# Cover Page for Protocol and Statistical Plan

| | |
|---|---|
| **Official Title:** | Objective Assessment of Pain Thresholds in Women with Vulvodynia |
| **NCT number**: | NCT04461210 |
| **Document Type:** | Study Protocol and Statistical Analysis Plan |
| **Date of the Document:** | 08/29/2024 |

# Complete Research Protocol (HRP-503)

## Table of Contents

## *Template Instructions*

***Sections that do not apply:***

- *In several sections, the addition of checkboxes for **Not Applicable** have been added to the template as responses.*
    - *If an N/A checkbox is present, select the appropriate justification from the list.*
    - *If an N/A checkbox is not present, or if none of the existing checkboxes apply to your study, you must write in your own justification.*
- *In addition:*
    - *For research where the only study procedures are records/chart review: Sections 6, 21, 22, 24, 25, 26 and 27 do not apply.*
    - *For exempt research: Section 6 may not apply. Section 6.1 will still apply if there is a study intervention.*

***Studies with multiple participant groups:***

- *If this study involves multiple participant groups (e.g. parents and children), provide information in applicable sections for each participant group. Clearly label responses when they differ. For example:*

| **Response Example** |
|---|
| Intervention Group: |
| Control Group: |

***Formatting:***

- *Do not remove template instructions or section headings when they do not apply to your study.*

*If you are pasting information from other documents using the "Merge Formatting" Paste option will maintain the formatting of the response boxes.*

***Amendments:***

- *When making modifications or revisions to this and other documents, use the **Track Changes** function in Microsoft Word.*
- *Update the version date or number **on Page 3.***

## PROTOCOL TITLE:

*Include the full protocol title.*

Response:

Objective Assessment of Pain Thresholds in Women with Vulvodynia

## PRINCIPAL INVESTIGATOR:

*Name* Vanessa M. Barnabei, MD, PhD
*Department* Obstetrics and Gynecology
*Telephone Number* 716-323-0615
*Email Address* vmbarnab@buffalo.edu

Response:

## VERSION NUMBER/DATE:

*Include the version number and date of this protocol.*

Response:

V2 1/13/2022**REVISION HISTORY**

| Revision # | Version Date | Summary of Changes | Consent Change? |
|---|---|---|---|
| V2 | 1/13/2022 | Added "One-Time Plastic Reward Card" to section 27.0 | No |
| V3 | 10/06/2023 | Updated Version # | No |
| | | | |
| V4 | 02/28/2024 | Addition of investigator | No |
| V5 | 08/29/2024 | Minor change to recruitment methods | No |

## FUNDING:

*Indicate any funding for this proposal. This should match the Funding Sources page in Click IRB.*

Response:

Jacobs School of Medicine and Biomedical Sciences, Clinical Translational Research Award

## GRANT APPLICABILITY:

*Indicate whether this protocol is funded by a grant (e.g. NIH, foundation grant). For a grant with multiple aims, indicate which aims are covered by this research proposal.*

*NOTE: This question does not apply to studies funded by a sponsor contract.*

 *Include a copy of the grant proposal with your submission.*

Response: Jacobs School of Medicine and Biomedical Sciences, Clinical Translational Research Award

## RESEARCH REPOSITORY:

*Indicate where the research files will be kept, including when the study has been closed. The repository should include, at minimum, copies of IRB correspondence (approval, determination letters) as well as signed consent documents. This documentation should be maintained for 3 years after the study has been closed.*

Response:

*Location:* Password-protected computer files

*Address:* 955 Main Street, Buffalo, NY

*Department:* Obstetrics and Gynecology

## 1.0 Study Summary

| | |
|---|---|
| **Study Title** | Objective Assessment of Pain Thresholds in Women with Vulvodynia |
| **Study Design** | Clinical Trial |
| **Primary Objective** | Develop annotated pain maps showing region and size of area sensitive to mechanical stimulus. The pain maps will be created by combining IR images, photographs, and clinical input, and will be correlated with patient co-morbidities. |
| **Secondary Objective(s)** | a-Determine changes in the location and size of sensitive regions following various conventional clinical interventions for vulvodynia.<br>b-Develop a large, information-rich database of annotated pain maps from patients, and use Artificial Intelligence to identify patterns and trends. |
| **Research Intervention(s)/ Investigational Agent(s)** | Infrared imaging of the vulva and assessment of pain intensity using cotton-tipped swab. |
| **IND/IDE #** | N/A |
| **Study Population** | Women with vulvodynia and healthy controls |
| **Sample Size** | 60 women (30 in each group) |
| **Study Duration for individual participants** | One day 1 hour |

| | |
|---|---|
| **Study Specific Abbreviations/ Definitions** | |

## 2.0 Objectives*

*2.1 Describe the purpose, specific aims, or objectives of this research.*

Response:

We have been developing a novel medical technique for the diagnosis and classification of vulvodynia. The technique will quantitatively quantify the magnitude and location of areas of sensitivity to touch/pressure and simultaneously use thermal and photo imaging to identify regions of inflammation. The technique builds on current methodology used in assessment and knowledge about the known pathophysiology of the disorder. For this aspect of study, we will assess thermal indicators of inflammation with an infrared camera and subjective pain sensitivity with traditional methods. Through this combination of measurements, we plan to expand the diagnostic tools used in patient care as well as on the classification of this heterogeneous disorder. Specific aims include developing annotated pain maps that show regions of sensitivity and changes in temperature; determining changes in the above parameters during and after traditional medical treatment for the condition; and developing a large database of annotated pain maps for use with artificial intelligence to identify patterns and trends which will be correlated with clinical outcome data.

*2.2 State the hypotheses to be tested, if applicable.*

*NOTE: A hypothesis is a specific, testable prediction about what you expect to happen in your study that corresponds with your above listed objectives.*

Response:

Women with vulvodynia will show specific patterns of pain sensitivity and inflammatory changes (identified by thermography) compared to women without vulvar pain.

