness) will also be recorded.
4. Women will ingest the assigned gabapentin 600 mg or placebo
    a. Stratified block randomization will occur to achieve even distribution of women based on vaginal parity (no prior vaginal delivery versus one or more prior vaginal deliveries). This strategy will ensure similar numbers of women with vaginal parity between gabapentin and placebo groups as this may be an important factor influencing pain with dilators in general.
    b. A UC Davis Investigational Drug Services (IDS) pharmacist will use computer-generated randomization to place active or placebo treatment in two groups of sequentially numbered vials (to account for block randomization based on parity)
5. The physician will proceed with dilator insertion via our existing standardized method (including standard cervical anesthesia with 1% xylocaine 20 mL, standard number of dilators based on gestational age). Number of dilators and any pharmacologic means of cervical preparation are already reported in a standardized template and will be available for chart review.
6. Post-dilator pain will be assessed via NRS at five minutes after dilator insertion. Additional symptoms (sedation and dizziness) will be recorded.
7. Women will be discharged home with:
    a. One additional study medication (Gabapentin 600 mg or placebo) to take at home 8 hours after the initial dose. This medication will be labeled by the IDS and completed by administering physician.
    b. Standard prescriptions for acetaminophen 300 mg/codeine 30 mg and ibuprofen 800 mg to take as needed.
    c. A reminder form that includes 24-hour research contact information, the times when they can expect text messages, a reminder to take the home dose of their assigned study medication at 8 hours after dilator insertion (exact time will be written out) and a reminder to bring the empty study medication bottle with them when they present for their procedure the next day.
    d. Recommendation that they have a ride to and from abortion procedure the subsequent day.
8. Participants will be sent a baseline text message from the study phone prior to leaving the clinic. Participants will be encouraged to enable privacy features on their personal phone. Examples of security features will be reviewed and included in the consent.
9. Participants will be contacted via text message at 2, 4, and 8 hours after dilator insertion.
    a. Text messages will originate from a password protected study cell phone. Android application “SMS scheduler” will be used to send standardized text messages to the participant at pre-programed time intervals from time of dilator insertion.
    b. Text message content:
        i. Current NRS pain score
        ii. Inventory of analgesic use since last contact
        iii. Presence of symptoms (sedation and dizziness)

iv. Reminder to take the assigned study medication (at 8 hours only)

10. Upon admission to the pre-operative ward prior to D&E, we will document the time and assess the current NRS pain score, additional analgesic use since 8 hour text message contact, and presence of symptoms (sedation and dizziness)

Blinding

Participants and providers will be blinded to study drug allocation as all study drug will be prepared by the pharmacist and placed into numbered drug bottles.

Privacy protection

Participant privacy is another ethical concern in this study. Participants may have people with access to their cell phones who do not know about the pregnancy or abortion. Compromising a woman's privacy about this matter could put her at risk depending on her life situation. To prevent this, I plan to use generic language that does not identify the context of the woman's care. Women will be counseled regarding their ability to rescind their participation at any point. Below is the verbatim content of each text message that will be sent to participants. These text messages will be sent in order, with a programmed one-minute interval between each question:

1. "What is your current pain level on a scale of 0-10? (Zero is no pain and ten is the worst pain imaginable)"
2. "How many pills of ibuprofen have you taken since the last text?"
3. "How many pills of acetaminophen with codeine have you taken since the last text?"
4. "Do you feel more dizzy than usual?"
5. "Do you feel more tired than usual?"

Participants will be told about the number, timing, and generic content of text messages. Women will be told that the text messages will contain questions regarding their pain, medication use, and other symptoms. This generic statement adequately represents the specific text message content as depicted above. Participants will not receive the verbatim text in advance. The primary reason for measuring pain via real time text message in this study, as opposed to home pain diary via VAS, is the benefit of spontaneous response which is more likely to reflect a participant's true state. By providing the verbatim questions up front, participants may consciously or unconsciously formulate a planned response, thereby compromising the internal validity of the data in this study.

Study drug

Gabapentin (Neurontin®) was initially approved by the U.S. Food and Drug Administration (FDA) for use as an antiepileptic. [25] The FDA expanded its use to include postherpetic neuralgia in 2002, as research revealed gabapentin to be an effective treatment for neuropathic pain. [25] Off-label use has expanded to include perioperative and cancer pain. [25]

Gabapentin is structurally similar to the gamma-aminobutyric acid (GABA) neurotransmitter. [26] The mechanism of action for both antiepileptic and analgesic uses

remains unknown. [26] Initiating gabapentin treatment for long term use typically starts at a dose of 300 mg every eight hours. [25] Dosing for perioperative use is typically higher though studies are heterogeneous in both dose and frequency. [25] The bioavailability of gabapentin actually decreases as the dose increases. For example, a dose of gabapentin 600 mg has 60% bioavailability, while increasing to 900 mg decreases to 47%. [26] For the purposes of this study, gabapentin 600 mg will balance concerns about lower analgesic efficacy at 300 mg doses with increased side effects without improved pain management at higher doses. [25] Using gabapentin 600 mg is also concordant with an existing fellow study investigating gabapentin use for pain during first trimester aspiration abortion and will add to the early research on gabapentin in abortion care.

