**Informed Consent Form**

**And**

**Authorization To Disclose Health Information**

|  |  |
| --- | --- |
| **Sponsors / Study Title:** | **Andrew T. Goldstein, Endoceutics Inc. / “A randomized placebo-controlled study examining the effects of Intrarosa**® **on the vulvar vestibule and vagina in women with Genitourinary Syndrome of Menopause.”** |
| **Principal Investigator:****(Study Doctor)** | **Andrew T. Goldstein, M.D.** |
| **Telephone:** | **(202) 887-0568****(410) 279-0209 (24-Hour)**  |
| **Address:** | **The Center for Vulvovaginal Disorders****3 Washington Circle NW, Suite 205****Washington, DC 20037** |

**INTRODUCTION:**

You are being invited to take part in a research study. Research studies are voluntary and include only those who wish to take part. This research study is to examine an approved treatment for Genitourinary Syndrome of Menopause (GSM). Before you decide if you want to participate in this research study, it is important for you to understand why the research is being done and what it will involve. This consent form describes the purpose, procedures, benefits, risks, discomforts, and precautions of the study. It also describes the alternative procedures available to you and your right to withdraw from the study at any time. No guarantees or assurances can be made as to the results of the study.

Please take time to read the following information carefully and discuss it with friends, relatives, or your family doctor if you wish. Please ask if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part. You will be given a signed and dated copy of this consent to take home with you.

If you are not completely truthful with your study doctor regarding your health history, you may harm yourself by participating in this study.

You may not use additional medications for GSM treatment while participating in this study.

**FINANCIAL DISCLOSURE:**

Dr. Andrew Goldstein, the principal investigator, is being paid by Endoceutics Inc to conduct this study. Due to this potential conflict of interest, Dr. Goldstein will not be involved in the informed consent process or recruitment for this study. Speak with the study doctor if you have additional questions.

**PURPOSE OF THE STUDY:**

The purpose of this study is to look at the effects of Intrarosa® on the tissue of the genitals (vulva and vagina) of women with GSM.

**BACKGROUND AND STUDY RATIONALE**

Tissues of the genitals of women are both androgen (testosterone) and estrogen dependent. The clitoris, vestibule, urethra, anterior vaginal wall, peri-urethral tissue, and pelvic floor all depend on androgens for normal function. In addition, the glands, which secrete lubrication during sexual arousal, also require androgens to function. Deficiencies of both estrogens and androgens occur naturally during menopause. Menopause-related deficiencies of these hormones lead to thinning in the tissues of the genital and urinary systems which have been termed Genitourinary Syndrome of Menopause (GSM). Patients with GSM will frequently complain of dryness and/or pain during sexual intercourse.

Historically, GSM treatment involved both androgens and estrogens, However, over the past few decades estrogen based therapies have become much more common. More recently, clinical trials have demonstrated that local vaginal dehydroepiandrosterone (Intrarosa®) improves symptoms in menopausal women who have moderate to severe pain with intercourse.

Intrarosa® vaginal inserts are a prescription medicine approved by the U.S. Food and Drug Administration (FDA) used in women after menopause to treat moderate to severe pain during sexual intercourse caused by changes in and around the vagina that happen with menopause.

**LENGTH OF THE STUDY AND NUMBER OF SUBJECTS:**

Up to 40 women may participate in this study.

The study will consist of 3 visits to the study center. Each visit is expected to last approximately one hour. The total amount of time you will participate in the study is 26 weeks. Your safety will be assessed for the entire 26-week study treatment period.

# WHO MAY PARTICIPATE:

You *may* participate if you:

* Are 50-70 years or older.
* Menopausal
* Have symptomatic GSM
* Signed written informed consent.
* Willing and able to comply with the study requirements.