## 3.0 Scientific Endpoints*

*3.1 Describe the scientific endpoint(s), the main result or occurrence under study.*

*NOTE: Scientific endpoints are outcomes defined before the study begins to determine whether the objectives of the study have been met and to draw conclusions from the data. Include primary and secondary endpoints. Some example endpoints are: reduction of symptoms, improvement in quality of life, or survival. Your response should* ***not*** *be a date.*

Response:

Thermographic evidence of inflammation in the areas of pain sensitivity in women with provoked vulvodynia compared to normal controls.

## 4.0 Background*

*4.1 Provide the scientific or scholarly background, rationale, and significance of the research based on the existing literature and how it will contribute to existing knowledge. Describe any gaps in current knowledge. Include relevant preliminary findings or prior research by the investigator.*

Response:

Vulvodynia is a heterogeneous group of clinical conditions defined by the International Society for the Study of Vulvovaginal Disease as chronic vulvar discomfort or pain, characterized by burning, stinging, irritation or rawness of the female genitalia [1]. The true prevalence is unknown but is estimated at 9-12% of the adult female population, with up to 2 million women affected. These chronic conditions cause significant burden in terms of quality of life and relationship dysfunction, especially for women with provoked vestibulodynia (pain at the opening of the vagina ("vestibule") with vaginal penetration or attempted vaginal penetration) which interferes with normal sexual function [2]. This is a "hidden" women's issue that is under-reported and under-treated because it causes embarrassment and feelings of inadequacy. The clinical management of localized, provoked vulvodynia has been disorganized and somewhat arbitrary [3]. Studies suggest that most women see a variety of providers over the course of months to years before the condition is diagnosed correctly. Diagnosis of these conditions is based on clinical picture, absence of other causes, and physical exam. During the exam, a cotton-tipped swab is used to assess for areas of tenderness and the patient is asked to rate her level of pain on a Likert scale. This has been the standard of care for many years, but reproducibility has not been assessed. In addition, monitoring response to therapy is also very subjective. Even return to sexual activity is not a reliable indicator of patient's pain, since many women will continue to engage in sexual activity to avoid relationship discord. We have been developing a novel medical technique for the diagnosis and classification of vulvodynia. The technique will quantitatively measure mechanical sensitivity to touch/pressure simultaneously with thermal indicators of inflammation. The technique builds on current methodology used in assessment and knowledge about the known pathophysiology of the disorder. Through this combination of measurements, we plan to expand the diagnostic tools used in patient care as well as on the classification of this heterogeneous disorder.

*4.2 Include complete citations or references.*

Response:

1. Bornstein J, Goldstein AT, Stockdale CK et al. 2015 ISSVD, ISSWSH, and IPPS Consensus Terminology and Classification of Persistent Vulvar Pain and Vulvodynia. L Lower Genit Tract Dis 2016;20:126-130.
2. Edwards L.. Vulvodynia. Clin Obstet Gynecol 2015;58;143-152
3. Falsetta ML et al. A review of the available clinical therapies for vulvodynia management and new data implicating proinflammatory mediators in pain elicitation. BJOG 2016;124:210-218.

## 5.0 Study Design*

*5.1 Describe and explain the study design (e.g. case-control, cross-sectional, ethnographic, experimental, interventional, longitudinal, observational).*

Response:

Prospective study of women with vulvodynia and normal controls. We plan to evaluate a novel technique that quantifies both pain intensity and records thermographic changes of the vulva in women with a clinical diagnosis of provoked vulvodynia and normal controls. The study subjects will have a new or prior diagnosis of provoked vulvodynia and will be invited to participate in this evaluation. Women with prior diagnosis of vulvodynia will be symptomatic and untreated at the time of assessment. Control subjects will be unaffected women presenting for routine care who do not have vulvar pain or other active vulvar or vaginal disorder as these may interfere with thermographic mapping.

# 6.0 Study Intervention/Investigational Agent

*6.1 Describe the study intervention and/or investigational agent (e.g., drug, device) that is being evaluated.*

Response: Thermographic imaging of the vulva combined with subjective pressure sensitivity assessments, overlaid onto a pain map of the vulva.

*6.2 Drug/Device Handling: If the research involves drugs or device, describe your plans to store, handle, and administer those drugs or devices so that they will be used only on subjects and be used only by authorized investigators.*

- *If the control of the drugs or devices used in this protocol will be accomplished by following an established, approved organizational SOP (e.g., Research Pharmacy SOP for the Control of Investigational Drugs, etc.), please reference that SOP in this section.*

Response:

NA

*6.3 If the drug is investigational (has an IND) or the device has an IDE or a claim of abbreviated IDE (non-significant risk device), include the following information:*

- *Identify the holder of the IND/IDE/Abbreviated IDE.*
- *Explain procedures followed to comply with sponsor requirements for FDA regulated research for the following:*

| | *Applicable to:* | | |
|---|---|---|---|
| ***FDA Regulation*** | ***IND Studies*** | ***IDE studies*** | ***Abbreviated IDE studies*** |
| ***21 CFR 11*** | ***X*** | ***X*** | |
| ***21 CFR 54*** | ***X*** | ***X*** | |
| ***21 CFR 210*** | ***X*** | | |
| ***21 CFR 211*** | ***X*** | | |
| ***21 CFR 312*** | ***X*** | | |
| ***21 CFR 812*** | | ***X*** | ***X*** |
| ***21 CFR 820*** | | ***X*** | |

Response:

The device has no contact with the patient, it takes IR and photo images remote from the patient, and so is not subject to IDE.

## 7.0 Local Number of Subjects

*7.1 Indicate the total number of subjects that will be enrolled or records that will be reviewed locally.*

Response: 60 (sixty)

*7.2 If applicable, indicate how many subjects you expect to screen to reach your target sample (i.e. your screen failure rate).*

Response: 100

*7.3 Justify the feasibility of recruiting the proposed number of eligible subjects within the anticipated recruitment period. For example, how many potential subjects do you have access to? What percentage of those potential subjects do you need to recruit?*

Response: The PI sees an average of 5 new patients per month diagnosed with vulvodynia and has many established patients who can be assessed when they come in for follow-up. For affected women, the goal would be to recruit close to 100% of them. The Ob/Gyn practice is an eight-person general Ob/Gyn practice that sees 50-70 women per week for routine gynecologic care. Only a small fraction of these women will need to be recruited.

