CLINICAL EVALUATION OF THE SAFETY AND EFFICACY OF USING MULTI-POLAR RF AND PEMF TECHNOLOGIES FOR THE TREATMENT OF THE MONS PUBIS, VAGINAL INTROITUS AND LABIA SKIN LAXITY

Clinical Study Protocol

Protocol Number:	CS2815
Approved: Amended: Amended:	February 25, 2016 July 27, 2016 November 25, 2016
Principal Investigator:	Dr. Allan Yang Wu, MD
Investigator Contact Details:	email: allanwumd@gmail.com Tel: (760) 605-1926 Fax: 1-800-453-2549
Study Location:	**Revive Wellness Center** 22330 Hawthorne Blvd., Suite J Torrance, CA 90505 (760) 605-1926
Study Sponsor:	Venus Concept 255 Consumers Road, Toronto, Canada
Sponsor Contact Details:	Joseph Reiz email: jreiz@venusconcept.com Tel: 888-907-0115, ext. 563 Fax: 855-907-0115

Study Synopsis

Study Title	Clinical evaluation of the safety and Efficacy of using Multi-Polar RF and PEMF technologies for the treatment of the Mons Pubis, Vaginal Introitus and Labia Skin Laxity	
Protocol No:	CS2815	
Device Name:	Modified Venus Versa $(MP)^2$ device with Freeze Diamondpolar and Investigational Applicators	
Design	Feasibility, single-center, baseline-controlled, prospective study	
Projected Study period	Initiation Date: **February 2016**	Completion Date: **February 2017**
Objectives	Primary objectives • To evaluate the safety of treating the mons pubis, labia and vaginal introitus with the Freeze Diamond Polar applicator. • To evaluate the safety of the internal treatment of the vagina with an investigational applicator • To verify the efficacy of using the Freeze Diamond Polar applicator for improving general skin appearance of the mons pubis, vaginal introitus and the labia including improvement of skin irregularities and skin laxity. • To determine and/or quantify any potential regenerative properties associated with the study treatments. Secondary objectives • To evaluate subject's assessment of comfort and pain associated with treatments. • To evaluate subject's satisfaction with treatment results and assessment of improvement. • To determine if any regenerative properties are associated with the Mons pubis, Vaginal Introitus and the Labia.	
Hypothesis	• The study will confirm that the Freeze Diamondpolar applicator is safe for treating the mons pubis, labia and vaginal introitus which will result in improvement in general skin appearance including an improvement in skin irregularities and skin laxity. • The study will confirm that the investigational applicator is safe for internal treatment of the vagina.	
Study population	1 site with 10 subjects	
Main Inclusion Criteria	• Healthy female between the ages of 25 and 65. • Sexual activity (vaginal intercourse once per month) in a monogamous relationship. • Requesting aesthetic benefit to the vaginal mons, introitus and labia.	

Main Skin Related Exclusion Criteria	• Pregnant or intending to become pregnant during the course of study. A urine pregnancy test will be given to women of childbearing potential and performed during initial visit. • Having any active electrical implant anywhere in the body, such as a pacemaker or an internal defibrillator. • Having a permanent implant in the treated area.
Investigational Treatment and Study Duration	• Each subject will receive three treatments at four week intervals and return for follow-up visit at one (± seven days) month after the last treatment for evaluation of the treated areas.
Criteria for Evaluation	Primary endpoints • Number and type of any adverse events throughout the study will be recorded. • General skin appearance improvement at FU3 compared to baseline as assessed by independent evaluators by photographic assessment, utilizing the GAI Scale. Secondary endpoints • Subject's assessment of pain associated with treatments using a VAS scale, following each of the 3 treatments. • Investigator assessment of immediate and short term response following each treatment, defined as type and intensity of response and the time it takes for it to subside. • Subject's satisfaction with the results and assessment of improvement in skin appearance using a GAI scale. • Subject's vaginal pH with results from pH paper sampling of the vaginal mucosa. • Subject's histologic and molecular pathology changes with standard molecular histopathology methods.

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1.0 Introduction

1.1 Rationale for Evaluation

The combination of Multi-Polar RF and PEMF technology has been shown in clinical studies to improve skin laxity, and to treat various skin conditions related to aging and alternate collagen structures such as wrinkles, rhytids, etc.

