SUBJECT INFORMATION AND CONSENT FORM

Research Project and Title	**LIBERATE International (VI-17-01): Evaluation of the Safety and Efficacy of the Viveve Treatment for Stress Urinary Incontinence**
Protocol Number	**VI-17-01**
Study Doctor:	**«PiFullName»**
Telephone:	**«IcfPhoneNumber»**
Additional Contact(s):	**«AdditionalStaffMemberContacts»**
Address:	**«PiLocations»**
Sponsor	Viveve Inc. 345 Inverness Drive South, Building B, Suite 250 Englewood, CO, 80112 USA

PLEASE READ THE FOLLOWING CAREFULLY

The purpose of this Consent Form and Authorization is to provide you with information that will enable you to decide if you want to take part in this research study. This form will also explain how your medical information will be used and who may see it. Please read the form carefully and take as much time as you need. This Consent Form may contain words that you do not understand. Please ask the study doctor or a member of the study personnel to explain any words that you do not clearly understand. You may take home an unsigned copy of this Consent Form to think about or discuss with family or friends or with your physician before making your decision. If you have any questions, you may ask your study doctor. When all your questions have been answered, you can decide if you want to be in the study or not. This process is called informed consent.

Participation in this study is voluntary, and refusal to participate will involve no penalty or loss of benefits to which you are otherwise entitled, and you may discontinue participation at any time without penalty or loss of benefits to which you are otherwise entitled.

Background/Rationale

Urinary incontinence is a significant health problem with considerable social and economic impact. Stress urinary incontinence (SUI), also known as stress incontinence, is the most common form of incontinence. It is due to inadequate strength of the closure of the bladder, which means a woman leaks urine when pressure is increased on the bladder, as when coughing, sneezing, or exercising. It happens when the muscles that support the bladder are weakened.

In women, physical changes resulting from pregnancy, childbirth, and menopause often contribute to stress incontinence. Stress incontinence can worsen during the week before the menstrual period. The incidence of stress incontinence increases following menopause due to lowered estrogen levels.

A company called Viveve has a nonsurgical radiofrequency treatment to effectively remodel the vaginal tissue without causing cellular damage or scarring. The study treatment works by heating and providing energy to the tissues that support the vaginal tissue. The procedure does not require any anesthesia or pre-treatment prior to the study treatment. The proposed treatment for SUI involves the application of 220 pulses of radiofrequency energy to the vaginal canal. This investigational treatment is intended to augment the effect observed through Viveve's standard treatment for vaginal laxity.

Viveve has received clearance from Health Canada to market and sell the Viveve System in Canada for the treatment of laxity of the vaginal introitus (opening) after vaginal childbirth to improve sexual function. This study is being conducted to assess the safety and efficacy of the Viveve SUI Treatment to treat stress urinary incontinence. Prior to this study, a small study was conducted to provide information that it is safe enough to proceed. Another study was conducted to gather information on the clinical outcomes from the study treatment, and another study was conducted to gather information how participants treated with the Viveve System felt after the treatment. While this treatment is approved and has some supporting data for use in treating vaginal laxity, there are no prior studies related to its use in SUI.

You are being invited to consider participation in this study because you have symptoms of stress urinary incontinence.

Nature and Purpose of the Study

The purpose of this study is to assess the safety and effectiveness of the Viveve Treatment, SUI protocol. Viveve is conducting this study to submit its results to Health Canada. If approved, the treatment will be available in Canada.

FDA has deemed that this investigational device is a "Significant Risk" device. A significant risk device presents a potential for serious risk to the health, safety, or welfare of a subject. Significant risk devices may include implants, devices that support or sustain human life, and devices that are substantially important in diagnosing, curing, mitigating or treating disease or in preventing impairment to human health.

Study Design

This research study aims to enroll approximately 99 subjects. Up to 10 sites in Canada will participate. If you agree to take part in this study, you will first voluntarily sign this Consent Form before any study-related procedures are performed. If you join this study, you will need to be willing and able to visit your doctor more often than would be necessary if you were not in the study. You will be asked to complete 5 scheduled study visits during the approximately 6 months that you will participate in the study. You may be required to come in more frequently if you are having side effects. You may also be contacted by the study personnel by phone for follow-up. No tests or procedures will be performed until you have had an opportunity to review and sign this Consent Form.

You will be assigned to receive one of two possible study treatments in this study:

- Active Study Treatment of RF energy of 90 Joules/cm2.
- Placebo (also known as a Sham/Control) Treatment of RF energy of less than or equal to 1 Joule/cm2. The placebo treatment does not provide enough energy to provide a treatment for a change in stress urinary incontinence symptoms.

