PARTNERS HUMAN RESEARCH COMMITTEE
PROTOCOL SUMMARY

Answer all questions accurately and completely in order to provide the PHRC with the relevant information to assess the risk-benefit ratio for the study. Do not leave sections blank.

PRINCIPAL/OVERALL INVESTIGATOR
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PROTOCOL TITLE
Liposomal Bupivacaine at Cesarean Delivery to Decrease Post-Operative Pain

FUNDING
Pacira Pharmaceuticals

VERSION DATE
April 4, 2017

SPECIFIC AIMS

Concisely state the objectives of the study and the hypothesis being tested.

This study is a pilot randomized trial to implement the infiltration of liposomal bupivacaine in the Pfannenstiel incision at the time of cesarean delivery.

Our aims are:
1. To measure pain scores with activity at 24-, 48-, and 72-hours postoperatively after cesarean delivery
2. To measure total post-operative opioid use after cesarean delivery.
3. To measure patient satisfaction with pain control, using a validated tool
4. To describe adverse events related to liposomal bupivacaine infiltration

We hypothesize that the addition of liposomal bupivacaine to multi-modal pain management after cesarean delivery will reduce pain scores with activity at 48- and 72-hours after cesarean delivery.

BACKGROUND AND SIGNIFICANCE

Provide a brief paragraph summarizing prior experience important for understanding the proposed study and procedures.

Cesarean delivery is the most common inpatient surgical procedure in the United States [1]. There were 1.3 million cesarean deliveries performed in 2014, accounting for 32% of all deliveries, and representing a 60% increase since 1996 [2,3]. Prescription opioids are one of the mainstays of pain management after cesarean delivery. For many women, a cesarean delivery is her first major surgical procedure and may also be her first exposure to prescription opioids. Although opioids are an effective pain management strategy, there are associated risks and side effects, including respiratory depression, nausea, vomiting, postoperative ileus,

sedation, constipation, and urinary retention, all of which have a negative impact on postoperative recovery.

In addition, there is an ongoing nationwide epidemic of prescription opioid abuse, accounting for over 300,000 emergency department visits per year [4]. Between 2000 and 2014, opioid overdoses far surpassed motor vehicle accidents as one of the leading causes of accidental death [5,6]. Moreover, opioids from legitimate prescriptions are a primary source of prescription or illicit opioids being used for recreational purposes, leading to adverse health consequences such as death from overdose [7,8]. Given the opioid epidemic, there is significant interest in refining opioid-sparing postoperative pain management strategies across a variety of disciplines.

There is a particular interest in the state of Massachusetts, which is experiencing a disproportionate burden of the opioid epidemic, with increasing rates of opioid deaths every year. To begin to combat this problem, the state of Massachusetts recently passed a law in March 2016 to restrict the prescription of a greater than 7-day supply of opioids, and the governor has made opioid abuse a top priority [9].

The current standard of care for pain management after cesarean delivery includes long-acting intrathecal morphine, acetaminophen, NSAIDs such as ibuprofen or ketorolac, and oral opioids.

Liposomal bupivacaine (trade name, Exparel [Pacira Pharmaceuticals, Inc]), is 1.3% bupivacaine suspended in a liposomal formulation that allows for a controlled released of local anesthetic over time. The half-life of liposomal bupivacaine is 24-34 hours; therefore, the impact of local anesthetic may be up to 72 hours post-operatively.

Liposomal bupivacaine has been studied in several settings. Most similar to an obstetric population is a randomized trial comparing bilateral TAP blocks with 40cc bupivacaine 0.5% to 60cc of liposomal bupivacaine at the time of abdominal hysterectomy via Pfannenstiel incision [10]. Relevant exclusion criteria included those with current use of opioids, history of drug addiction, current pain at the time of surgery, and contraindications to acetaminophen or NSAIDs. Intrapartum anesthetic management was standardized across both groups. Postoperative pain management was with morphine PCA with standardized settings for 24h, followed by as-needed oral opioids, and scheduled NSAIDs and acetaminophen throughout the postoperative period. The study was powered to detect a 2-point difference in the mean visual analog scale (VAS) for overall postoperative pain, from 4 to 2. The study met enrollment goals, and demonstrated improved pain scores and decreased postoperative use of IV and oral opioids, approximately 17mg less in IV morphine equivalents [10].

Liposomal bupivacaine has not been studied in the setting of cesarean delivery, and has the potential to significantly decrease the use of opioids in a large population of women. It is currently FDA-approved to be used in any surgical site, and is also approved for women who are currently breastfeeding.