The objective of this clinical study is to evaluate the modified Venus Versa $(MP)^2$ system™ clinical performance in improving the mons pubis and labia general skin appearance including skin laxity and loss of vaginal introitus coaptation (normal closure of vaginal opening) and various skin irregularities using the Freeze Diamondpolar applicator. The safety of an investigational applicator for treatment of the vagina will also be investigated.

The use of the modified Venus Versa has been determined to present non-significant risk in accordance with 21 CFR 812.3 for the intended use in this study, **because the device is not:**

- Intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;
- Is purported or represented to be for use supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;
- Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or
- Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

Furthermore, RF technology has been used previously for the external and internal female genitalia without incident or complications, see for example Millheiser LS et al., 2010 ; Sekiguchi Y. et al. , 2013; and Dover RR., 2002. (Use of Multi-Polar RF and PEMF technology was already demonstrated to be safe and efficient in delivering heat to the tissue (Nils Krueger et al., 2012; Dover J. et al. , 2014). The study device therefore poses no clinically significant risk to the subjects or operator(s) of the device.

This study will be conducted in compliance with the protocol and according to Good Clinical Practice (GCP) standards.

2 Study Design

This is a single center, baseline-controlled, prospective study. Ten (10) and up to three hundred (300) subjects that meet the inclusion criteria will be enrolled from the site's pool of patients. Subjects should be female, at the age of 25-65 years, and have a suitable treatment area (e.g. skin irregularities and/or unwanted skin laxity in the mons pubis, introitus and/or labia area).

Subjects will receive three treatments with the study device and both applicators, at four week intervals, followed by one month follow-up visits after the last treatment.

3 Study Objectives

3.1 Primary Objectives

- To evaluate the safety of treating the mons pubis, labia and vaginal introitus with the Freeze Diamondpolar applicator.
- To evaluate the safety of the internal treatment of the vagina with the investigational applicator.
- To verify the efficacy of using the Freeze Diamondpolar applicator for improving general skin appearance of the Mons pubis and Labia including improvement of skin irregularities and skin laxity of the female genitalia and introitus.
- To determine and/or quantify any potential regenerative properties associated with the study treatments.

3.2 Secondary Objectives

- Subject's assessment of discomfort/pain associated with treatments using a VAS scale, following each of the 3 treatments.
- Subject's satisfaction with the results and assessment of improvement in skin appearance using a GAI scale.
- Subject's vaginal pH with results from pH paper sampling of the vaginal mucosa.
- Subject's histologic and molecular pathology changes with standard molecular histopathology methods.

4 Outcome Measures

4.1 Primary Effectiveness Endpoints

- General skin appearance improvement at FU3 compared to baseline as assessed by independent evaluators by photographic assessment, utilizing the GAI Scale.

4.2 Secondary Endpoints

- Subject's assessment of discomfort/pain associated with treatments using a VAS scale, following each of the 3 treatments.
- Subject's satisfaction with the results and assessment of improvement in skin appearance using a GAI scale.
- Subject's vaginal pH with results from pH paper sampling of the vaginal mucosa.
- Subject's histologic and molecular pathology changes with standard molecular histopathology methods.

4.3 Safety Endpoint

- Immediate and short term response as assessed by the investigator following treatment, defined as type and intensity of response and the time it takes for it to subside.
- Any adverse events associated with various setting(s) used during the treatment and follow-up period.

5 Patient Population

5.1 Source and Sample Size

Subjects shall be recruited by the investigator from within the investigator's patient population. Subjects shall

be with skin type I-VI and have unwanted skin laxity in the mons pubis and/or labia area. Each subject (no less than 10 subjects and no more than 300 subjects) included for treatment will receive three treatments at four week intervals and return for follow-up visit at one month (± seven days) after the last treatment for evaluation of the treated areas. Enrolled subjects that did not complete the full course of the study will not be replaced.

5.2 Eligibility

Each subject will be evaluated by the Investigator to assess her suitability for entry into this study according to the following criteria:

5.2.1 Inclusion Criteria

Subjects must meet all of the following inclusion criteria to be entered into the study:

1. Healthy female between the ages of 25 and 65.
2. Able to read, understand and voluntarily provide written Informed Consent.
3. Able and willing to comply with the treatment/follow-up schedule and requirements.
4. Fitzpatrick skin type I-VI.
5. Sexual activity (vaginal intercourse once per month) in a monogamous relationship.
6. Women of child-bearing age are required to be using a reliable method of birth control at least 3 months prior to study enrollment and have a negative Urine Pregnancy test at baseline.
7. Women requesting aesthetic benefit to the vaginal mons, introitus and labia.