You will be randomly assigned, like flipping a coin, to a study treatment group. All study subjects will be randomized in a 2:1 ratio. This means that there is a 2 in 3 chance that you will be assigned to active study treatment. There is a 1 in 3 chance that you will be assigned to the placebo treatment. The study treatment you will receive will be blinded, meaning neither you nor study personnel will know which study treatment you receive until after the study is completed.

Pre-Screening and Informed Consent Visit (Visit 1)

You will come to the study clinic for a pre-screening visit to review and sign the informed consent form

and complete study-related procedures. You will spend 30 to 60 minutes at the clinic for the pre-screening assessment. The following procedures will be performed:

- Signing of the Informed Consent Form. ***You must sign this consent form before having any study-related tests or procedures performed.***
- Study personnel will ask you questions to review your eligibility for the study.
- A complete medical history will be taken, including any medications you are currently taking.
- Study site personnel will measure your height and weight.
- You will be provided with and trained on a 3-day bladder voiding diary that will be completed during the 3 days prior to your next visit.
    - A voiding diary provides valuable information about your bladder control and helps you and your doctor understand the number of accidental leakage episodes that you experience each day (for 3 days).
- You will be provided with pads to collect urine leakage for a 24-hr period prior to your next visit.

Screening Visit (Visit 2)

You will come to the study clinic to complete assessments to see if you are eligible for the study. You will spend approximately 2 hours at the clinic. It is important that you come to this visit with a full bladder.

- Study personnel will ask you questions to review your eligibility for the study.
- Study personnel will collect and score your 3-day bladder voiding diary.
- You will be asked to complete questionnaires related to urinary incontinence and sexual function.
- You will be asked if there have been any changes to your medical history or medication use since the last study visit.
- Your vital signs (e.g., blood pressure, pulse, temperature and respiration) will be measured.
- A urine dipstick will be performed.
- A urine pregnancy test will be performed.
- A physical exam will be performed, including a neurologic and pelvic exam.
- Your bladder will be scanned so the study personnel can ensure that your bladder is full.
- To confirm the diagnosis of mild to moderate stress urinary incontinence due to urethral hypermobility, the following tests will be performed:
    - A Q-tip test will be performed
        - A Q-tip that with numbing gel will be gently inserted into your urethra to test for movement of your urethra while you cough or strain. You may feel pressure but it should not be painful.
    - A cough stress test: You will be asked to cough or bear down and the doctor will observe if there is urine loss from the urethra.
    - 1-hr pad weight test: This will evaluate the amount of urine lost into a pad during a set of activities, such as: walking, climbing stairs, standing up from sitting, coughing vigorously and washing hands under running water.
- A 24-hr pad weight test will be done using the pads you were provided at the Pre-Screening visit. You will wear several pads over a 24-hr period while you perform normal daily activities. The pads will be collected in an airtight bag, which you will bring with you to this visit.
- You will have your blood drawn to assess your overall health, including kidney function. Less than a teaspoon of blood is needed for the laboratory to complete the assessments.

Randomization Visit (Visit 3)

This visit will last about 1 ½ hours. One or more Viveve representatives may be present during the procedure to assist with any technical issues that may arise and to provide guidance to the research team as needed. The following procedures will be performed:

- You will be asked if there have been any changes to your medical history or medication use since the last study visit.
- Your vital signs (e.g., blood pressure, pulse, temperature and respiration) will be measured.
- A urine pregnancy test will be performed.
- A urine dipstick will be performed.
- You will be provided with and trained on a 3-day bladder voiding diary that will be completed during the 3 days prior to your next visit.
- You will receive the study treatment, which includes the following steps:
    - A flat pad will be attached to your lower back or side (above the hip).
    - You will lie on an examination table with your feet in stirrups as if you are receiving a pelvic exam.
    - A gel will be applied to the device tip during the procedure to allow for contact between the device tip and vaginal tissue.
    - The study doctor, or designee, will insert the device tip in the opening of your vagina.
    - The study treatment RF pulses will be applied in a circular fashion inside the vaginal opening until 220 study treatment pulses have been applied.
    - The procedure should take approximately 50 minutes.

During the study treatment, you may feel a sensation of cold and/or heat. If you experience pain or discomfort during the procedure, you will have the option to stop study treatment. If you receive partial study treatment, you will be asked to complete the remainder of the study visits to ensure you are not experiencing any side effects.

Follow-Up Telephone Call

Approximately 10 days after you receive the procedure a study staff member will contact you by telephone. You will be asked as to how you are feeling and if you have experienced any side effects from the procedure. Additionally, any changes in therapies or medications will be recorded.