A reduction in pain and inpatient opioid use will decrease opioid-related side effects and may translate to a reduction in outpatient opioid use, thus decreasing the risks of opioid abuse and misuse, ultimately resulting in fewer opioid-related adverse events and deaths.

RESEARCH DESIGN AND METHODS

Briefly describe study design and anticipated enrollment, i.e., number of subjects to be enrolled by researchers study-wide and by Partners researchers. Provide a brief summary of the eligibility criteria (for example, age range, gender, medical condition). Include any local site

restrictions, for example, "Enrollment at Partners will be limited to adults although the sponsor's protocol is open to both children and adults."

This study is a randomized controlled trial. A total of 80 patients will be randomized 1:1 to intervention (liposomal bupivacaine) versus control (placebo solution).

Inclusion criteria:

(1) Scheduled cesarean delivery via Pfannenstiel incision;
(2) Planned neuraxial anesthetic with intrathecal morphine and fentanyl administration.

Exclusion criteria:

(1) Current or prior use of methadone, buprenorphine, or other opioids before cesarean delivery;
(2) Contraindication to neuraxial anesthetic;
(3) Allergy to local anesthetic;
(4) Planned general anesthetic;
(5) Age less than 18 years on the date of enrollment.

Women will not be excluded if they received general anesthesia after neuraxial anesthesia with intrathecal morphine was administered.

Briefly describe study procedures. Include any local site restrictions, for example, "Subjects enrolled at Partners will not participate in the pharmacokinetic portion of the study." Describe study endpoints.

The planned intervention is the infiltration of liposomal bupivacaine (or placebo) at the time of fascial closure at a Pfannenstiel incision, after the delivery of the infant and repair of the hysterotomy. We will instill a total of 80cc (20cc liposomal bupivacaine diluted into 60cc of normal saline, or 80cc placebo) into the surgical site.

The total 80cc will be divided in to 4 20cc syringes with a 22G needle. The dilutions and aliquoting into the syringes will be performed by the injecting clinician.

The procedure to instill the drug is as follows: Once the patient is in the operating room, neuraxial anesthesia will be administered per routine practice. A Pfannenstiel skin incision will be made. The usual cesarean delivery procedure will be performed at the discretion of the surgeon. Once the surgical team is about to begin fascial closure, the study drug will then be infiltrated by a member of the study team (WHB, BJW, MP, or MAC – all of whom are obstetricians and trained in drug infiltration), with 50% of the study solution in subcutaneous space and 50% in the fascial plane, taking care to evenly spread the drug in the superior and inferior aspects of the incision. For the fascial infiltration, liposomal bupivacaine will be preferentially infiltrated laterally. The remainder of the cesarean delivery will proceed according to the usual fashion. We recommend suture closure for a subcutaneous wound > 2cm and suture closure of the skin, as both of these are evidence-based practices to decrease wound complications. We also recommend not using Mastozol for improved application of steri-strips. At any point in the cesarean delivery, the surgeon may chose to administer or withhold ketorolac.

Post-operative pain management will be: intrathecal morphine, scheduled ketorolac 30mg IV x 24h followed by ibuprofen 600mg q6h x 24h, scheduled Tylenol 650mg q6h x 48h, and prn oxycodone 5-10mg q4h. This is the current pain management protocol for postoperative women

after cesarean delivery. If Tylenol or NSAIDs are contraindicated, either due to the discretion of the clinical team or pre-existing patient contraindication, these will not be administered but are not a reason for study exclusion. After the first 48 hours of scheduled NSAIDs and Tylenol, these medications will be available as needed for additional pain control.

Outcomes include:
The primary outcome is pain score with activity at 48-hours and 72-hours postoperatively. A visual analog scale will be shown to the patient at both time points.