5.2.2 Exclusion Criteria

Any of the following will exclude the subject from the study:

1. Pregnant or intending to become pregnant during the course of study. A urine pregnancy test will be given to women of childbearing potential and performed during initial visit.
2. Having any active electrical implant anywhere in the body, such as a pacemaker or an internal defibrillator.
3. Having a permanent implant in the treated area.
4. Prior use of retinoids in treated area within 2 weeks of initial treatment or during the course of the study.
5. Use of oral Isotretinoin (Accutane®) within 6 months of initial treatment or during the course of the study.
6. Patient on systemic corticosteroid therapy 6 months prior to and throughout the course of the study.
7. Prior skin treatment with laser in treated area within 6 months of initial treatment or during the course of the study.
8. Prior use of collagen, fat injections and /or other methods of skin augmentation (enhancement with injected or implanted material) in treated area within 4-6 weeks of initial treatment or during the course of the study. Treatment may not be performed at all over permanent dermal implants.
9. Prior ablative resurfacing procedure in treated area with laser or other devices within 12 months of initial treatment or during the course of the study.
10. Any other surgery in treated area within 12 months of initial treatment or during the course of the study.
11. History of keloid formation or poor wound healing in a previously injured skin area.
12. History of epidermal or dermal disorders (particularly if involving collagen or microvascularity).
13. Open laceration or abrasion of any sort on the area to be treated.
14. Active STD (e.g. genital Herpes Simplex, condylomata) or vaginosis; any tissue biopsy will be deferred or

delayed to a later time point until the infection is resolved.

15. Chronic vulvar pain or vulvar dystrophy.
16. History of immunosuppression/immune deficiency disorders (including HIV infection or AIDS) or use of immunosuppressive medications.
17. Having any form of active cancer at the time of enrollment and during the course of the study.
18. Significant concurrent illness, such as uncontrolled diabetes i.e. any disease state that in the opinion of the Investigator would interfere with the treatment, or healing process.
19. Participation in a study of another device or drug within 1 month prior to study enrollment or during this study, and as per the Investigator's careful discretion, as long as not contradictory to any of the above criteria.
20. Tattoos in the treatment area.
21. Mentally incompetent, prisoner or evidence of active substance or alcohol abuse.
22. Having any stage 3-4 cystocele, rectocele, enterocele paravaginal defect or major pelvic organ prolapse beyond the hymenal ring.

6 Materials

6.1 Device Description

The modified Venus Versa $(MP)^2$ by Venus Concept Ltd. is a non-invasive dermatological treatment system based on patented and proprietary $(MP)^2$ technology combines Multi Polar Radiofrequency (RF) and Pulsed Magnetic Fields. The RF energy penetrates the skin and resulted in RF-generated tissue heating that has known effect on skin laxity[1], the magnetic field that is simultaneously induced increases fibroblast collagen production through non-thermal mechanism and contributes to the clinical effect of skin laxity improvement. The system is paired with the Freeze Diamondpolar applicator (with 4 electrodes) which will be used to treat the mons pubis, vaginal introitus and labia. For the internal vaginal treatments, an investigational handpiece (applicator) will be used, however no change in range of energy modality or amount of energy delivered will occur at any point during the study.

6.2 Measurement Equipment

6.2.1 Standard High Resolution Digital Camera

The investigative site will ensure the digital photography equipment including photo storage media and adequate lighting equipment is available for use during this study. Photographs of the treated areas will be taken at various visits as detailed in the schedule of events chart.

For consistency purposes, all images throughout the study must be taken, using the same camera and lighting settings, preferably by the same photographer, the photography should be taken from the same angle.

Subject anonymity will also be assured for the images by deleting any ID detail. Only the code for the Case Number in the study will appear on the records being transferred to the sponsor.

[1] Noninvasive Radio Frequency for Skin Tightening and Body Contouring. Weiss, 2013

6.2.2 pH Paper

The investigative site will ensure pH paper is available for use during this study. pH measurements will be taken at various visits as detailed in the schedule of events chart. For consistency purposes, all pH measurements throughout the study shall be taken from the mid posterior wall of the vaginal mucosa.

6.2.3 Histopathology and Molecular Studies

The investigative site will ensure Tischler biopsy forceps or the equivalent of a small punch biospsy (2-3mm) for skin/mucosal biopsy is available for use during this study. Histopathology and molecular study specimens will be taken at various visits as detailed in the schedule of events chart (Appendix A). For consistency purposes, all histopathology and molecular study specimens taken throughout the study shall be taken from any of the anatomic sites treated.