Follow-Up Study Visit (Month 3, Visit 4)

The following procedures/information will be collected at each of the monthly follow-up visits after the Day 10 visit:

- You will be asked if you have experienced any adverse events and if there have been any changes to your medical history or medication use since the last study visit.
- Your vital signs (e.g., blood pressure, pulse, temperature, and respiration) will be measured.
- Study personnel will collect and score your 3-day bladder voiding diary.
- You will be provided with and trained on a 3-day bladder voiding diary that will be completed during the 3 days prior to your next visit (except at the Month 6 Visit).
- You will be asked to complete questionnaires related to urinary incontinence and sexual function.
- You will be asked to complete a 1-hr pad weight test.

Final Visit (Month 6, Visit 5)

The following procedures/information will be collected at Visit 5/ Month 6. It is important that you come to this visit with a full bladder.

- You will be asked if you have experienced any adverse events and if there have been any changes to your medical history, therapies and/or medication use since the last study visit.
- Study personnel will collect and score your 3-day bladder voiding diary.

- Study site personnel will measure your weight.
- You will be asked to complete questionnaires related to urinary incontinence and sexual function.
- Your vital signs (e.g., blood pressure, pulse, temperature, and respiration) will be measured.
- A urine pregnancy test will be performed.
- A physical exam will be performed, including a neurologic and pelvic exam.
- You will be asked to complete questionnaires related to urinary incontinence and sexual function.
- Your bladder will be scanned so the study personnel can ensure that your bladder is full.
- You will be asked to complete a 1-hr pad weight test.
- You will be asked to complete a 24-hr pad weight test prior to this visit.

Potential Risks

Procedure

Potential risks may include:

- Pain or discomfort during the procedure related to heat and/or cold in the treated area
- Brief swelling or redness in the treated area
- Vaginal discharge
- Pelvic pain or discomfort after the procedure
- Sensitivity if you have an allergy to any component of the device
- Focal, brief tingling in the vulvar and/or vaginal pelvic region
- Excessive vaginal tightness resulting in interference with sexual activity
- Damage to the urinary bladder and/or urethra
- Temporary worsening for urinary incontinence symptoms

To minimize these risks in sensitive areas of the vagina, no study treatment is being performed in the urethral area. Doctors will not treat subjects with physical features in the study treatment area that may be more sensitive than others (such as excessive scar tissue).

Unknown Risks

This is a feasibility study using the Viveve system to treat SUI. The study treatment uses 220 pulses of radiofrequency energy, which is twice that previously studied. Therefore, the degree of risk and potential adverse events are unknown.

In addition to the risks listed above, there may be some unknown or infrequent and unforeseeable risks associated with the use of this device. You will be informed in a timely manner of any new information, findings, or changes to the way the research will be performed that may be important to your health or that might influence your willingness to continue your participation in this study.

Pelvic Exam

Some women experience discomfort from the pressure applied during a manual pelvic exam.

Q-tip Test

Some women experience pressure and discomfort during the Q-tip assessment. Analgesic gel will be applied to the Q-tip to minimize discomfort.

Blood Draws

Blood samples will be drawn from a vein with a sterile needle, usually in the arm. The risks with drawing

blood are pain, swelling, bruising, feeling faint, and rarely, infection at the site of the needle stick.

Reproductive Risks
The risks to an unborn human fetus or a nursing child from the Viveve Study Treatment are not known. If you are a woman who is able to become pregnant, it is expected that you will use an effective method of birth control throughout the study to prevent exposing a fetus to unknown risks. If you are taking oral contraceptives, you must have been taking them for 3 months prior to the start of your participation in this study and continue taking them for the duration of the study. If you are using an IUD, it must be in place for at least 3 months prior to the procedure. If a vasectomy is done for your partner, it must be 30 days prior to the study treatment or a sperm count of zero (0) will suffice to ensure optimal efficacy and safety to reduce the risk of pregnancy and possible harm to the fetus.

If you are pregnant or currently breastfeeding, you may not participate in this study. You understand that if you are pregnant, if you become pregnant, or if you are breastfeeding during this study, your child may be exposed to unknown risks.

Contraindications of the Study Treatment
The Viveve Study Treatment is not intended for use in patients with either an Implantable Pacemaker or an Automatic Implantable Cardioverter/Defibrillator (AICD) or any other implantable electrical device, as they may be adversely affected by RF fields or current. If you have an implantable electrical device, you must notify the study doctor, and you will not be able to be a participant in this research study.

In addition to the risks listed above, there may be some unknown or infrequent and unforeseeable risks associated with the use of this device. You will be informed in a timely manner of any new information, findings, or changes to the way the research will be performed that may be important to your health or that might influence your willingness to continue your participation in this study.