Additional outcomes to be collected from the participants include:
1. Total opioid use, converted to morphine milligram equivalents using this converter (http://www.globalrph.com/narcotic.cgi) at 48- and 72-hours postoperatively. This will be abstracted from the chart.
2. Satisfaction with post-operative pain control, using a validated tool (Pain OUT) (at 48h only)
3. Opioid-related adverse events: nausea, vomiting, urinary retention, dizziness, drowsiness, based on patient self-report.
4. Pain scores with rest and activity at 24h post-operatively
5. Pre-operative anxiety, using validated tool (GAD7)
6. Planned mode of feeding (antepartum), and actual mode of feeding upon discharge and at 6 weeks postpartum
7. Adverse wound complication, through chart abstraction and follow-up phone call at 6 weeks postpartum
8. Leftover opioids in the home, at 6 weeks postpartum

Additional outcomes to be collected through medical record abstraction include:
1. Hospital length of stay.
2. Inpatient or outpatient (followed for 6 weeks from delivery) wound complication (breakdown, seroma, hematoma, infection). This is already recorded in the medical record.
3. Allergic reaction attributable to local anesthetic. This is already recorded in the medical record.
4. Local anesthetic toxicity. This is already recorded in the medical record.
5. Operative time of cesarean delivery (skin incision to skin closure). This is already recorded in the medical record.
6. Number of oral opioids provided upon discharge. This is already recorded in the medical record.

For studies involving treatment or diagnosis, provide information about standard of care at Partners (e.g., BWH, MGH) and indicate how the study procedures differ from standard care. Provide information on available alternative treatments, procedures, or methods of diagnosis.

Current pain management for a cesarean delivery includes administration of intrathecal morphine, followed by administration of ketorolac, ibuprofen, acetaminophen, and opioids, most commonly oxycodone. If a patient has a contraindication to any of these medications, they will not be administered.

Describe how risks to subjects are minimized, for example, by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk or by using procedures already being performed on the subject for diagnostic or treatment purposes.

Subjects in the study are already planning to have a cesarean delivery, thus there is no coercion regarding having an unindicated procedure. Subjects will have appropriate informed consent discussions, with an in-person interpreter if indicated. No decisions to participate will be made under duress of maternal well-being or fetal well-being, as all subjects will be presenting for scheduled cesarean deliveries. Prior studies have already demonstrated surgical safety with the use of liposomal bupivacaine for the study subject, and the drug is FDA-approved. Thus, this is not experimental and geared more towards establishing efficacy in a new population. Patients with any form of local anesthestic intolerance or allergy are automatically excluded. There is minimal impact on the subject's experience of their inpatient hospitalization, with the majority of their care proceeding according to routine care.

Subjects enrolled in this study will be monitored for unanticipated problems, including adverse events, and if these occur, they will be reported to the Partners Human Research Committee/IRB, in accordance with the guidelines *Reporting Unanticipated Problems including Adverse Events*.

Describe explicitly the methods for ensuring the safety of subjects. Provide objective criteria for removing a subject from the study, for example, objective criteria for worsening disease/lack of improvement and/or unacceptable adverse events. The inclusion of objective drop criteria is especially important in studies designed with placebo control groups.

At the time of infiltration, subjects' vitals signs and stability are closely monitored by the anesthesiologist. Should there be any immediate local anesthetic toxicity, this would identified by the anesthesiologist.

Subjects will be monitored routinely on the postpartum floor for signs of local anesthetic toxicity. In general, the postoperative stay after a cesarean delivery is 3-4 days, allowing for ample time to detect any safety concerns.

Pfannenstiel incisions are examined at least daily by the rounding clinician. Should the subject or nurse have any wound concerns, the subjects clinician, as well as the study physician, will be able to be contacted. Once subjects are discharged, they have access to their physician for any wound concerns. We will be closely monitoring the charts of study subjects for any reported wound complications.

If any adverse event does occur, this will be recorded, and a subject will not be removed from the study, as the intervention has already been performed, and the remainder of the data collection is non-invasive. However, if a subject decides no longer to participate due to an adverse event, we will respect this decision.

FORESEEABLE RISKS AND DISCOMFORTS

Provide a brief description of any foreseeable risks and discomforts to subjects. Include those related to drugs/devices/procedures being studied and/or administered/performed solely for research purposes. In addition, include psychosocial risks, and risks related to privacy and confidentiality. When applicable, describe risks to a developing fetus or nursing infant.

Potential risks include increased bleeding in the subcutaneous space or subfascial space, with infiltration of liposomal bupivacaine to create a field block. If this bleeding were to occur, it is not likely that it would be concealed and lead to an unanticipated hematoma; however, additional hemostatic measures may be necessary. These measures are commonly employed at cesarean delivery, even in the absence of infiltration of a substance, as these are areas that are

at risk of hematoma formation. To minimize this risk, we will ensure adequate hemostasis prior to subcutaneous space closure.