## 8.0 Inclusion and Exclusion Criteria*

*8.1 Describe the criteria that define who will be **included** in your final study sample.*

*NOTE: This may be done in bullet point fashion.*

Response:

Women > 18 years of age

Women seeking care for vulvar pain

Controls: Women seeking routine gynecologic care

*8.2 Describe the criteria that define who will be **excluded** from your final study sample.*

*NOTE: This may be done in bullet point fashion.*

Response:

Women < 18 years of age

Pregnancy

Women with vulvar or vaginal disorder other than pain

*8.3 Indicate specifically whether you will include any of the following special populations in your study using the checkboxes below.*

***NOTE: Members of special populations may not be targeted for enrollment in your study unless you indicate this in your inclusion criteria.***

Response:

☐ Adults unable to consent

☐ Individuals who are not yet adults (infants, children, teenagers)

☐ Pregnant women

☐ Prisoners

*8.4 Indicate whether you will include non-English speaking individuals in your study. **Provide justification if you will exclude non-English speaking individuals.***

*In order to meet one of the primary ethical principles of equitable selection of subjects, non-English speaking individuals may **not** be routinely excluded from research as a matter of convenience.*

*In cases where the research is of therapeutic intent or is designed to investigate areas that would necessarily require certain populations who may not speak English, the researcher is required to make efforts to recruit and include non-English speaking individuals. However, there are studies in which it would be reasonable to limit subjects to those who speak English. Some examples include pilot studies, small unfunded studies with validated instruments not available in other languages, studies with numerous questionnaires, and some non-therapeutic studies which offer no direct benefit.*

Response:

Non-English speakers are not eligible for inclusion in the study. This is a non-therapeutic study which will offer no direct benefit.

## 9.0 Vulnerable Populations*

*If the research involves special populations that are considered vulnerable,* ***describe the safeguards included to protect their rights and welfare.***

*NOTE: You should refer to the appropriate checklists, referenced below, to ensure you have provided adequate detail regarding safeguards and protections. You do not, however, need to provide these checklists to the IRB.*

*9.1 For research that involves* ***pregnant women,*** *safeguards include:*
*NOTE CHECKLIST: Pregnant Women (HRP-412)*

Response:

☒ **N/A**: This research does not involve pregnant women.

*9.2 For research that involves* ***neonates of uncertain viability or non-viable neonates,*** *safeguards include:*
*NOTE CHECKLISTS: Non-Viable Neonates (HRP-413), or Neonates of Uncertain Viability (HRP-414)*

Response:

☒ **N/A:** This research does not involve non-viable neonates or neonates of uncertain viability.

*9.3 For research that involves* ***prisoners****, safeguards include:*
*NOTE CHECKLIST: Prisoners (HRP-415)*

Response:

☒ **N/A:** This research does not involve prisoners.

*9.4 For research that involves* ***persons who have not attained the legal age for consent to treatments or procedures involved in the research ("children")****, safeguards include:*
*NOTE CHECKLIST: Children (HRP-416)*

Response:

☒ **N/A:** This research does not involve persons who have not attained the legal age for consent to treatments or procedures ("children").

*9.5 For research that involves* ***cognitively impaired adults****, safeguards include:*
*NOTE CHECKLIST: Cognitively Impaired Adults (HRP-417)*

Response:

☒ **N/A:** This research does not involve cognitively impaired adults.

*9.6 Consider if other specifically targeted populations such as students, employees of a specific firm, or educationally or economically disadvantaged persons are vulnerable.* ***Provide information regarding their safeguards and protections, including safeguards to eliminate coercion or undue influence.***

Response:

N/A

## 10.0 Eligibility Screening*

*10.1 Describe* ***screening procedures*** *for determining subjects' eligibility. Screening refers to determining if prospective participants meet inclusion and exclusion criteria.*

*Include all relevant screening documents with your submission (e.g. screening protocol, script, questionnaire).*

Response: Exclusion criteria include pregnancy, age < 18 years, and active vulvar and vaginal disorder other than pain, to be assessed in two ways: during the recruitment interview and at the time of the exam.

☐ **N/A:** There is no screening as part of this protocol.

## 11.0 Recruitment Methods

☐ **N/A:** This is a records review only, and subjects will not be recruited. NOTE: If you select this option, please make sure that all records review procedures and inclusion/exclusion screening are adequately described in other sections.

*11.1 Describe when, where, and how potential subjects will be recruited.*

*NOTE: Recruitment refers to how you are identifying potential participants and introducing them to the study. Include specific methods you will use (e.g. searching charts for specific ICD code numbers, Research Participant Groups, posted advertisements, etc.).*

Response: Women will be approached by the PI when they come to the clinical suite for evaluation of vulvar pain (subjects). Women will be approached by their own provider prior to routine annual exam to ask permission for the PI or study coordinator to discuss the study with them (controls). Some women will be called by the study coordinator in advance of their scheduled clinic visit and invited to participate in the study to save time on the day of the visit. The consent form will be discussed with them and then signed when they arrive for their clinic visit.

*11.2 Describe how you will protect the privacy interests of prospective subjects during the recruitment process.*

*NOTE: Privacy refers to an individual's right to control access to him or herself.*

Response: Women will be approached by telephone prior to their study visit or in private once they have been ushered into an exam room by clinical staff. If a patient agrees to consider recruitment, study staff will then explain the study and patient's participation in a private room.