Subject anonymity will also be assured for histopathology slides and molecular assay results by deleting any associated ID detail. Only the code for the Case Number in the study will appear on the records being transferred to the sponsor.

7 Study Procedures

7.1 Study duration and timelines

Each subject will be enrolled and scheduled for three treatments at approximately four week intervals and return for a follow-up visit at one month (± seven days) after the last treatment for evaluation of the treated areas. During each visit various tasks will be performed as detailed in the study flow chart (Appendix A).

Each subject will therefore participate in the study for a period of at least 3 months. The study is anticipated to be completed within six months.

7.2 Evaluation Assessments

Various assessments will be performed throughout this clinical study. The grading of the photographs of the treated area will be performed by independent evaluators. See Table 1.

7.2.1 Post Treatment Responses

Immediate and short term responses (erythema, edema, purpura, etc.) will be assessed by the investigator immediately and up to 30 min post treatment, by a 5 level scale: 1=none; 2=trace; 3=moderate; 4=marked; 5=severe.

In addition, subject reporting on duration of post-treatment adverse events questionnaire will be collected after each treatment and at the follow-up visit.

7.2.2 Skin improvement assessment

The assessment of general improvement in skin appearance will be accomplished by an independent evaluation of photographs.

At baseline and in FU3, a photograph of each of the treated areas will be taken per the photography guidelines. A copy of the images will be sent to independent reviewers. The reviewers will evaluate, for each time point, the improvement in skin appearance in comparison to base line based on the GAI scale (See Appendix B). The results of the evaluation will be recorded in the Photographs assessment log (see appendix

C).

7.2.3 Histopathology and Molecular Assay documentation

The documentation of histopathologic and molecular assays will be accomplished by use of standard laboratory and pathology methods and commercially available assay kits suitable and designated for research. The results of the documentation (i.e. slide serial and catalogue numbers and assay results) shall be recorded in the Histopathology and Molecular Assay log (see appendix D).

7.2.4 Subject Subjective Assessments

7.2.4.1 Level of discomfort/pain

Treatment associated level of discomfort/pain experienced by the subjects will be measured on a 10cm Visual Analogue Scale (VAS) were 0 cm is 'no pain' and 10 cm is 'intolerable pain'. The subjects will be given a VAS and be asked to mark their perception of discomfort/pain immediately following each treatment (see appendix E)

7.2.4.2 Level of improvement and satisfaction

Subject's Improvement and Satisfaction with treatment will be recorded by using the GAI scale at the last follow up visit (see Appendix B).

Table 1 - Clinical Evaluation Tools

Claim/task	When to conduct?	Tool
Photography	Baseline, immediately before treatments 2, 3, FU 3	Standardized digital photographs
Vaginal pH	Baseline, immediately before treatments 2, 3, FU 3	Standard pH paper
Histopathology & Molecular Studies	Baseline, immediately before treatments 2, 3, FU 3	Histology slides, special staining and assays.
Immediate and short term response evaluation by investigator	Immediately following treatments 1-3	Examination of skin in the treated area based on 5 level scale (Appendix F)
Subject's duration of post-treatment adverse events questionnaire	Before treatments 2, 3, FU 3	Subject Questionnaire on post treatment response (Appendix G)
Subjects discomfort/pain assessment	Immediately following treatments 1-3	VAS (Appendix E)
Subjects improvement/ satisfaction assessment score	FU3.	GAI (see Appendix B)
Independent reviewers score	At the end of the study	GAI (see Appendix B)

7.3 Screening Procedures

7.3.1 Subject Enrollment

If the subject has met the preliminary study criteria the study doctor, and/or his designee, will obtain an informed consent from the subject, clearly indicating her understanding of the requirements and possible risks involved with study participation and other applicable treatment options.

During the first visit, the study investigator, and/or his designee, will screen the subject for eligibility to participate in the clinical study using the Inclusion, Exclusion criteria. During screening the study doctor will review the subject's medical history, and examine the subject's targeted area to ensure that it meets the study criteria. The subject will complete screening and the treatment will be scheduled. Treatment may be performed on the day the subject was enrolled or no later than one week following enrollment and screening.

During the first visit, the investigator will ask women of child-bearing potential for the date of their last period, if not applicable the investigator shall inquire about the form of contraceptive they use to confirm they meet the inclusion criteria.