Another potential intraoperative risk is increased operative time. We anticipate that the time needed to complete liposomal bupivacaine infiltration is approximately 2-3 minutes. However, if a patient's regional anesthetic is inadequate to complete surgery, additional anesthetic may need to be administered to account for the longer operative time. One surgeon will perform all infiltrations both to standardize the procedure and to minimize time spent performing the infiltration.

Post-operatively, the risk of wound complication may be increased by the infiltration of additional fluid near the incision. There is no reported data to support this concern in the prior study of liposomal bupivacaine during abdominal hysterectomy.

After enrollment, we may discover the patient has untreated anxiety, based on the GAD7. If the score suggests significant anxiety (GAD7 score >=10), we will alert the patient's primary obstetrician.

Finally, potential risks include a small amount of bupivacaine entering the breastmilk. Although the goal of this formulation is for the drug to not become systemic, this may occur. Liposomal bupivacaine is FDA-approved for breastfeeding women. Moreover, bupivacaine ingested into a neonate's gut cannot be absorbed systemically, thus minimizing the risk to the neonate.

Psychosocial risks include creating an expectation of improved pain control that may not be borne out, either because the patient may receive the placebo, or because liposomal bupivacaine may not be effective.

In addition to the risks above, there may be additional unanticipated risks to subjects or other persons that are encountered through the course of this study. We will monitor subjects and other persons for unanticipated problems, including adverse events, and if these occur, they will be reported to the Partners Human Research Committee/IRB, in accordance with the guidelines *Reporting Unanticipated Problems including Adverse Events*.

EXPECTED BENEFITS

Describe both the expected benefits to individual subjects participating in the research and the importance of the knowledge that may reasonably be expected to result from the study. Provide a brief, realistic summary of potential benefits to subjects, for example, "It is hoped that the treatment will result in a partial reduction in tumor size in at least 25% of the enrolled subjects." Indicate how the results of the study will benefit future patients with the disease/condition being studied and/or society, e.g., through increased knowledge of human physiology or behavior, improved safety, or technological advances.

Potential benefits to participating individuals include improved pain control in the immediate post-operative period, thus resulting in fewer opioids used. This may lead to other benefits, including earlier ambulation, earlier return of bowel function, possibly earlier readiness for discharge.

Potential benefits to our patient population include the possibility for increasing opioid-minimizing strategies for pain management after cesarean delivery, the most common surgery performed in the U.S.

EQUITABLE SELECTION OF SUBJECTS

The risks and benefits of the research must be fairly distributed among the populations that stand to benefit from it. No group of persons, for example, men, women, pregnant women, children, and minorities, should be categorically excluded from the research without a good scientific or ethical reason to do so. Please provide the basis for concluding that the study population is representative of the population that stands to potentially benefit from this research.

We will approach all women having scheduled cesarean deliveries. Among those patients who do not speak English, we will have an in-person interpreter to discuss the study and obtain informed consent. If the non-English speaking subject desires to participate, an interpreter will also be used for both post-operative encounters to collect outcomes data.

When people who do not speak English are excluded from participation in the research, provide the scientific rationale for doing so. Individuals who do not speak English should not be denied participation in research simply because it is inconvenient to translate the consent form in different languages and to have an interpreter present.

For guidance, refer to the following Partners policy:
Obtaining and Documenting Informed Consent of Subjects who do not Speak English
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Non-English_Speaking_Subjects.1.10.pdf

RECRUITMENT PROCEDURES

Explain in detail the specific methodology that will be used to recruit subjects. Specifically address how, when, where and by whom subjects will be identified and approached about participation. Include any specific recruitment methods used to enhance recruitment of women and minorities.

All obstetric providers (physicians, midwives, clinic nurses, labor nurses, postpartum nurses) at MGH will be made aware of this study.

One study physician (MP) will identify patients with scheduled cesarean deliveries and contact the patient's primary provider to inform the patient that this study physician will approach them about the study. If the patient's primary provider feels the patient is not an appropriate study candidate, or the patient declines to hear about the study, the patient will not be approached by the study physician. A flier will be used to educate patients in outpatient obstetric clinics about the study.

If the patient agrees to hear more, she will be approached by a study physician during a routine clinic visit 1-6 weeks before the scheduled surgical date, or contacted via phone to set up a time to meet in person. At this visit, a member of the study team will describe the standard of care, the intent of the study, and the potential risks and benefits. If a patient desires to enroll,

informed consent will be obtained. At the time of presentation for cesarean delivery, desire to participate in the study will be affirmed. Patients with scheduled cesarean deliveries who we are unable to approach prior to the scheduled surgical date will not be approached on the day of admission.