*11.3 Identify any materials that will be used to recruit subjects.*

*NOTE: Examples include scripts for telephone calls, in person announcements / presentations, email invitations.*

*For advertisements, include the final copy of printed advertisements with your submission. When advertisements are taped for broadcast, attach the final audio/video tape. NOTE: You may submit the wording of the advertisement prior to taping to ensure there will be no IRB-required revisions, provided the IRB also reviews and approves the final version.*

Response: N/A – we are using a direct recruitment method.

## 12.0 Procedures Involved*

*12.1 Provide a description of **all research procedures or activities** being performed and when they are performed once a subject is screened and determined to be eligible. Provide as much detail as possible.*

*NOTE: This should serve as a blueprint for your study and include enough detail so that another investigator could pick up your protocol and replicate the research. For studies that have multiple or complex visits or procedures, consider the addition of a schedule of events table in in your response.*

Response:

All procedures will be performed on the same day as screening and consent and are expected to take 30-60 minutes. An annotated pain map of the vulva will be created based on subjective assessment of pain, and thermographic imaging.
A. Images and Thermographic readings will be taken with an infrared camera prior to any physical contact with the vulva of the patient other than by placing a calibrated paper drape circumferentially on the vulva outside of the area of interest. The drape will be calibrated to maintain pain map/image size comparison between patients.
B. Subjective pain at several predetermined loci will be assessed with a cotton swab (standard of care) and rated on a Likert scale of 0-10. This data will be added to the thermographic map.
C. Comparative analysis of the two measures will be performed (separate from visit). Patient demographic and health data (see table below) will be collected by direct participant interview and review of the patient's chart in Allscripts.

*12.2 Describe what data will be collected.*

*NOTE: For studies with multiple data collection points or long-term follow up, consider the addition of a schedule or table in your response.*

Response:

Vulvar images, both plain and infrared.

Pain sensitivity data on a Likert scale of 0-10 using cotton-tipped swabs.

Status (PVD or Control)
Race
Gravida
Para
Vaginal Births
Cesarean Births

Sexually Active
Dyspareunia
Smoking
Marital Status
Education Level

Medical History
Depression
Anxiety
Fibromyalgia
Chronic Pelvic Pain
Interstitial Cystitis
Endometriosis
Irritable Bowel Syndrome
TMJ
Other
h/o yeast infections
h/o BV
h/o abuse

PVD Patients Only
Symptom Duration
Pain Map Score
Pain Diary Score
FSDS
Previous Rx (Y/N)
Previous Rx (type)

*12.3 List any instruments or measurement tools used to collect data (e.g. questionnaire, interview guide, validated instrument, data collection form).*

*Include copies of these documents with your submission.*

Response: Please see the attached data collection form.

*12.4 Describe any source records that will be used to collect data about subjects (e.g. school records, electronic medical records).*

Response: Electronic medical records (Allscripts) will be accessed to obtain information for the data collection form only if the patient-provided information is incomplete or unclear.

*12.5 Indicate whether or not **individual** subject results, such as results of investigational diagnostic tests, genetic tests, or incidental findings will be shared with subjects or others (e.g., the subject's primary care physician) and if so, describe how these will be shared.*

Response: No

*12.6 Indicate whether or not **study** results will be shared with subjects or others, and if so, describe how these will be shared.*

Response: No, although study results of de-identified data may be presented or published in a scientific context.

## 13.0 Study Timelines*

*13.1 Describe the anticipated duration needed to enroll all study subjects.*

Response: Two years

*13.2 Describe the duration of an individual subject's participation in the study. Include length of study visits, and overall study follow-up time.*

Response: Participant will only have one study visit lasting from 30-60 minutes.

*13.3 Describe the estimated duration for the investigators to complete this study (i.e. all data is collected and all analyses have been completed).*

Response: Three years

## 14.0 Setting

*14.1 Describe all facilities/sites where you will be conducting research procedures. Include a description of the security and privacy of the facilities (e.g. locked facility, limited access, privacy barriers). Facility, department, and type of room are relevant. Do not abbreviate facility names.*

*NOTE: Examples of acceptable response may be: "A classroom setting in the Department of Psychology equipped with a computer with relevant survey administration software," "The angiogram suite at Buffalo General Medical Center, a fully accredited tertiary care institution within New York State with badge access," or, "Community Center meeting hall."*

Response:

The Obstetrics and Gynecology clinical suite at Conventus Office Building, 4th floor for data acquisition; and Dr. Glenna Bett's laboratory at Sherman Hall, South Campus of the University at Buffalo for data analysis. The de-identified data will be shared through UB-Box.

*14.2 For research conducted outside of UB and its affiliates, describe:*

- *Site-specific regulations or customs affecting the research*
- *Local scientific and ethical review structure*

*NOTE: This question is referring to UB affiliated research taking place outside UB, i.e. research conducted in the community, school-based research, international research, etc. It is not referring to multi-site research. UB affiliated institutions include Kaleida Health, ECMC, and Roswell Park Cancer Institute.*

Response:

☒ **N/A:** This study is not conducted outside of UB or its affiliates.

## 15.0 Community-Based Participatory Research

*15.1 Describe involvement of the community in the design and conduct of the research.*

*NOTE: Community-Based Participatory Research (CBPR) is a collaborative approach to research that equitably involves all partners in the research process and recognizes the unique strengths that each brings. CBPR begins with a research topic of importance to the community, has the aim of combining knowledge with action and achieving social change to improve health outcomes and eliminate health disparities.*

Response:

☒ **N/A:** This study does not utilize CBPR.

*15.2 Describe the composition and involvement of a community advisory board.*

Response:

☒ **N/A:** This study does not have a community advisory board.

