**Informed Consent**

**And**

**Authorization To Disclose Health Information**

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| **Sponsor / Study Title:** | **Investigator Sponsored Trial: “A Double Blind Placebo Controlled Trial of Autologous Platelet Rich Plasma (PRP) Peri-urethral and Clitoral Injections for the Treatment of Female Orgasmic Disorder.”** |
| **Principal Investigator:****(Study Doctor)** | **Andrew Goldstein, M.D.** |
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| **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 for an experimental treatment for Female Orgasmic Disorder (FOD). It is not known if this experimental treatment will be an effective (good) treatment for FOD. 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 FOD treatment while participating in this study.

**Financial Disclosure:**

Dr. Andrew Goldstein, the principal investigator is receiving funding from the Cellular Medicine Association and ISTO Biologics to pay for some of the costs of this study. Additional costs of this study are being funded by the Center for Vulvovaginal Disorders, the medical practice of Dr. Andrew Goldstein. Speak with the study doctor if you have additional questions.

**Purpose of the Study:**

Female Orgasmic Disorder (FOD) is defined as a female sexual disorder with the presence of the following “on all or almost all (75%-100%) occasions of sexual activity”:

1. Marked delay in, marked infrequency of, or absence of orgasm

2. Marked reduced intensity of orgasmic sensations.

3. The absence of orgasm must cause personal distress (bother) in order for these symptoms to be considered a disorder. (for example, women who are not very bothered by their lack of orgasm do not have FOD).

Symptoms must have been present for at least 6 months and are not better explained by a mental disorder or because of a relationship problems or other significant stress in your life and not due to effects of substance abuse or new medications or other medical conditions.

Approximately one in twenty women have FOD and it is the second most frequently reported sexual problem in American women. FOD can either be lifelong (primary) or acquired (secondary).

There are no currently FDA approved treatments or devices for FOD. Therefore, common off-label treatments include psychotherapy/sex therapy, hormone therapy, and medications that increase blood flow to the genitals.

Platelet-rich plasma (PRP) is a platelet concentrate that may help to speed up tissue healing, without serious side effects, in some medical conditions. It has been tried as treatment for diabetic foot ulcers, muscle injury, tendon injury, and in a variety of cosmetic procedures. The only condition for which there are high-quality data and clear demonstration of effectiveness is arthritis of the knee. It is also apparent from the majority of published studies that PRP therapy has minimal risk of scar tissue formation or significant bad side effects.

There are some reports that physicians using the PRP as an injection near the urethra and clitoris have seen some patients with improvement in FOD after the injections. This is the first study that uses an objective comparative study to find out if this treatment works or not.

It has been suggested by many scientists that in some women FOD may be caused by decreased clitoral and genital blood flow secondary to blockage in the small blood vessels going to the clitoris (similar to that seen in erectile dysfunction (ED) in men) and/or diminished nerve conduction (also as seen in ED). PRP activates cells to develop into new tissue—nerves, collagen, and blood vessels. As such, PRP may potentially reverse the changes responsible for FOD. In addition, it has been shown that improved sexual function in women is highly linked with increased blood flow through the clitoris. One component of PRP is known to cause growth of new blood vessels. Therefore, we anticipate PRP injections may potentially improve blood flow through both the clitoris and the tissue around the urethra, thereby improving sexual function and decreasing FOD.

In addition, it has been shown that women who easily achieve orgasm are more likely than women with FOD to have a larger clitoris and a clitoris positioned closer to the vaginal wall. Since PRP has been shown to increase connective tissue, injection of PRP into the clitoris may potentially enlarge the clitoris and may bring the clitoris closer to the vaginal wall, thereby improving orgasm.

However, your personal and individual cause for FOD may be unrelated to a lack of circulation to your clitoris or the size or location of your clitoris. If so, the proposed study treatment may not work.

In addition, the study treatment is not proven to do and may not do for you what this study suggests it might. If not, then the study treatment may not work for you.

Lastly, there are no prior studies that prove that if the proposed study treatment increases circulation to your clitoris, and/or increases its size, and/or changes its location, that the changes will improve your FOD.

**Length of the Study and Number of Subjects:**

The study will consist of three visits to the study center; at weeks 0, 6, 12. Each visit is expected to last approximately one hour. The total amount of time you will participate in the study is 42 weeks. You will fill out questionnaires at each visit and online at week 29 and week 42. Your safety will be assessed during the initial 12-week study period.