For non-English speaking patients, they will be approached with an in-person interpreter in the outpatient setting to discuss the study, and will sign a short-form consent after reviewing the full English consent form, verbally translated with the interpreter.

For English speaking patients who are unable to meet in person prior to the scheduled surgical date, but who have heard about the study over the telephone and would like to participate, we will pursue phone recruitment and consent if the following conditions can be met: (1) have a means to receive and return the consent form electronically; (2) have the time to go through each section of the consent form with the study physician on the phone; (3) affirm their comfort with English as the primary language. If this is possible, an email will be sent securely with "send secure" in the subject line. The faxed/emailed back copy will be printed in the chart, with the consenting study physician signing the copy upon receiving it, and the patient will be requested to bring their version on the scheduled surgical date so that the same study physician can sign the consent form. A note will be made in the chart regarding the patient's participation and phone consent.

There will also be recruitment fliers posted in the outpatient clinic restrooms, as this is the designated space in the outpatient clinic for all recruitment fliers for research studies.

The study has been named the PENGUIN study, for ease of remembering, for patients and providers alike. Postperative pain: Exparel iNjection with the Goal of Understanding the Impact on Numeric Pain Score. Cartoon penguins are pictured on the recruitment flier.

Provide details of remuneration, when applicable. Even when subjects may derive medical benefit from participation, it is often the case that extra hospital visits, meals at the hospital, parking fees or other inconveniences will result in additional out-of-pocket expenses related to study participation. Investigators may wish to consider providing reimbursement for such expenses when funding is available

There will be no remuneration for study participation.

For guidance, refer to the following Partners policies:

Recruitment of Research Subjects
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Recruitment_Of_Research_Subjects.pdf

Guidelines for Advertisements for Recruiting Subjects
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Guidelines_For_Advertisements.1.11.pdf

Remuneration for Research Subjects
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Remuneration_for_Research_Subjects.pdf

CONSENT PROCEDURES

Explain in detail how, when, where, and by whom consent is obtained, and the timing of consent (i.e., how long subjects will be given to consider participation). For most studies involving more than minimal risk and all studies involving investigational drugs/devices, a licensed physician investigator must obtain informed consent. When subjects are to be enrolled from among the investigators' own patients, describe how the potential for coercion will be avoided.

Consent will be obtained by a study physician (MP) at a clinic visit 1-6 weeks prior to the date of the scheduled cesarean delivery. If the patient is unable to meet with a study physician before her scheduled surgery, the consent discussion may occur remotely via phone conversation as described above.

The enrolling study physician, MP, will not have a private obstetric clinic or work in another faculty obstetric outpatient clinic for the duration of this study.

NOTE: When subjects are unable to give consent due to age (minors) or impaired decision-making capacity, complete the forms for Research Involving Children as Subjects of Research and/or Research Involving Individuals with Impaired Decision-making Capacity, available on the New Submissions page on the PHRC website:
https://partnershealthcare.sharepoint.com/sites/phrmApply/aieipa/irb

For guidance, refer to the following Partners policy:
Informed Consent of Research Subjects:
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Informed_Consent_of_Research_Subjects.pdf

DATA AND SAFETY MONITORING

Describe the plan for monitoring the data to ensure the safety of subjects. The plan should include a brief description of (1) the safety and/or efficacy data that will be reviewed; (2) the planned frequency of review; and (3) who will be responsible for this review and for determining whether the research should be altered or stopped. Include a brief description of any stopping rules for the study, when appropriate. Depending upon the risk, size and complexity of the study, the investigator, an expert group, an independent Data and Safety Monitoring Board (DSMB) or others might be assigned primary responsibility for this monitoring activity.

NOTE: Regardless of data and safety monitoring plans by the sponsor or others, the principal investigator is ultimately responsible for protecting the rights, safety, and welfare of subjects under his/her care.

As this is a small trial, we do not plan an external committee to monitor outcome data. One study physician (MP) will receive all safety reports. There will be no interim analysis of primary outcome data. However, safety and adverse event data will be reviewed by 1 study physician as the events occur. If >20% of patients have a wound complication (approximately three times our normal rate), the study team will gather and terminate the study early. Adverse events will be

reported in accordance with the CONSORT extension to better report trial harms. The adverse events of interest include any local anesthetic allergic reaction, wound complication, and opioid-related side effects.