Interest in gabapentin for perioperative pain management is increasing in part due to its favorable safety profile. There are few contraindications to gabapentin use. It is excreted by the kidneys unchanged from its ingested form. [26] The absence of hepatic metabolism enables use in patients with hepatic disease or on medications that influence hepatic enzymes. [26] Renal insufficiency can increase the clearance time of gabapentin so dosage adjustment or avoidance of gabapentin is needed depending on the severity of renal disease. [26] Gabapentin is well tolerated in the pediatric population as well. [26] Most common side effects include dizziness and somnolence with less common reporting coordination or balance issues, peripheral edema, or gastrointestinal symptoms. [26] These reports are among chronic users of gabapentin. Studies investigating perioperative use focus more on immediate side effects experienced by gabapentin naïve patients such as dizziness and somnolence. [26]

Study drugs will be obtained from the UC Davis Investigational Drug Services (IDS). The IDS is a division of UC Davis Pharmacy Services that can procure gabapentin and over-encapsulate it to match an identical placebo. The IDS controls participant randomization, maintains randomization log, and provides additional support for study drug administration along with accountability and adherence with state drug dispensing regulations. The IDS has already reviewed this research study and has formulated a plan for study execution with investigators. Peter Trovitch, PharmD (Senior IDS Pharmacist) has shadowed the Principal Investigator in the preoperative clinic to formulate a concrete plan for IDS drug preparation and medication accountability.

Participant Compensation:

Participants will be compensated $30 for initial study drug ingestion and completing baseline data collection. They will be provided based on fully answering all five text messages at each scheduled encounter. Compensation will include an additional $10 for completion of 2 hour and 4 hour text messages, and $20 for the 8 hour contact. Participants will receive a final $30 for completion of the assessment when presenting for D&E. Compensation will occur via gift cards provided to participants when presenting for their procedure the subsequent day. Maximum compensation per participant will be $100, with partial compensation possible based on participation level. Participants will be provided with the compensation levels.

8) Data and/or Specimen Management and Confidentiality

Sample size calculation

For the purpose of calculating sample size, there is no existing data that truly mirrors the objective of this study (context of pain, use of NRS, and use of change in pain score from baseline). The closest approximation is the mean immediate post-dilator insertion pain score of 5.2 (SD 1.2) via NRS from Borgatta, et al (2012). However, when using this data point and a commonly cited clinically significant decrease in NRS pain score of 2 points, computation with SAS 9.1 (factoring in power at 80% (α=0.05), normal distribution) yielded a small sample size of only 12 women per group. [27-33] Based on the block randomization there are four groups for a total of 48 women. To account for up to 20% of subjects not responding to text messaging for the primary outcome the sample size estimate will increase to 58 total women. To ensure we gather sufficient data to truly outline pain experience during the dilator-procedure interval, we will more than double the sample size to recruit 121 women. We will stratify these 121 women by presence or absence of prior vaginal parity. Ensuring similar distribution of vaginal parity between the gabapentin and placebo groups is important as vaginal parity may affect pain with osmotic dilators.

Statistical Analysis

We will use non-parametric testing to assess the primary outcome variable because we do not expect normal distribution of the data. Chi square analysis and fisher exact tests will be used to compare demographics and dichotomous variables as appropriate. I plan to describe the pain course for the total study cohort using means and medians as appropriate.

Data Management

Participants will be assigned a unique study number for use on source documents and participant study charts. These documents will be kept in a locked file cabinet accessible only to study staff. Data from participant's study charts and text message contact will be entered into a secure database. No identifying information will be entered into the study database. Only password-protected, institutionally secured UC Davis computers will be used for data entry and analysis. Data will be reviewed by the principal investigator and research coordinator to ensure accuracy and completeness. The research database will be banked indefinitely for the purpose of future research questions and will contain only de-identified information as above.

A cell phone will be purchased for the purposes of this study. This phone line will be dedicated to the study and will be password protected. It will stay with the principal investigator or research assistant during the times when participant follow-up is occurring. Outside of this time, the secured cell phone will be kept in a locked file cabinet with restricted access. Since the phone will not be attended at all times, participants will be given the standard UC Davis contact information for all clinical and study-related questions at any time. Our division has a dedicated phone line for family planning research patients that is covered by research personnel during the day (who have close access to an assigned family planning physician) and forwarded to the on call family

planning attending or fellow at night. All family planning attendings and fellows will be trained as study personnel. The cell phone's remote data erase function and location service will both be activated to protect study data in the event that the phone is lost or stolen.