7.3.2 Subject Identification

At enrollment, each subject will receive a unique identifying number that will be composed of a consecutive number and her initials. This unique identifier will be used throughout the entire study and will be entered in the subject's CRF for each treatment and photographs.

7.4 Pre-Treatment Procedures

7.4.1 Subject Skin care and medication

- Before attending the first treatment, the subject will shave the treatment area at home, using foam or gel to minimize skin irritation.
- Apply medical Grade Glycerin on the treated area

7.4.2 Photography

7.4.2.1 Photography

Photographs will be taken prior to treatment and throughout the study according to specified time points detailed in Table 1, utilizing standard scientific equipment.

The photos should be taken in a private room or area of the clinic under controlled conditions, including the distance, angle, background and lighting in order to achieve high-quality before & after sets. Do not use direct illumination. The subject should be placed in the same position each time. As each photograph is taken, it should be viewed to ensure that it is in focus and is similar to its baseline counterpart in all technical aspects, including lighting, distance and angle.

For consistency purposes, the same person should ideally take all study photographs, especially per subject. The digital files should follow a consistent standard naming scheme, for example: 001TM_Tx1_Mons Pubis.

7.5 Treatment

All patients will receive treatment of the mons pubis, labia and vaginal introitus with the Freeze Diamondpolar

applicator. Patients will also receive an internal vaginal treatment with the investigational handpiece/applicator.

A dedicated Freeze Diamondpolar applicator will be used for each patient. Each applicator will be clearly labeled with the name of the patient. The patient will take the applicator or disposable head with her at the end of the first treatment session (Tx1) and will bring it back to the clinic for each of the additional treatment sessions (Tx2 and TX3). The applicator should not stay in the clinic possession during the study period. At the end of the study the applicators will return to Venus Concept.

The internal vaginal system consists of an the handheld applicator and disposable cover. The applicator contains 3 pairs of electrodes that deliver the Multi Polar Radiofrequency (RF) and Pulsed Magnetic Fields (PEMF) energy contained in a plastic housing with thermal sensors for detecting the tissue temperature. The disposable cover comes in 2 sizes to accommodate patient sizes.

Based on the mild nature of treatment, anesthesia is not required. Treatment procedure should include positioning of the patient in a manner that enables comfortable access to the treated anatomical site. The positioning of subjects during treatment will be contingent on the location of the treated anatomical site.
The following steps should be followed in each treatment session:

1. Set the treatment parameters (see Venus Versa (MP)^2 User Manual for the Diamondpolar applicator). Set the desired energy level between 10%-35% according to the skin type, severity of the treated condition, treatment area, etc. Set conservative parameters for the first treatment, and then gradually increase during treatment or in subsequent treatments according to desired impact, patient's comfort, AEs and results.
2. External treatment consists of a multiple passes over the treatment area with treatment parameters adjusted according to patient's comfort and temperature measurements by an external thermometer.
3. Move the applicator over the treated area, to maintain a temperature of 40^{o}C-42^{o}C when treating the labia area and 40^{o}C-45^{o}C when treating the mons pubis.
4. Maintain the temperature of the skin for 10 minutes on the labia tissue or 15 minutes on the mons pubis.
5. Apply ultrasound gel as a lubricant for the internal applicator.
6. Internal treatment consists of insertion of the investigational applicator into the vagina with treatment parameters adjusted according to the patient's comfort and temperature measurements by the applicator's thermometers.
7. Maintain a temperature of between 40^{o}C-45^{o}C for 10 minutes.
8. After both treatments are complete, the treated area will be examined by the investigator who will report immediate and short term response using 5 points scale (see Appendix F).
9. The assessment of discomfort/pain based on the subject's report should also be documented immediately after each treatment using the VAS.

The normal response to these treatments is transient erythema and edema. If any side effects occur, as indicated in the protocol, they will be recorded.

Applicator cleaning and disinfection:

At the end of the treatment session the cover for the investigational applicator should be disposed of (as per the site's standard operating procedures).

Both applicators should be thoroughly cleaned using a wet single use cloth with tap water and soap. After the

cleaning the applicators should be disinfected using high level disinfectant (Maxicide or Cavacide). The disinfection should be done by thoroughly rubbing the electrodes and plastic parts of the applicators with cloth immersed with the disinfectant.

At the end of the cleaning and disinfection procedure, inspect all applicator external parts if any sign of damage to the electrodes or plastic parts appears (i.e. damage to the electrodes cover) do not use this applicator and contact the Manufacturer. The Freeze Diamondpolar applicator is then packaged for the patient to take home.