Possible Benefits
There may be no direct benefit to you for participating in this study. However, if you are assigned to receive the active study treatment, you may experience a decrease in stress urinary incontinence symptoms. Additionally, the information learned from this study may benefit other women with problems with stress urinary incontinence in the future.

Note that this investigational device will not be able to address all physical changes that may cause stress urinary incontinence. Two components contribute to stress urinary incontinence: urethral hypermobility (instability of the urethra) and internal sphincter dysfunction (weak muscles at the bladder opening). Although many women may have both issues contributing to their stress urinary incontinence symptoms, in some patients, intrinsic sphincter dysfunction may be the primary cause of their stress urinary incontinence. The Viveve Treatment, SUI protocol is thought to be most helpful to women with urethral hypermobility as the primary cause of their stress urinary incontinence symptoms. In addition, some types of trauma following vaginal childbirth result in the detachment of the pelvic floor muscles from the pubic bone. The study treatment is not designed to address detached pelvic floor muscles that may be responsible for symptoms in many women.

Alternatives to Participation
Your participation in this study is voluntary. You are free to choose not to participate. Your medical care will not be affected if you decide not to participate. Various treatments exist for the alleviation of stress urinary incontinence symptoms in women, ranging from non-invasive treatments such as pelvic floor muscle exercises, pelvic floor stimulation, pessaries (a device worn in the vagina to support the

pelvic organs), and periurethral injection therapy (Bulking agents are injected into the bladder neck and around the urethra), to surgical approaches using various bladder sling or mesh devices. Pharmaceutical approaches may also be used, including topical estrogen or other medications (e.g., alpha-adrenergic stimulants, duloxetine).

Cost to Subjects

If you are a candidate for this clinical study and you wish to participate, the study procedure and all study costs (e.g., examinations and tests, study treatment procedure, and all post-procedure visits) will be paid by the Sponsor, Viveve. There is no cost to you, your private medical insurance (if any), or the public health insurance plan, for study procedures.

Payment for Participation

Participants in this study will receive monetary compensation to cover costs for their time and travel or any other costs incurred to participate in the study up to the amounts listed in the table below per study visit. Subjects who complete the 6-month follow-up will receive a total of $520 that will be allocated over the study treatment visits. Subjects who withdraw from the study before 6 months will receive compensation for the visits they have completed.

Patient Payment Schedule	
Visit 1	$50
Visit 2	$150
Visit 3	$100
TC	$20
Visit 4	$100
Visit 5	$100

Compensation for Injury

In the event that you are physically injured as a result of participating in this research, emergency care will be available. You and/or your insurer will, however, be responsible for the charges for the emergency care. Medications used to control adverse health effects may result in costs to you that may not be covered by your insurance. This could include a diagnostic work-up. The Sponsor of this study, Viveve, has an Insurance Policy in place to cover damages due to injury or death which arise from your direct participation in this study. No other compensation will be provided by the Sponsor. Under no circumstances will the Sponsor be responsible or liable for medical or other expenses related to pregnancy, or the cost of health expenses and rearing of any child (children) conceived before, during, or after participation in this study. In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment, by signing this form, nor release the study doctor or sponsors from their legal and professional obligations. Please talk with the study personnel if you are injured or if you would like further information.

Withdrawal from Study

Participation in this study is entirely voluntary. If you do not wish to take part in the study, this in no way will affect your current or future treatment at this doctor's office. If you do take part, you can withdraw (stop participating in this study) at any time. Withdrawal will not affect your future medical treatment at this doctor's office. However, if you decide not to further participate in this study, you will be asked to provide a reason for not participating in the study. It will be recorded as a part of the study records. If you decide to withdraw before the study is completed, you must contact the study doctor or

a member of the study personnel. You will be asked to complete all the procedures required in the final study visit. If you withdraw, your previously collected de-identified personal health information may still be used by the study doctor and/or Sponsor to help assess how safe and effective the study treatment is. No new information will be collected.

The study doctor or the study Sponsor, Viveve, may decide to stop your participation in the study at any time without your consent if they believe it is in your best interest to do so. The study can also be ended at any time by the Sponsor, a regulatory agency (such as Health Canada), and you would then be taken off the study without your consent. This does not entitle you to receive any additional study treatments, study procedures, or compensation other than what you are entitled to receive up to the time your participation in the study is cancelled.

Who Can Answer My Questions?

If you have additional questions, you should not hesitate to ask your study doctor or study personnel at any time during the study, and they will try to explain any issues you do not understand.

What If I Have Concerns About the Study?