Describe the plan to be followed by the Principal Investigator/study staff for review of adverse events experienced by subjects under his/her care, and when applicable, for review of sponsor safety reports and DSMB reports. Describe the plan for reporting adverse events to the sponsor and the Partners' IRB and, when applicable, for submitting sponsor safety reports and DSMB reports to the Partners' IRBs. When the investigator is also the sponsor of the IND/IDE, include the plan for reporting of adverse events to the FDA and, when applicable, to investigators at other sites.

NOTE: In addition to the adverse event reporting requirements of the sponsor, the principal investigator must follow the Partners Human Research Committee guidelines for Adverse Event Reporting

Study staff will closely monitor all adverse events as above. Any serious adverse events will be reported to the sponser, Pacira Pharmaceuticals, also the drug manufacturer, and the IRB, particularly if it is a reason to halt the trial or terminate the trial early. Unanticipated problems or harms to study subjects or others, including adverse events, will be reported to the IRB, in accordance with the guidelines *Reporting Unanticipated Problems including Adverse Events*.

MONITORING AND QUALITY ASSURANCE

Describe the plan to be followed by the principal investigator/study staff to monitor and assure the validity and integrity of the data and adherence to the IRB-approved protocol. Specify who will be responsible for monitoring, and the planned frequency of monitoring. For example, specify who will review the accuracy and completeness of case report form entries, source documents, and informed consent.

NOTE: Regardless of monitoring plans by the sponsor or others, the principal investigator is ultimately responsible for ensuring that the study is conducted at his/her investigative site in accordance with the IRB-approved protocol, and applicable regulations and requirements of the IRB.

One study physician (MP) will primarily be responsible for adhering to this protocol, with recruitment methods, administration of intervention, and assessment of outcomes in the post-operative period. The PI (WHB) and 1 study physician (MP) will ensure the accuracy and completeness of consent forms and data entry forms. The PI (WHB), study physician, and research coordinator will meet at every 2 week intervals to discuss recruitment, study implementation, and adherence to study protocol. The study team will be blinded to the intervention performed until the groups are revealed by the Research Pharmacy after the analysis is complete. The injecting clinician for a particular patient will not be blinded as to what was injected, but will not be involved in that same patient's outcomes assessment.

For guidance, refer to the following Partners policies:
Data and Safety Monitoring Plans and Quality Assurance
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/DSMP_in_Human_Subjects_Research.pdf

Reporting Unanticipated Problems (including Adverse Events)
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Reporting_Unanticipated_Problems_including_Adverse_Events.pdf

PRIVACY AND CONFIDENTIALITY

Describe methods used to protect the privacy of subjects and maintain confidentiality of data collected. This typically includes such practices as substituting codes for names and/or medical record numbers; removing face sheets or other identifiers from completed surveys/questionnaires; proper disposal of printed computer data; limited access to study data; use of password-protected computer databases; training for research staff on the importance of confidentiality of data, and storing research records in a secure location.

NOTE: Additional measures, such as obtaining a Certificate of Confidentiality, should be considered and are strongly encouraged when the research involves the collection of sensitive data, such as sexual, criminal or illegal behaviors.

Data forms will be stored in a locked room, in a locked filing cabinet. Only members of the study team will have access to this data. Once the data is transcribed to a database, this will be a password-protected database that is de-identified, with randomly assigned study IDs. At the conclusion of the analysis, the data forms will be destroyed, and only the de-identified, password protected database saved.

SENDING SPECIMENS/DATA TO RESEARCH COLLABORATORS OUTSIDE PARTNERS

Specimens or data collected by Partners investigators will be sent to research collaborators outside Partners, indicate to whom specimens/data will be sent, what information will be sent, and whether the specimens/data will contain identifiers that could be used by the outside collaborators to link the specimens/data to individual subjects.

Not applicable.

Specifically address whether specimens/data will be stored at collaborating sites outside Partners for future use not described in the protocol. Include whether subjects can withdraw their specimens/data, and how they would do so. When appropriate, submit documentation of IRB approval from the recipient institution.

Not applicable

RECEIVING SPECIMENS/DATA FROM RESEARCH COLLABORATORS OUTSIDE PARTNERS

When specimens or data collected by research collaborators outside Partners will be sent to Partners investigators, indicate from where the specimens/data will be obtained and whether the

specimens/data will contain identifiers that could be used by Partners investigators to link the specimens/data to individual subjects. When appropriate, submit documentation of IRB approval and a copy of the IRB-approved consent form from the institution where the specimens/data were collected.

Not applicable.