7.6 Post-treatment Instructions

7.6.1 Post treatment care

1. Transient skin erythema and edema, as well as heat or tingling sensations, may last up to a few hours after the treatment, but typically no longer. In the event of post-treatment discomfort, it is recommended to cool the treated area immediately following treatment with air cooling. Cold packs (not frozen) may also be placed on the treated area.
2. During the day following treatment, care should be taken to prevent trauma to the treated site: avoid hot baths, massage, contact sports, swimming etc. The skin should be kept clean to avoid contamination or infection; any mechanical or thermal damage to the area must be avoided.

7.7 Follow-up regimen

Follow-up visits will be combined with treatments visits 2 and 3 and an additional follow up visit will occur one month (± seven days) after the last treatment as detailed in Appendix A.

8 Study Analysis Plan

8.1 Study Hypothesis

The study will confirm that the Freeze Diamond Polar applicator is safe for the treatment of the mons pubis, vaginal introitus and labia, and will result in improvement in skin laxity and skin irregularities.

The study will also confirm that the investigational applicator is safe for internal treatment of the vagina.

8.2 Sample Size Justification

The proposed study is a feasibility study for evaluating the safety and the efficacy of using the Freeze Diamond Polar applicator for treatment of the mons pubis, vaginal introitus and labia anatomical areas and the investigational applicator for treatment of the vagina. Based on previous experience with other RF devices, we believe that the proposed study sample of 10 subjects per each anatomical area (total of 10) will be sufficient to evaluate the safety and the efficacy of the treatment and to obtain qualitative assessments of comfort levels experienced during treatments.

8.3 Study Analysis

- An intermediate safety report based on qualitative analysis of immediate and short term reaction and on AEs will be produced based on analysis of data collected immediately post treatment number one of all the enrolled subjects. This data will be used to adjust further treatments parameter. The interim

reports will not affect the continuation of the study. The study will, regardless of the interim report results, be finalized according to this protocol.

- After FU3, the photographs will be sent to independent evaluators that will grade on a GAI scale the change in skin laxity according to photograph of FU3 compare to baseline. Descriptive statistics and correlations between variables will be performed on these results.
- After FU3 the subject assessment on the change in skin laxity on a GAI scale will be analyzed. These results will be correlated with the evaluation done by the independent evaluators in order to learn on the relationships between objective and subjective improvements assessments.
- After FU3 all data collected by response and discomfort/pain level (VAS) and the 5-level short term response scale results will be analyzed using descriptive statistics.
- After FU3, the vaginal pH values will be sent to the PI for formal data entry and analysis. These results will be correlated with the evaluation done by the independent evaluators in order to learn on the relationships between objective and subjective improvements assessments.
- After FU3, the histology slides and molecular assay results will be sent to the PI for formal data entry and analysis and archive storage (histology slides). These results will be correlated with the evaluation done by the independent evaluators in order to learn on the relationships between objective and subjective improvements assessments.

The study reports will provide information for use in research & development, and future planned studies. Descriptive statistics and correlations between variables will be performed.

Safety: Adverse events reported will be listed, documenting course, outcome, severity, and possible relationship to the treatment.

9 Adverse Events

9.1 Adverse Events Definitions

In this study, an Adverse Event (AE) is any undesirable clinical occurrence (sign, symptom, illness, or other medical event), that appears or worsens during the clinical study, or requires medical treatment or intervention to a subject, whether it is considered to be device-related or not. If an adverse event occurs, the first concern will be the safety and welfare of the patient. Appropriate medical intervention will be made.

Any AE or complication reported by the patient or observed by the physician that occurs during or after treatment with the device will be recorded in the medical record or source document and on the Case Report Form (CRF). The investigator will determine if the AEs are device-related or procedure-related. This assessment shall include the onset date, resolution date, severity, seriousness, frequency, treatment and outcome.

Each AE should be assessed according to the following criteria:

9.1.1 Severity

Each AE should be assessed for its severity, or the intensity of an event experienced by the subject.

Mild: Awareness of a sign or symptom that does not interfere with the subject's activity or is transient

resolved without treatment and has no sequelae.

Moderate: May interfere with the subject's usual activity and require additional intervention and/or treatment, and may have additional sequelae.

Severe: Significant discomfort to the subject and/or interferes with the subject's activity. Additional intervention and or treatment are necessary. Additional sequelae occur. Severe is used to describe the intensity of an event experienced by the subject.