Prior to first contact, the research assistant will program the participant into the phone contact list with their study number and preferred phone number. The Android SMS Scheduler application will record all scheduled and sent text messages. The application's template function will be used to ensure all outgoing text messages are uniform. Incoming text messages are returned to the cell phone's default text message application. The study cell phone will only be connected to the password protected, secure institutional wireless internet connection. The study cell phone's mobile data will be turned off at all times to improve security. Text message responses will be input into the study database on a weekly basis and the participant's contact information and text messages deleted from the phone.

9) Data Banking

The entire research study database, which will contain only de-identified data, will be banked indefinitely for the purposes of future research analysis.

10) Provisions to Monitor the Data to Ensure the Safety of Subjects

- Safety data will be collected throughout the study – participants will be asked about potential medication side effects.
- Adverse event (AE): adverse experience such as symptom, physical exam finding, or worsening of a preexisting condition that has a temporal association with research participation. Causal relationship with study treatment is not necessary to designate an AE.
- Given the contact of participants via text message in this study, significant breech in participant privacy will also be classified as an adverse experience. At enrollment, participants will be counseled to ensure they are making a fully informed decision to participate knowing that there will be text message contact with them. They will be counseled regarding ways to withdrawal if safety becomes a concern. If this occurs, study staff will list safety-related withdrawal as an AE and review as below.
- Serious adverse event (SAE): adverse event that requires hospitalization, causes significant disability, is life threatening or results in death.
- AEs will be logged and reviewed by an investigator for study drug relationship
- Any SAE will be reported to the principal investigator once identified. The participant will be managed medically as indicated. All source data will be

reviewed. Physician investigators will assess for causality or relatedness of the adverse experience to the study.

- In accordance with UC Davis institutional review board (IRB) reporting policy, AEs will be reported at annual IRB renewal submission. SAEs that are unanticipated and thought to be related to the study (thereby placing research subjects at higher risk of harm than originally thought) will be reported to the IRB by the principal investigator within five days of becoming aware of the event.
- The study will be reviewed semimonthly at the Family Planning division research meeting, which includes all research staff. Any concerns regarding individual or trends in AEs will prompt further review of the study and consideration of study termination.
- Study allocation will remain concealed except in a scenario in which revealing allocation is clinically important for the participant's management

11) Withdrawal of Subjects

Based on the safety of existing research on both gabapentin for peri-procedure pain and an existing abortion-related study using text messaging of subjects, we do not anticipate frequent circumstances for participant withdrawal. There are both investigator and participant-initiated modes for subject withdrawal. Participants will be withdrawn from the study pending investigator review of AE that warrants removal or any SAE (see Section 10). Participants will be counseled at enrollment about how to withdrawal themselves from the study for any reason. If a participant is withdrawn from the study, no further data will be collected. We will inquire about the reason for withdrawal so we can monitor for AE/SAE.

12) Risks to Subjects

There are two primary categories of risk in this study:

1. ***Study medication risk (Gabapentin):***

   As noted in Section 7, Gabapentin is a safe, well tolerated medication that is an established agent of interest for peri-procedure analgesia. Contraindications and medication interactions are few. This study will be monitoring for the more common side effects that can happen (though not frequently in prior studies), including increased self-reported sedation and dizziness from baseline.[25]

   The FDA label for gabapentin lists adverse events reported by studies investigating the drug for management of either epilepsy or postherpetic neuralgia. Both FDA approved indications for gabapentin use a wide range of drug dosing and a significantly longer duration compared to this study. Studies investigating gabapentin for peri-procedure analgesia are powered to detect their primary outcome of pain reduction. Those studies reporting side effects ask about sedation and dizziness most commonly. [34] Gynecologic studies, typically in the context of abdominal hysterectomy, report no statistically significant increase in sedation or dizziness compared to placebo. [13-14] Both studies started with initial doses of gabapentin 1200 mg, which is twice the dosing of this study.[13-14] Dierking et al continued gabapentin dosing for a total of 3000 mg over 24 hours (year). While

participants may be able to understand the FDA risk stratification, delineating frequent, infrequent, and rare adverse events, the risks in the label do not accurately simulate the clinical context of this study.
To minimize risks, the dose of Gabapentin used in this study is comparable to that of prior peri-procedure studies and the same as an ongoing randomized controlled trial through the family planning division at Emory University that is investigating Gabapentin 600 mg versus placebo for pain control during first trimester aspiration abortion. [25] Out of caution, participants will be required to have a ride home from the clinic as criteria for study eligibility so they aren't driving after study medication dosing. Frequency of reported side effects will be closely monitored, as well as any AE or SAEs, per Section 11.