Up to 40 women may participate in this study.

Who May Participate:

You *may* participate if you:

* Are a woman between 25-55 years old.
* Are premenopausal (are still getting regular periods).
* Are in a continuous, stable sexual relationship with the same partner for at least the most recent 12 months.
* Have all of the diagnostic criteria to be diagnosed with FOD.
* Previously had satisfying orgasms.
* Score between 0-4 on a questionnaire that measures the severity of your FOD.
* Score at least 11 on the Female Sexual Distress Questionnaire-Revised
* Have seen at least one medical provider (doctor, nurse-practitioner, midwife, physician assistant, sex therapist) for your sexual complaint
* Have tried at least one intervention for your sexual complaint
* Are willing to comply with the study requirements.

You *may not* participate if you:

* Have not previously had satisfying orgasms
* Are not in a continuous, stable sexual relationship with the same partner for at least the most recent 12 months.
* If you are immunocompromised (for example, lymphoma, AIDS, Wiskott-Aldrich Syndrome) or have an uncontrolled malignant disease.
* If you suffer from systemic or generalized infections (bacterial, viral or fungal).
* Taking medications for depression, anxiety, attention deficit disorder, attention deficit hyperactivity disorder or other psychiatric conditions including selective serotonin re-uptake inhibitors, selective norepinephrine re-uptake inhibitors, tricyclic antidepressants, mood stabilizers, bupropion, and stimulants such as Adderall.
* Taking sildenafil, vardenafil, or tadalafil.
* Using topical or systemic estrogen, testosterone, or progesterone.
* Are taking oral contraceptive pills
* Have an allergy to lidocaine, tetracaine, or bupivacaine
* Have been diagnosed with lichen sclerosus, lichen planus, psoriasis, candidiasis, intraepithelial neoplasia, or carcinoma of the vulva.
* Have received an investigational drug within four weeks prior to the study or who plan to use other investigational drugs during the course of this study.
* Have severe medical condition(s) that in the view of the study doctor prohibits participation in the study.
* Have a history of substance abuse or any factor, which limits your ability to cooperate with the study procedures.
* Are uncooperative or are not willing to attend regular visits.

**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 and enrollment**

This visit will include a detailed history and physical examination. You will fill out three questionnaires. 1) a questionnaire about your FOD 2) a questionnaire about your sexual distress 3) a questionnaire about any possible incontinence (loss) of urine that you may be having.

If you meet the inclusion criteria, you will have sixty ccs of blood drawn (4 tablespoons) from your arm to make the PRP and for hormonal blood tests. You will then be randomized to either receive the PRP or a placebo (saline). Half of the women (20 out of 40) will receive the PRP and half (20 out of 40) will receive the placebo. Only a research coordinator will know if you will be receiving the PRP or the placebo. Neither you nor Dr. Goldstein will know if you are to receive the PRP or placebo. If you have been randomized to receive the PRP you will get it throughout the entire study. If you have been randomized to receive placebo, you will get it throughout the entire study and you will not be getting PRP. If you are randomized to receive the placebo, 3ccs of your PRP may be tested to determine the number of platelets in your PRP and the rest of the PRP will be discarded.

You will then have a numbing medicine (lidocaine, tetracaine, and bupivacaine cream) applied to your genital area and this will stay on for approximately 15 minutes. Then you will receive an injection of a numbing medicine (lidocaine). You will then receive either the PRP injections or placebo injections into the mucosa (skin) near the urethra and near the glans clitoris. (SEE THE END OF THIS DOCUMENT FOR A DIAGRAM OF THE TWO INJECTION SITES) The syringe containing the PRP or placebo is blackened so that neither you, nor Dr. Goldstein, will know if you are receiving the PRP or placebo.

**Visit 2**

You will return approximately 6 weeks after visit 1. You will tell the study doctor if you are having any side effects from the prior injections. You will fill out three questionnaires. Sixty cc of blood will be drawn (4 tablespoons) from your arm to make the PRP. You will then have a numbing medicine (lidocaine and bupivacaine cream) applied to your genital area and this will stay on for approximately 15 minutes. Then you will receive an injection of a numbing medicine (lidocaine). You will then receive either the PRP injections or placebo injections into the mucosa (skin) near the urethra and near the clitoris.

**Visit 3**

You will return approximately 6 weeks after visit 2. You will tell the study doctor if you are having any side effects from the prior injections. You will have a physical exam. You will fill out two questionnaires.