9.1.2 Relationship of AE to the Device

Each AE should be assessed for its relationship to the device or procedure as identified as follows:

Device: This category should be restricted to adverse events directly attributable to the modified Venus Concept Versa

Procedure: A procedure is any activity that supports the usage of the device

Use the following categories for assigning the certainty of the relatedness:

Related – The AE is known to occur with the study agent, there is a reasonable possibility that the study agent caused the AE, or there is a temporal relationship between the study agent and event. Reasonable possibility means that there is evidence to suggest a causal relationship between the study agent and the AE.

Not Related – There is not a reasonable possibility that the administration of the study agent caused the event, there is no temporal relationship between the study agent and event onset, or an alternate etiology has been established.

9.1.3 Serious Adverse Events

NOTE: The term serious is not synonymous with severity, which may be used to describe the intensity of an event experienced by the subject). An AE that does not meet any of the below criteria will be classified as non- serious.

A serious AE is any event that:

- Results in, or contributes to a death;
- Is immediately life- threatening (injury or illness);
- Results in hospitalization, or prolongs an existing hospitalization;
- Results in permanent impairment of body structure or function, or in persistent or significant disability/incapacity;
- Results in an injury that requires medical intervention to prevent permanent impairment of body structure or function;
- Is a device malfunction or deterioration in the characteristics and/or performance of the device that results in death or serious deterioration in health;
- Is a device malfunction or deterioration in the characteristics and/or performance of the device that, if it were to occur again, could result in death or serious deterioration in health;
- Results in a congenital anomaly or birth defect.
- Is any medically significant injury, event or experience that requires medical/surgical intervention to

prevent one of the outcomes listed above;

- Results in end- organ toxicity, including hematological, renal, cardiovascular, hepatic, gastrointestinal, and central nervous system events;

9.1.4 Pre-existing Conditions

A pre-existing condition should not be reported as an adverse event unless there has been a substantial increase in severity or frequency of problems, which has not been attributed to natural history.

9.1.5 Diagnosis of Adverse Event

There should be an attempt to report a "diagnosis" rather than the individual signs, symptoms and abnormal laboratory values associated with the diagnosis. However, a diagnosis should be reported only if, in the Investigator's judgment, it is relatively certain (i.e., definite or possible). Otherwise individual signs, symptoms and abnormal laboratory values should be reported as the adverse events.

9.1.6 Anticipated Outcome Related Adverse Events

Anticipated adverse events in this study include pain, tenderness, purpura, persistent erythema, edema, burn, blistering, crusting, hyperpigmentation, hypopigmentation, scarring and potential for damage to hair follicles within the treatment area and subsequent loss of hair within the treatment area.
Any anticipated AE that occurs at any time during or after the use of the study device must be recorded by the Investigator. If the anticipated AE, in the opinion of the Investigator, is likely to affect the safety of the subjects or the conduct of the study, the ethic committee will be notified of the effect within 10 working days. In this study if an adverse event occurs the Investigator will continue following the subject until the case is resolved or up to 1 month following the last visit, whichever comes first.

9.1.7 Unanticipated Adverse Device Effects

In the event of a serious (or unanticipated) adverse event, the Investigator will immediately notify the study monitor by telephone. If such an adverse event is being reported after normal working hours, the Investigator will leave a voice message with accompanying report of the AE.

9.2 Reporting

9.2.1 Adverse Events (AE) and Severe Adverse Events (SAE) Reporting

All serious AEs, whether or not deemed expected or device-related, must be reported to the clinical monitor immediately or within 24 hours by telephone (see contact details below).

Name: Joseph Reiz, Director of Clinical Research
Phone: 888-907-0115 ext. 563
Email: *jreiz@venusconcept.com*
Address: 255 Consumers Road, #110, Toronto, Ontario, Canada, M2J 1R4

A written report prepared by the Principal Investigator must follow within seven working days to the clinical

monitor and should include a full description of the event and sequence.

9.2.2 Device Malfunctions

Each device failure will be assessed for its possible influence on the patient safety. The investigator should contact the manufacturer n case additional information is required in order to understand the possible implications of a device malfunction.