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the Investigator at the telephone number listed on the first page of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research subjects. If you have any questions about your rights as a research subject, and/or concerns or complaints regarding this research study, contact**:**

- By mail:
  Study Subject Adviser
  Advarra IRB
  6940 Columbia Gateway Drive, Suite 110
  Columbia, MD 21046
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00023755

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all your questions.

Posting on ClinicalTrials.gov

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Primary Care Physician / Specialist Notification Option

Please indicate below, by initialing, whether you want us to notify your primary care physician or your specialist of your participation in this study.

	Yes, I want the study doctor to inform my primary care physician/specialist of my participation in this study
	No, I do not want the study doctor to inform my primary care physician/specialist of my participation in this study.
	I do not have a primary care physician/specialist.
	The study doctor is my primary care physician/specialist.

Authorization to Use or Disclose (Release) Health Information that Identifies You for a Research Study

Your confidentiality will be maintained throughout the clinical study to the extent permitted by law. That is every attempt will be made to remove information that could reveal your identity from clinical study documents. For this purpose, a unique subject identification code will be assigned and used to allow identification of all data reported about you.

Because information about you and your health is personal and private, it generally cannot be used in this research study without your written authorization. If you sign this below, it will provide that authorization. The authorization is intended to inform you about how your health information will be used or disclosed in the study. Your information will only be used in accordance with this authorization and the Informed Consent Form and as required or allowed by law. Please read it carefully before signing it.

If you sign this document, you give permission to the study doctor to use or disclose (release) your health information that identifies you for the research study described in this consent form. Your study records including confidential information about you collected during the study will be kept at a secure location.

The health information that we may use or disclose (release) for this research includes:

- information in a medical record,
- results of physical examinations,
- medical history,
- lab tests, or
- certain health information indicating or relating to a particular condition.

The health information listed above may be used by and/or disclosed (released) to the following persons in order to monitor the research and verify the accuracy of the study data:

- The Study Doctor and his/her research personnel (namely its monitors and auditors);
- Sponsors who want access to PHI or who will actually own the research data;
- Institutional Review Boards - Advarra IRB (an independent ethics committee that reviewed the ethical aspects of this study to help protect the rights and welfare of study participants), or Data Safety and Monitoring Boards;
- Food and Drug Administration (FDA), Health Canada and/or to other government health oversight agencies; and/or
- Governmental health agencies in other countries where the study device may be considered for approval

The Study Doctor is required by law to protect your health information. By signing this document, you authorize the Study Doctor to use and/or disclose (release) your health information for this research.

Because of the need to release information to these parties, absolute confidentiality cannot be guaranteed. The results of this research study may be presented at scientific meetings or in publications in medical journals. However, your identity will not be disclosed in those presentations. Additionally, information from the study may be exported to countries where different data protection laws apply.

You do not have to sign this authorization, but if you do not you will not be able to participate in this research study. Signing the authorization is not a condition for receiving any medical care outside the study.

If you decide to participate, you are free to withdraw your authorization regarding the use and disclosure of your health information (and to discontinue any other participation in the study) at any time. After any revocation, your health information will no longer be used or disclosed in the study, except to the extent that the law allows us to continue using your information (e.g., necessary to maintain integrity of research). If you wish to revoke your authorization for the research use or disclosure of your health information in this study, you must inform the Study Doctor.

I have read the foregoing, understand how my health information will be used, and consent to and authorize the use of my health information as described above.

Subject Name (printed)	Subject Name (signed)	Date (dd/mmm/yyyy)

CONSENT

I have read and understand the information regarding participation in this research study and agree to participate as a subject.

- I understand that my participation is voluntary.
- I understand that if I decide not to participate or discontinue my participation in this study, there will be no penalty or loss of benefits that I am otherwise entitled to at this site.
- I was given the opportunity to ask questions regarding this Consent Form, the study, and any other areas of concern. All my questions were answered to my satisfaction by a member of the research personnel.
- I agree to participate in this research study under the direction of the Study Doctor**.**
- I authorize the use and disclosure of my Personal Health Information under the terms and conditions described in this form.
- I understand that I will receive a signed and dated copy of this form for my records.
- By signing this form, I have not waived any of the legal rights which I otherwise would have as a subject in a research study.

Subject Signature	Date (dd/mmm/yyyy)*
Subject Name (Printed)	
Signature of Person Conducting Informed Consent Discussion	Date (dd/mmm/yyyy)
Name of Person Conducting Informed Consent Discussion (Printed)	
Study Doctor Signature (if different from above)	Date (dd/mmm/yyyy)
Name of Study Doctor (Printed)	

* Please write dates in this format: 01/Jan/2016.

END OF CONSENT FORM