## 16.0 Resources and Qualifications

*16.1 Describe the qualifications (e.g., education, training, experience, expertise, or certifications) of the Principal Investigator **and** staff to perform the research. When applicable describe their knowledge of the local study sites, culture, and society. Provide enough information to convince the IRB that you have qualified staff for the proposed research.*

*NOTE: If you specify a person by name, a change to that person will require prior approval by the IRB. If you specify a person by role (e.g., coordinator, research assistant, co-investigator, or pharmacist), a change to that person will not usually require prior approval by the IRB, provided that the person meets the qualifications described to fulfill their roles.*

Response:

Dr. Vanessa M. Barnabei, the Principal Investigator of the study and Emeritus Professor at UB, is a board-certified Ob/Gyn with over 40 years of clinical and research experience. Dr. Barnabei is the only provider in Western New York with significant clinical experience and expertise in the care of women with vulvodynia. Dr. Tova Ablove is Associate Professor of Ob/Gyn is an expert in female pelvic health and has many years of research experience in gynecologic health. Dr. Glenna Bett is Associate Professor of Ob/Gyn and Physiology and Biophysics and Dr. Randall Rasmusson is Professor of Physiology and Biophysics. Drs. Bett and Rasmusson are fulltime UB faculty members and have many years of experience in development and medical applications of electrophysiologic devices. Study coordinator TBD.

***Describe other resources available to conduct the research.***

*16.2 Describe the time and effort that the Principal Investigator and research staff will devote to conducting and completing the research.*

*NOTE: Examples include the percentage of Full Time Equivalents (FTE), hours per week. The question will elicit whether there are appropriate resources to conduct the research.*

Response:

0.1 FTE for each of the investigators.

*16.3 Describe the availability of medical or psychological resources that subjects might need as a result of anticipated consequences of the human research, if applicable.*

*NOTE: One example includes: on-call availability of a counselor or psychologist for a study that screens subjects for depression.*

Response:

NA – We do not anticipate a need for additional medical or psychological resources.

*16.4 Describe your process to ensure that all persons assisting with the research are adequately informed about the protocol, the research procedures, and their duties and functions.*

Response:

The study team has regular meetings to discuss and design the research project. All investigators are CITI trained. Only the PI, Dr. Barnabei, and the study coordinator, will have direct contact with the study patients.

## 17.0 Other Approvals

*17.1 Describe any approvals that will be obtained prior to commencing the research (e.g., school, external site, funding agency, laboratory, radiation safety, or biosafety).*

Response:

☒ **N/A:** This study does not require any other approvals.

## 18.0 Provisions to Protect the Privacy Interests of Subjects

*18.1 Describe how you will protect subjects' privacy interests during the course of this research.*

*NOTE: Privacy refers to an individual's right to control access to him or herself. Privacy applies to the person. Confidentiality refers to how data collected about individuals for the research will be protected by the researcher from release. Confidentiality applies to the data.*

*Examples of appropriate responses include: "participant only meets with a study coordinator in a classroom setting where no one can overhear", or "the participant is reminded that they are free to refuse to answer any questions that they do not feel comfortable answering."*

Response:

Participants will meet with the PI or the study coordinator in a private exam room in the clinical suite where no one can overhear. They will be given ample time to consider study participation, ask questions, and sign the consent. All patients will be reminded that participation is voluntary and will not affect the care they receive.

*18.2 Indicate how the research team is permitted to access any sources of information about the subjects.*

*NOTE: Examples of appropriate responses include: school permission for review of records, consent of the subject, HIPAA waiver. This question **does apply** to records reviews.*

Response:

Consent and HIPAA authorization will be obtained for access to the patient's medical record to confirm medical history and medications which may impact patient's participation.

## 19.0 Data Management and Analysis*

*19.1 Describe the data analysis plan, including any statistical procedures. This section applies to both quantitative and qualitative analysis.*

Response: Both visible and infrared images will be acquired using our state-of-the-art FLIR E-95 camera. The E-95 is one of the best IR cameras available. It has very high spatial resolution and temperature sensitivity. In summation: if there is any correlation between temperature and vulvodynia, this camera will be able to see it. The camera's software stores both of these images along with metadata in a single jpeg. We have already designed our own custom software to extract the raw temperature data from these files. Our software will control the camera remotely through a USB link. This, along with mounting the camera on a tripod, will ensure that there is minimal "smearing" of the image due to small uncontrollable movements of the person operating the camera. This will give us the highest accuracy possible. In addition, our graphical software interface will allow the user to mark the image to indicate where sensitivity to pressure or an increase in thermal activity was observed. As we expect spatial variation in temperature from the affected area to the unaffected, we will provide the user with a variety of options for subtracting the average body temperature to make the difference more visible. All data will be stored securely to maintain patient confidentiality. Once we have collected enough data, we can begin the process of establishing the metrics by which we can diagnose the patients. Considering all of our data (pressure, temperature, color (from visible light image)) we can determine the connection of each to a positive diagnosis and assign a finally probability to our result.

*19.2 If applicable, provide a power analysis.*

*NOTE: This may not apply to certain types of studies, including chart/records reviews, survey studies, or observational studies. This question is asked to elicit whether the investigator has an adequate sample size to achieve the study objectives and justify a conclusion.*

Response: This is a pilot study. No power analysis will be performed.

*19.3 Describe any procedures that will be used for quality control of collected data.*

Response: We are focusing on detecting vulvodynia alone, so we will choose patients that are otherwise healthy. Any patient with a pre-existing condition that may affect the outcome of our experiments will be excluded from the study.

## 20.0 Confidentiality*

## A. Confidentiality of Study Data

*Describe the local procedures for maintenance of confidentiality of **study data and any records that will be reviewed for data collection**.*

*20.1 A. Where and how will all data and records be stored? Include information about: password protection, encryption, physical controls, authorization of access, and separation of identifiers and data, as applicable. Include physical (e.g. paper) **and** electronic files.*

Response:

All study data, including images, will be maintained on a password-protected, HIPAA-compliant computer in the Department of Obstetrics and Gynecology, Jacobs School of Medicine. Data on this computer will identify patients only by a code. The key code with patient identifiers, stored as an Excel spreadsheet, will be kept in a separate, secure location on a password-protected, HIPAA-compliant computer in the Department of Obstetrics and Gynecology.

*20.2 A. How long will the data be stored?*

Response:

Indefinitely.