**Exclusion criteria:**

You *may not* participate if you are:

* Non-menopausal (have had a menstrual period within one year)
* Have undiagnosed vaginal bleeding
* Have a known or suspected history of breast cancer
* Have a current vaginal infection
* Known sensitivity or allergy to Intrarosa®
* Currently being treated with topical or systemic estrogen, testosterone, or DHEA.
* Take raloxifene, ospemifene, tamoxifen, bazedoxifene

**YOUR ROLE IN THE STUDY:**

Taking part in a research study can be an inconvenience to your daily life. Please consider the study time commitments and responsibilities as a research subject when you are deciding to take part. Your responsibilities as a study subject include the following:

* Tell the truth about your medical history and current conditions.
* Tell the study doctor if you have been in a research study in the last 30 days or are in another research study now.
* Tell the study doctor about any problems you have during the study.

**PROCEDURES TO BE FOLLOWED DURING THE STUDY:**

**Visit 1 Screening**

* A detailed history and physical examination will be performed.
* You will fill out questionnaires about your GSM and current sexual function.
* A digital photograph of your vulva and vagina will be taken.
* A vaginal swab will be taken.
* A cotton swab will be applied to your vulvar vestibule and the amount of pressure necessary to cause moderate discomfort (5/10 on a pain scale) will be determined
* A 4mm (¼ inch) skin biopsy of the vulva will be taken. Prior to the biopsy, a numbing medication (lidocaine) will be injected in the biopsy site. After the biopsy, you will get one or two stitches at the biopsy site. These stitches dissolve and do not have to be removed.
* A 3mm x 7mm (¼ inch) biopsy of the vaginal mucosa will be taken. Prior to the biopsy, a numbing medication (lidocaine) will be injected in the biopsy site.
* 10cc of blood (2 teaspoons) will be removed from your arm to test blood hormone levels.
* You will be randomized (like the flip of a coin) to receive either Intrarosa or placebo. Half of the women (20 out of 40) will receive Intrarosa® and half (20 out of 40) will receive the placebo treatment. The research coordinator will know if you will be receiving Intrarosa® or the placebo. Neither you, nor Dr. Goldstein will know if you are to receive Intrarosa® or placebo. If you have been randomized to receive Intrarosa® you will get it throughout the entire study. If you have been randomized to receive the placebo, you will get it throughout the entire study and you will not be getting Intrarosa®.

You will need to refrain from sexual intercourse until the biopsies heal.

**Visit 2**

You will return approximately 13 weeks after visit 1.

* You will have a gynecologic examination.
* You will tell the study doctor if you are having any side effects from the study treatment.

**Visits 3**

You will return approximately 13 weeks after visit number 2.

* You will have a gynecologic examination.
* You will tell the study doctor if you are having any side effects from the study treatment.
* You will fill out questionnaires about your GSM and current sexual function.
* A digital photograph of your vulva and vagina will be taken.
* A cotton swab will be applied to your vulvar vestibule and the amount of pressure necessary to cause moderate discomfort (5/10 on a pain scale) will be determined
* A vaginal swab will be taken.
* Two 4mm (¼ inch) skin biopsies of the vulva will be taken. Prior to the biopsies, a numbing medication (lidocaine) will be injected in the biopsy sites. After the biopsies, you will get one or two stitches at each biopsy site. These stitches dissolve and do not have to be removed.
* A 3mm x 7mm (¼ inch) biopsy of the vaginal mucosa will be taken. Prior to the biopsy, a numbing medication (lidocaine) will be injected in the biopsy site.
* 10cc of blood (2 teaspoons) will be removed from your arm to test blood hormone levels.

You will need to refrain from sexual intercourse until the biopsies heal.

**FORESEEABLE DISCOMFORTS AND RISKS OF THE STUDY:**

1. **If the Intrarosa®** **is not an effective study treatment of GSM or if you receive placebo:**
* Your symptoms of vaginal dryness or pain during intercourse may not improve, or it may get worse.
1. **Possible side effects from the intervention during this study:**

Risks related to the Intrarosa®include:

Less likely

* Increased vaginal discharge

Rare but potentially serious

* You will have an abnormal pap smear

**3) Risks related to the vulvar and vaginal biopsies:**

Very Likely:

* Pain from injection of anesthetic
* Mild or moderate discomfort while the biopsies heal (typically less than 10 days)