2. ***Privacy risk*:**
As noted in Section 7, participant privacy is a consideration as participants will be contacted while outside the healthcare setting and other individuals may have access to their cell phone. To protect participants' privacy, only the above text content will be sent, which is generic in nature and does not identify pregnancy or abortion. Participants will be given a form listing the times when the text messages will be sent to them so they can keep the phone with them. Participants will be advised to also password protect their own phone and change settings so text message content is not displayed on their phone without unlocking it. Participants will also be given the 24-hour contact information for family planning research coordinators/physicians that can remove them from the study and discontinue any future text message contact if they wish.

The study cell phone will only be used in the small research office/preoperative clinic area and will be in a locked cabinet when not in the hands of research staff. As noted, it will not be connected to the mobile data network and will only be used over the secure, password protected UC Davis wireless internet. Data will be erased from the phone on a weekly basis after import into the secure database. The phone's remote erase and location functions will be enabled for another layer of security. Family planning physicians at the University of Hawaii who are completing a similar study (randomized controlled trial of Pregabalin versus placebo for pain with medication abortion, communicating with participants at home via text message through the SMS Scheduler Android App) have provided insight into use of the text messaging app/privacy protection and have reported no privacy-related adverse events.

The form given to participants that includes text message times will identify the UC Davis Department of Obstetrics and Gynecology, as well as Family Planning physicians, in the contact information for participant questions or concerns. This does not pose additional risk to our participants as **all** patients in our pre-operative abortion clinic are given a folder containing copies of their signed abortion

consents, post-dilator and pre/post abortion care instructions, along with abortion support references.

13) Potential Benefits to Subjects

There are no direct benefits to participants.

14) Community-Based Participatory Research

Not applicable

15) Sharing of Results with Subjects

Results will not be shared with participants or other providers.

16) Prior Approvals

A concept paper detailing the background, hypotheses, design and methods of this study has been approved by the funding organization (Society of Family Planning). A full proposal has been submitted and is under review. The study will not be initiated until funder approval of the proposal is obtained.

17) Provisions to Protect the Privacy Interests of Subjects

See section 12 for acknowledgement of privacy risk and steps undertaken to minimize this risk.

Participants will be made to feel at ease with the research situation by study staff using lay language to describe the study and to reinforce the fact that patient's care will not be influenced by participation in or declination of the study. The baseline history questions, such as reason for abortion, substance abuse, mental health, and medical/obstetric history are asked of all of our pre-operative abortion patients. Obtaining answers to these questions ensures that we not only provide medically safe abortion procedures but that we can provide additional support (such as counseling resources, social work referrals) to patients that endorse active issues. We ask all patients about the reason for their abortion so we can ensure they are making an autonomous decision to terminate the pregnancy and are not being coerced. Additionally, we can provide support as above depending on the situation around the abortion (such as fetal anomaly, etcetera). As family planning specialists, our physicians are well trained to provide sensitive care to women seeking abortion every day and are thus adept to asking these standard history questions.

The research staff will have access to the participant's medical records for study purposes only. Participants will be notified of this and research staff will review and sign an institutional HIPAA release to grant this access.

18) Compensation for Research-Related Injury

The University of California, Davis Health System will provide care needed to treat injuries directly resulting from taking part in this research. Insurance or third party payers may be billed, if appropriate, for the costs of the care subjects received. Subjects

may be responsible for some of the costs. The University of California, Davis does not plan to compensate subjects for injuries.

19) Economic Burden to Subjects

The only potential economic cost to participants would occur if their cell phone plan required additional payment for text messaging responses. The compensation structure for the study should cover these costs if they do occur.

20) Drugs or Devices

The UC Davis Investigational Drug Service has been notified regarding this research study. Meetings between the principal investigator and IDS staff have occurred to formulate a plan for study drug formulation (over-encapsulated Gabapentin 600 mg with an identical placebo) along with drug storage, labeling, randomization, and overall administration oversight. Regular drug reconciliation checks will occur by the study team. As noted, Peter Trovitch, PharmD (Senior IDS Pharmacist) has shadowed the Principal Investigator in the preoperative clinic to ensure the plan formulated can be reasonably executed based on clinic work flow. Study drugs will be administered only by family planning physicians (all family planning attendings and fellows will be trained on the study) in accordance with IDS instructions. The study drug will only be administered to enrolled study participants. Participants will administer the second dose of study drug at home and will have clear instructions on both the drug label (through IDS) and research participant form.

☒ I confirm that all investigational drugs will be received by the Investigational Drug Service (IDS). The IDS will store, handle, and administer those drugs so that they will be used only on subjects and be used only by authorized investigators.

☒ I confirm that all investigational devices will be labelled in accordance with FDA regulations and stored and dispensed in such a manner that they will be used only on subjects and be used only by authorized investigators.

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