*20.3 A. Who will have access to the data?*

Response:

The PI and co-investigators.

*20.4 A. Who is responsible for receipt or transmission of the data?*

Response:

The PI and co-investigators.

*20.5 A. How will the data be transported?*

Response:

On a password-protected, HIPAA-compliant flash drive.

## B. Confidentiality of Study Specimens

*Describe the local procedures for maintenance of confidentiality of **study specimens**.*

☒ **N/A:** No specimens will be collected or analyzed in this research. *(Skip to Section 21.0)*

*20.6 B. Where and how will all specimens be stored? Include information about: physical controls, authorization of access, and labeling of specimens, as applicable.*

Response:

*20.7 B. How long will the specimens be stored?*

Response:

*20.8 B. Who will have access to the specimens?*

Response:

*20.9 B. Who is responsible for receipt or transmission of the specimens?*

Response:

*20.10 B. How will the specimens be transported?*

Response:

## 21.0 Provisions to Monitor the Data to Ensure the Safety of Subjects*

☐ **N/A:** This study is not enrolling subjects, or is limited to records review procedures only. This section does not apply.

***NOTE: Minimal risk studies may be required to monitor subject safety if the research procedures include procedures that present unique risks to subjects that require monitoring. Some examples include: exercising to exertion, or instruments that elicit suicidality or substance abuse behavior. In such cases, N/A is not an acceptable response.***

*21.1 Describe the plan to periodically evaluate the data collected regarding both harms and benefits to determine whether subjects remain safe.*

Response:

UB Box will be monitored to ensure that only study investigators have accessed the data files.

*21.2 Describe what data are reviewed, including safety data, untoward events, and efficacy data.*

Response:

NA

*21.3 Describe any safety endpoints.*

Response:

None.

*21.4 Describe how the safety information will be collected (e.g., with case report forms, at study visits, by telephone calls with participants).*

Response:

NA

*21.5 Describe the frequency of safety data collection.*

Response:

NA

*21.6 Describe who will review the safety data.*

Response:

NA

*21.7 Describe the frequency or periodicity of review of cumulative safety data.*

Response:

NA

*21.8 Describe the statistical tests for analyzing the safety data to determine whether harm is occurring.*

Response:

NA

*21.9 Describe any conditions that trigger an immediate suspension of the research.*

Response:

Data breach.

## 22.0 Withdrawal of Subjects*

☐ **N/A:** This study is not enrolling subjects. This section does not apply.

*22.1 Describe **anticipated** circumstances under which subjects may be withdrawn from the research without their consent.*

Response:

Participants who consent but cannot complete the study procedures, if for example they have abnormal findings at the time of the exam, will be withdrawn from the study at the time of the study visit.

*22.2 Describe any procedures for orderly termination.*

*NOTE: Examples may include return of study drug, exit interview with clinician. Include whether additional follow up is recommended for safety reasons for physical or emotional health.*

Response:

If patient cannot complete the study at the time of the study visit, no additional procedures will be performed at that time

*22.3 Describe procedures that will be followed when subjects withdraw from the research, including retention of already collected data, and partial withdrawal from procedures with continued data collection, as applicable.*

Response:

If a patient chooses to return to complete the study procedures, her biographical and demographic data will be saved. If she cannot return, previously collected data will be destroyed for control participants and saved for affected women, since this data would be collected for the routine assessment anyway. If a participant decides to leave the research, she can contact the investigator so that the investigator can remove any personal medical information from the study records.

## 23.0 Risks to Subjects*

*23.1 List the reasonably foreseeable risks, discomforts, hazards, or inconveniences to the subjects related to their participation in the research. Consider physical, psychological, social, legal, and economic risks. Include a description of the probability, magnitude, duration, and reversibility of the risks.*

*NOTE: Breach of confidentiality is always a risk for identifiable subject data.*

Response:

There is minimal risk to subjects from participation in this study except minor discomfort from the cotton-tipped swab. There is no immediate risk to the imaging. Breach of confidentiality is a small risk of participation although every effort will be done to maintain security of PHI.

*23.2 Describe procedures performed to lessen the probability or magnitude of risks, including procedures being performed to monitor subjects for safety.*

Response: See section 20.1 for ways to mitigate the risk of breach of confidentiality.

*23.3 If applicable, indicate **which procedures** may have risks to the subjects that are currently unforeseeable.*

Response: N/A

*23.4 If applicable, indicate which research procedures may have risks to an embryo or fetus should the subject be or become pregnant.*

Response:

None.

NA

*23.5 If applicable, describe risks to others who are not subjects.*

Response:

NA

## 24.0 Potential Benefits to Subjects*

*24.1 Describe the potential benefits that individual subjects may experience by taking part in the research. Include the probability, magnitude, and duration of the potential benefits. Indicate if there is no direct benefit.*

*NOTE: Compensation **cannot** be stated as a benefit.*

Response:

There is no benefit directly to subjects for participation. Data from this study may improve the diagnosis and care of women with vulvodynia in the future.

## 25.0 Compensation for Research-Related Injury

☒ **N/A:** The research procedures for this study do not present risk of research related injury (e.g. survey studies, records review studies). This section does not apply.

*25.1 **If the research procedures carry a risk of research related injury,** describe the available compensation to subjects in the event that such injury should occur.*

Response: There is no possibility of research-related injury.

*25.2 Provide a copy of contract language, if any, relevant to compensation for research related injury.*

*NOTE: If the contract is not yet approved at the time of this submission, submit the current version here. If the contract is later approved with **different language regarding research related injury**, you must modify your response here and submit an amendment to the IRB for review and approval.*

Response: N/A

## 26.0 Economic Burden to Subjects

*26.1 Describe any costs that subjects may be responsible for because of participation in the research.*

*NOTE: Some examples include transportation or parking.*

Response:

The study procedures may extend the length of time the patients are in the clinic which means more time away from work and may increase the cost of parking slightly.

☐ **N/A:** This study is not enrolling subjects, or is limited to records review procedures only. This section does not apply.