Less Likely

* Infection at biopsy site requiring antibiotics

Rare but Serious

* Long-lasting discomfort at the biopsy site

**4) Risks of Lidocaine Injection**

Tell the study doctor or study staff at once if you have any of these serious side effects:

* Feeling anxious, shaky, dizzy, restless, or depressed
* Drowsiness, vomiting, ringing in your ears, blurred vision
* Confusion, twitching, seizure (convulsions)
* Fast heart rate, rapid breathing, feeling hot or cold
* Weak or shallow breathing, slow heart rate, weak pulse
* Feeling like you might pass out

Less serious side effects include:

* Mild bruising, redness, itching, or swelling where the medication was injected
* Mild dizziness
* Nausea
* Numbness in places where the medicine is accidentally applied

Get emergency medical help if you have any of these signs of an allergic reaction: hives; difficulty breathing; swelling of your face, lips, tongue, or throat.

**5) Blood Draw Risks**

You may have pain or bruising at the site where the blood is drawn. You may feel faint. An infection at the site of the blood draw is possible.

**6) Personal Questions Risk**

You will be asked questions about personal issues during this study. There may be questions about your sexual functioning, etc. These types of questions may make some subjects uncomfortable.

**7) Risks of Loss of Confidentiality**

In order to protect you from the risk of loss of confidentiality, individual subject names will not be used for any purpose and you will be tracked only by a unique subject number. All data files will be password-protected and no hard copies with medical record numbers or account numbers will be printed. All of your study data will be kept in a secure location. Information published will be in group form without individual identifying facts.

**8) Unknown Risks**

You might have side effects or discomforts that are not listed in this form. Some side effects may not be known yet. New ones could happen to you. Tell the study doctor or study staff right away if you have any problems.

**NEW FINDINGS:**

Any new important information which is discovered during the study and which may influence your willingness to continue participation in the study will be made available to you in a timely fashion.

**POTENTIAL BENEFITS OF THE STUDY:**

There is the hope that your vaginal dryness and pain during intercourse will be decreased. However, there is no guarantee that you will benefit from your participation in this study.

**ALTERNATIVES TO BEING IN THE STUDY:**

You do not need to take part in this research study. Risks of not treating GSM include worsening of pain during intercourse and increased risk of urinary tract infections. Alternative treatments for GSM include estrogen creams, tablets, and vaginal rings. The FDA has mandated that the package inserts for all types of vaginal estrogen therapy state that there is an increased risk of breast cancer, endometrial cancer, dementia, heart attack and stroke associated with these products.

Your study doctor can discuss the alternatives and the risks and benefits of these alternatives with you.

**COMPENSATION:**

You will receive $1000 for participation for the entire study. You will receive $200 for completion of the first study visit, $150 for the completion of the second study visit, and $650 for completion of the third study visit. All of your compensation will be given at the end of your participation in the study. In addition, you may be eligible for reimbursement for travel and lodging of up to $500 for the entire study. Receipts will be required for travel reimbursement that must be submitted within 2 weeks of your last study visit.

**DISCLOSURE OF PROTECTED HEALTH INFORMATION (HIPAA):**

For purposes of this study:

* The study doctors and the sponsors (Dr. Andrew Goldstein and Endoceutics) will use medical information collected or created as part of the study, such as medical records and test results, that identifies you by name or in another way.
* Your consent to participate in the study means that you agree that the study doctors may obtain your medical information for study purposes from your physicians and your other health care providers.
* You are also agreeing that the study doctors may use and share this information with the parties described below. In addition, you agree that, during the study, you may not have access to some of your medical information obtained or created as part of this study. You will be allowed to access this information once the study is finished.
* Unless required by law, the study doctors will share this medical information only with the study team and other professionals involved in the study, the sponsors, the US Food and Drug Administration (FDA), governmental agencies in other countries where the study insert may be considered for approval, and Advarra Institutional Review Board.
* The purpose for using and sharing this information with these parties is to perform the study and to ensure the accuracy of the study data. Not all of the parties who will have access to your medical information as part of the study are prohibited by federal law from further sharing it, so the information, once received by them, may no longer be protected by federal law.
* You have the right to cancel this consent at any time by giving written notice to the study doctor at the address listed on the first page of this form. If you cancel this consent, then the study doctors will no longer use or disclose your medical information, unless it is necessary to do so to preserve the scientific integrity of the study. However, canceling this consent will not affect previous uses and disclosures and your medical information would not be removed from the study records.
* If you fail to give your consent by signing and dating this document, or if you cancel your consent later, then you will not be eligible to participate in this study and will not receive any study treatment provided as part of the study. Unless and until you cancel the consent, it will remain valid and effective.
* All documents will be retained for 10 years after completion of the study.