**Online Questionnaires**

You will be contacted via email and/or text message at weeks 29 and weeks 42 and instructed to go to a secure HIPAA compliant website and fill out three questionnaires.

**Foreseeable Discomforts and Risks of the Study:**

1) If the PRP is not an effective study treatment of FOD:

Your symptoms of decreased orgasm will not improve

2) Possible side effects from the intervention during this study:

Because the PRP is derived from your own blood there is no risk of an allergic or immune reaction.

The risks related to the PRP injections include:

Very likely:

1. mild or moderate pain from the injections

Less likely

1. Bruising at injection sites
2. Pain with urination
3. Incontinence (loss of urine)
4. Urinary retention (inability to start the flow of urine)
5. A pressure sensation around the injection sites
6. Sensation of unwanted sexual arousal

Rare but potentially serious

Very unlikely

 1) infection at injection sites

The risks related to the venipunctures (blood removal):

Very likely:

1. mild discomfort

Less likely

1. bruising
2. anemia

Risks of lidocaine Injection

Likely

1. Pain from injection of anesthetic

Tell your study doctor at once if you have any of these serious side effects:

1. feeling anxious, shaky, dizzy, restless, or depressed;
2. drowsiness, vomiting, ringing in your ears, blurred vision;
3. confusion, twitching, seizure (convulsions);
4. fast heart rate, rapid breathing, feeling hot or cold;
5. weak or shallow breathing, slow heart rate, weak pulse; or
6. feeling like you might pass out.

Less serious side effects include:

1. mild bruising, redness, itching, or swelling where the medication was injected;
2. mild dizziness;
3. nausea;
4. 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.

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.

**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 possibility that you will have an increased ability to have an orgasm or have stronger orgasms. You might have decreased incontinence if you lose urine when you cough or sneeze.

**Alternatives to Being in the Study:**

You do not need to take part in this research study. There are no FDA approved treatments for FOD. You could try sex therapy, hormonal therapy, or medications that increase blood flow to the genitals. Your study doctor can discuss the alternatives and the risks and benefits of these alternatives with you.

**Compensation:**

You will not receive compensation for participation in this study. However, if you received the placebo **and** the study has shown statistical improvement in its intended effect, you will be entitled to receive one peri-urethral and peri-clitoral PRP treatment at no charge by Dr. Andrew Goldstein within one year of the study’s completion.

**Disclosure of Protected Health Information (HIPAA):**

For purposes of this study:

* The study doctor 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 doctor may obtain your medical information that he requests for study purposes from your physicians and your other health care providers.
* You are also agreeing that the study doctor 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 doctor will share this medical information only with the Study Team and other professionals involved in the Study, and the US Food and Drug Administration (FDA), governmental agencies in other countries where the study centrifuge may be considered for approval, and Chesapeake 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 any of the study doctor. If you cancel this consent, then the study doctor 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 understand that 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 other 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 study doctor, 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 Chesapeake IRB Officer within 24 hours of the report being received by Dr. Goldstein.

**Getting Answers to Your Questions or Concerns About the Study:**

You can ask questions about this consent form or the study (before you decide to start the study, at any time during the study, or after completion of the study).  Questions may include:

* Who to contact in the case of a research-related injury or illness;
* Payment or compensation for being in the study, if any;
* Your responsibilities as a study subject;
* Eligibility to participate in the research;
* The study doctor’s or study site’s decision to exclude you from participation;
* Results of tests and/or procedures;
* Other questions, concerns, or complaints.

***Contact the study doctor or study staff listed on the first page of this form with any questions, concerns or complaints.***

**Getting Answers to Your Questions About Your Rights as a Research Subject:**

This study has been reviewed by an Institutional Review Board (IRB). This Committee reviewed this study to help ensure that your rights and welfare are protected and that this study is carried out in an ethical manner.

For questions about your rights as a research subject, contact:

* By mail:

Study Subject Adviser

Chesapeake IRB

6940 Columbia Gateway Drive, Suite 110

Columbia, MD 21046

* or call **toll free**:        877-992-4724
* or by **email**:              adviser@chesapeakeirb.com

Please reference the following number when contacting the Study Subject Adviser: Pro00021800.

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. 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 to your satisfaction. Based on this information, you voluntarily agree to participate in the study. 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.

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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.

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Printed Name of Person Signature Date Time

Obtaining Consent

**Injection Diagram**

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