## 27.0 Compensation for Participation

*27.1 Describe the amount and timing of any compensation to subjects, including monetary, course credit, or gift card compensation.*

Response:

Upon completion of study procedures, subjects will be given a $25 One-Time Plastic Reward Card to compensate them for time spent and transportation costs.

☐ **N/A:** This study is not enrolling subjects, or is limited to records review procedures only. This section does not apply.

☐ **N/A:** There is no compensation for participation. This section does not apply.

## 28.0 Consent Process

*28.1 Indicate whether you will be obtaining consent.*

*NOTE: This does not refer to consent documentation, but rather whether you will be obtaining permission from subjects to participate in a research study. Consent documentation is addressed in Section 29.0.*

☒ ***Yes*** *(If yes, Provide responses to each question in this Section)*
☐ ***No*** *(If no, Skip to Section 29.0)*

*28.2 Describe where the consent process will take place. Include steps to maximize subjects' privacy.*

Response:

Consent will be obtained in a private exam room within the Obstetrics and Gynecology suite at the Conventus Office Building, 1001 Main Street, Buffalo.

*28.3 Describe how you will ensure that subjects are provided with a sufficient period of time to consider taking part in the research study.*

*NOTE: It is always a requirement that a prospective subject is given sufficient time to have their questions answered and consider their participation. See "SOP: Informed Consent Process for Research (HRP-090)" Sections 5.5 and 5.6.*

Response:

Subjects will be allowed as much time as they need to review the requirements of study participation and ask to questions.

*28.4 Describe any process to ensure ongoing consent, defined as a subject's willingness to continue participation for the duration of the research study.*

Response:

Prior to and during the exam, the investigator will verbally confirm that subject wishes to continue.

*28.5 Indicate whether you will be following "SOP: Informed Consent Process for Research (HRP-090)." Pay particular attention to Sections 5.4-5.9. If not, or if there are any exceptions or additional details to what is covered in the SOP, describe:*

- *The role of the individuals listed in the application who are involved in the consent process*
- *The time that will be devoted to the consent discussion*
- *Steps that will be taken to minimize the possibility of coercion or undue influence*
- *Steps that will be taken to ensure the subjects' understanding*

Response:

HRP-090 will be followed.

☒ We have reviewed and will be following "SOP: Informed Consent Process for Research (HRP-090)."

***Non-English Speaking Subjects***

☒ **N/A:** This study will not enroll Non-English speaking subjects. *(Skip to Section 28.8)*

*28.6 Indicate which language(s) other than English are likely to be spoken/understood by your prospective study population or their legally authorized representatives.*

*NOTE: The response to this Section should correspond with your response to Section 8.4 of this protocol.*

Response:

*28.7 If subjects who do not speak English will be enrolled, describe the process to ensure that the oral and written information provided to those subjects will be in that language, how you will ensure that subjects are provided with a sufficient period of time to consider taking part in the research study, and any process to ensure ongoing consent. Indicate the language that will be used by those obtaining consent.*

*NOTE: Guidance is provided on "SOP: Informed Consent Process for Research (HRP-090)."*

Response:

***Cognitively Impaired Adults***

☒ **N/A**: This study will not enroll cognitively impaired adults.
*(Skip to Section 28.9)*

*28.8 Describe the process to determine whether an individual is capable of consent.*

Response:

***Adults Unable to Consent***

☒ **N/A**: This study will not enroll adults unable to consent.
(*Skip to Section 28.13)*

*When a person is not capable of consent due to cognitive impairment, a legally authorized representative should be used to provide consent (Sections 28.9 and 28.10)* ***and, where possible, assent of the individual should also be solicited*** *(Sections 28.11 and 28.12).*

*28.9 Describe how you will identify a Legally Authorized Representative (LAR). Indicate that you have reviewed the "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)" for research in New York State.*

*NOTE: Examples of acceptable response includes: verifying the electronic medical record to determine if an LAR is recorded.*

Response:

☐ We have reviewed and will be following "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)."

*28.10* ***For research conducted outside of New York State****, provide information that describes which individuals are authorized under applicable law to*

*consent on behalf of a prospective subject to their participation in the research. One method of obtaining this information is to have a legal counsel or authority review your protocol along with the definition of "legally authorized representative" in "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)."*

Response:

*28.11 Describe the process for **assent of the adults**:*

- *Indicate whether assent will be obtained from all, some, or none of the subjects. **If some, indicate which adults will be required to assent and which will not.***

Response:

- ***If assent will not be obtained from some or all subjects, provide an explanation of why not.***

Response:

*28.12 Describe whether **assent of the adult** subjects will be documented and the process to document assent.*

*NOTE: The IRB allows the person obtaining assent to document assent on the consent document using the "Template Consent Document (HRP-502)" Signature Block for Assent of Adults who are Legally Unable to Consent.*

Response:

***Subjects who are not yet Adults (Infants, Children, and Teenagers)***

☒ **N/A**: This study will not enroll subjects who are not yet adults. *(Skip to Section 29.0)*

*28.13 Describe the criteria that will be used to determine **whether a prospective subject has not attained the legal age for consent to treatments or procedures involved in the research** under the applicable law of the jurisdiction in which the research will be conducted **(e.g., individuals under the age of 18 years)**. For research conducted in NYS, review "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)" to be aware of which individuals in the state meet the definition of "children."*

*NOTE: Examples of acceptable responses include: verification via electronic medical record, driver's license or state-issued ID, screening questionnaire.*

Response:

*28.14* ***For research conducted outside of New York State****, provide information that describes which persons have not attained the legal age for consent to treatments or procedures involved the research, under the applicable law of the jurisdiction in which research will be conducted. One method of obtaining this information is to have a legal counsel or authority review your protocol along the definition of "children" in "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)."*

Response:

*28.15 Describe whether parental permission will be obtained from:*

Response:

☐ One parent even if the other parent is alive, known, competent, reasonably available, and shares legal responsibility for the care and custody of the child.