**IN CASE OF RESEARCH- RELATED INJURY:**

If you become ill or are hurt while you are in the study, get the medical care that you need right away. You should inform the healthcare professional treating you that you are participating in this study.

You must report any suspected study-related illness or injury to the study doctor immediately. Medical therapy will be arranged for you by the study doctor (Dr. Andrew Goldstein) for any physical injuries or illnesses which occur as a direct result of your participation in this research. You will not be reimbursed for your medical expenses that are not covered by your medical insurance or third-party coverage. Compensation for lost wages and/or direct or indirect losses is not available. Dr. Andrew Goldstein will not provide any form of compensation for injury. You will not lose any of your legal rights as a research subject by signing and dating this form nor does it relieve the investigators, Sponsor or involved institutions from their legal and professional responsibilities.

**COSTS:**

There will be no charge to you for your participation in this study. The study treatment, study related procedures, tests, and study visits will be provided to you at no charge to you or your insurance company. Routine medical care not required for this study is not covered.

**SERIOUS ADVERSE EVENTS:**

Every serious adverse medical event, whether related to, or not related to the investigational protocol will be reported to the Advarra IRB Officer within 24 hours of the report being received by Dr. Goldstein.

**WHOM TO CONTACT ABOUT THIS 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: Pro00027673.

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.

**VOLUNTARY PARTICIPATION/WITHDRAW:**

Your participation in this study is voluntary. You may decide not to participate or you may withdraw from this study at any given time without penalty or loss of benefits to which you are otherwise entitled and without effect on your future medical care. If you stop the study, you should tell the study staff and follow the instructions they may give you. There will be no change in your medical care or eligibility to participate in future research studies.

In addition, the study doctor can stop your participation at any time without your consent for the following reasons: if it appears to be medically harmful to you, if you fail to follow directions for participating in the study, if it is discovered that you do not meet the study requirements, if you become pregnant, at the discretion of the study doctor, or if the study is cancelled.

If you withdraw from the study, please be aware that to meet regulatory requirements, the information collected about you will still be processed and used in submissions to regulatory agencies.

**PRIMARY CARE PHYSICIAN NOTIFICATION:**

Participation in this study should not be considered a substitute for treatment by your primary care physician or specialist. Please ask your study doctor questions about the results of your laboratory tests or diagnostic procedures. Please review this information with your primary care physician or specialist. Unless specifically requested, your primary care physician or specialist will not be contacted by your study doctor regarding your participation in this study.

**CONSENT:**

This consent form contains important facts so that you can decide if it is in your best interest to participate in this research study. If you have any questions that are not answered in this consent form, the study doctor can give you further information.

All of your questions about the study have been answered. Based on this information, you voluntarily agree to participate in the study. You also voluntarily agree to allow study staff to collect, use and share my health data as specified in this form. All oral and written information and discussion about the study are in English, a language you can read and understand. You will not lose any of your legal rights as a research subject by signing and dating this consent form. You will receive a copy of this signed and dated consent form.

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ \_\_\_\_\_ \_\_\_\_\_\_

Printed Name of Subject Signature Date Time

**STATEMENT OF PERSON EXPLAINING CONSENT:**

I have carefully explained to the subject the nature and purpose of the above study. There has been an opportunity for the subject to ask questions about this research study. I have been available to answer any questions that the subject has about this study.

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ \_\_\_\_\_ \_\_\_\_\_\_

Printed Name of Person Signature Date Time

Obtaining Consent