☐ Both parents unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

☐ Parent permission will not be obtained. A waiver of parent permission is being requested.

*NOTE: The requirement for parent permission is a protocol-specific determination made by the IRB based on the risk level of the research. For guidance, review the "CHECKLIST: Children (HRP-416)."*

*28.16 Describe whether permission will be obtained from individuals* ***other than parents****, and if so, who will be allowed to provide permission. Describe your procedure for determining an individual's authority to consent to the child's general medical care.*

Response:

*28.17 Indicate whether assent will be obtained from all, some, or none of the* ***children****. If assent will be obtained from some children, indicate which children will be required to assent.*

Response:

*28.18 When assent of children is obtained, describe how it will be documented.*

Response:

## 29.0 Waiver or Alteration of Consent Process

***Consent will not be obtained, required information will not be disclosed, or the research involves deception.***

☒ **N/A:** A waiver or alteration of consent is not being requested.

*29.1 If the research involves a waiver or alteration of the consent process, please review the "CHECKLIST: Waiver or Alteration of Consent Process (HRP-410)" to ensure that you have provided sufficient information for the IRB to make the determination that a waiver or alteration can be granted.*

*NOTE: For records review studies, the first set of criteria on the "CHECKLIST: Waiver or Alteration of Consent Process (HRP-410)" applies.*

Response:

*29.2 If the research involves a waiver of the consent process for planned emergency research, please review the "CHECKLIST: Waiver of Consent for Emergency Research (HRP-419)" to ensure you have provided sufficient information for the IRB to make these determinations. Provide any additional information necessary here:*

Response:

## 30.0 Process to Document Consent

☐ **N/A:** A Waiver of Consent is being requested.
*(Skip to Section 31.0)*

*30.1 Indicate whether you will be following "SOP: Written Documentation of Consent (HRP-091)." If not or if there are any exceptions, describe whether and how consent of the subject will be obtained including whether or not it will be documented in writing.*

*NOTE: If your research presents no more than minimal risk of harm to subjects and involves no procedures for which written documentation of consent is normally required outside of the research context, the IRB will generally waive the requirement to obtain written documentation of consent. This is sometimes referred to as 'verbal consent.' Review "CHECKLIST: Waiver of Written Documentation of Consent (HRP-411)" to ensure that you have provided sufficient information.*

*If you will document consent in writing, attach a consent document with your submission. You may use "TEMPLATE CONSENT DOCUMENT (HRP-502)". If you will obtain consent, but not document consent in writing, attach the script of the information to be provided orally or in writing (i.e. consent script or Information Sheet).*

Response:

☒ We will be following "SOP: Written Documentation of Consent" (HRP-091).

## 31.0 Multi-Site Research (Multisite/Multicenter Only)*

☒ **N/A:** This study is not an investigator-initiated multi-site study. This section does not apply.

*31.1 Indicate the total number of subjects that will be enrolled or records that will be reviewed across all sites.*

Response:

*31.2 If this is a multi-site study **where you are the lead investigator**, describe the processes to ensure communication among sites, such as the following.*

- *All sites have the most current version of the IRB documents, including the protocol, consent document, and HIPAA authorization.*
- *All required approvals have been obtained at each site (including approval by the site's IRB of record).*
- *All modifications have been communicated to sites, and approved (including approval by the site's IRB of record) before the modification is implemented.*
- *All engaged participating sites will safeguard data as required by local information security policies.*
- *All local site investigators conduct the study appropriately in accordance with applicable federal regulations and local laws.*
- *All non-compliance with the study protocol or applicable requirements will be reported in accordance with local policy.*

Response:

*31.3 Describe the method for communicating to engaged participating sites.*

- *Problems (inclusive of reportable events)*
- *Interim results*
- *Study closure*

Response:

*31.4 If this is a multicenter study **where you are a participating site/investigator**, describe the local procedures for maintenance of confidentiality.*

- *Where and how data or specimens will be stored locally?*

- *How long the data or specimens will be stored locally?*
- *Who will have access to the data or specimens locally?*
- *Who is responsible for receipt or transmission of the data or specimens locally?*
- *How data and specimens will be transported locally?*

Response:

*31.5 If this is a multicenter study and subjects will be recruited by methods not under the control of the local site (e.g., call centers, national advertisements) describe those methods. Local recruitment methods are described elsewhere in the protocol.*

- *Describe when, where, and how potential subjects will be recruited.*
- *Describe the methods that will be used to identify potential subjects.*
- *Describe materials that will be used to recruit subjects. (Attach copies of these documents with the application. For advertisements, attach the final copy of printed advertisements. When advertisements are taped for broadcast, attach the final audio/video tape. You may submit the wording of the advertisement prior to taping to preclude re-taping because of inappropriate wording, provided the IRB reviews the final audio/video tape.)*

Response:

## 32.0 Banking Data or Specimens for Future Use*

☐ **N/A:** This study is not banking data or specimens for future use or research outside the scope of the present protocol. This section does not apply.

*32.1 If data or specimens will be banked (stored) for **future use, that is, use or research outside of the scope of the present protocol**, describe where the data/specimens will be stored, how long they will be stored, how the data/specimens will be accessed, and who will have access to the data/specimens.*

*NOTE: Your response here must be consistent with your response at the "What happens if I say yes, I want to be in this research?" Section of the Template Consent Document (HRP-502).*

Response:

Data will be stored on an encrypted password-protected UB server in the Department of Obstetrics and Gynecology for 10 years.

*32.2 List the data to be stored or associated with each specimen.*

Response:

Clinical data collected during the exam (infrared photos and pain map) and demographic data from the data collection sheet.

*32.3 Describe the procedures to release banked data or specimens for future uses, including: the process to request a release, approvals required for release, who can obtain data or specimens, and the data to be provided with specimens.*

Response:

Only the investigators will have access to stored data.

All future use of data from this study outside the scope of this protocol will be submitted to the IRB for review.