9.3 Risk/ Benefit Analysis

9.3.1 Risks

The potential risks for adverse effects of the treatment procedure include but are not limited to mainly to transient edema or erythema in the treated area the following events were also identified as low probability anticipated adverse effects: pain, tenderness, erythema lasting longer than 6 hours, mild to moderate edema lasting more than 6 hours, burn, blistering, crusting, hyperpigmentation, hypopigmentation, scarring, potential damage to hair follicles and loss of hair within the treatment zones and eye irritation. (See Appendix I for Additional Safety Background).

9.3.2 Anticipated Benefits

If the subject agrees to participate in this study, she will be contributing to the understanding of the device's impact and the biological processes that are occurring in the different skin layers. This understanding may lead to optimization of the treatment of these devices. In addition the subject may benefit from improvement in skin laxity in the treated areas.

10 Administrative Procedures

10.1 Investigator Selection

The investigator must be of good standing as an investigator, board certified in OBGYN (or appropriate specialty) and knowledgeable in relevant areas of clinical research to ensure adherence to the requirements of the protocol, including the protection of human subjects. Other site personnel must have appropriate research experience and infrastructure to ensure adherence to the protocol and enrollment of sufficient numbers of evaluable subjects. The curriculum vitae (CV) of the Investigator will be maintained in the study files as documentation of previous medical training. The Principal Investigator will sign the signature page of this protocol, agreeing to comply with all applicable regulations and the requirements of this study.

10.2 Ethics committee Approval

This study will be conducted in accordance with the International Conference on Harmonization (ICH) Harmonized Tripartite Guideline for Good Clinical Practice (GCP), 1996; the US Code of Federal Regulations (CFR) Title 21 parts 50, 56 and 812; applicable national laws and regulations and the ethical principles that have their origin in the Declaration of Helsinki.

10.3 Informed Consent

Prior to the procedure, the Investigator must explain to each subject the nature of the study, its purpose, expected duration, and the benefits and risks of study participation. After this explanation and before

entering the study, the subject must voluntarily sign and date the approved Informed Consent form.

10.4 Subject Withdrawal/Dropouts

The subjects will be advised in the written Informed Consent form that they have the right to withdraw from the study at any time without prejudice, and may be withdrawn at the Investigator's discretion at any time. In the event that a subject drops out of the study or is withdrawn from the study, the Exit/Termination CRF form should be completed. On the withdrawal page the Investigator should record the date of the withdrawal, the person who initiated withdrawal and the reason for withdrawal.

Reasonable effort should be made to contact any subject lost to follow-up during the course of the study in order to complete assessments and retrieve any outstanding data and study medication/supplies. The records of subjects who terminate prior to completing the study will be retained and the reason for termination will be documented.

The following are possible reasons for subject dropout/withdrawal:

- Adverse event that would prevent subject compliance with the protocol;
- Subject withdrawal of consent;
- Subject lost to follow-up (e.g., subject cannot be located or contacted and does not return for follow-up visits);
- Subject death;
- Investigator requested subject to be withdrawn.

However, every effort should be made to see that subject is followed for the remainder of the study even if subject is unable or unwilling to comply with the protocol.

10.5 Case Report Forms (CRFs)/Data Collection

The Investigator is responsible for completely and accurately recording study data in the appropriate sections of the CRFs.

Data recorded on the CRF and photographs will serve as a source document for the study data.

10.6 Subject's Financial Compensation

Subjects will not pay for any office visits, examinations and procedures as part of this clinical study.

10.7 Device Use/Accountability

The evaluation site personnel will maintain records of the model and serial number of the devices (if appropriate) used for treatment during the conduct of the study.

10.8 Training Requirements

Prior to any independent use of the modified Venus Versa $(MP)^2$ system™, study personnel, will receive proper training from the Venus Versa $(MP)^2$ Manufacturer clinical training team. Training requirements will be discussed during study initiation and will include site responsibilities, training of device use and study documentation.

10.9 Modification of Protocol

The protocol may be amended with the agreement of the sponsor and upon notification of and approval by the IRB or other relevant ethics committees.

Investigators should review the contents of this protocol. Subsequent alterations should only be made in written conjunction with the sponsor.

Medically significant amendments to the protocol (e.g., changes that increase the risk or the inconveniences for the patient, inclusion of new categories of patients, etc.) must be approved by the local IRB prior to implementation.

10.10 Data Retention/Archiving Data

The Investigator must keep the following documents in a secure place for at least two years after the last clearance of a marketing application or at least two years have elapsed since the formal discontinuation of clinical development of the investigational product.

- A signed copy of the final protocol and amendments.
- Copies of the subjects' evaluation forms, data clarification forms and any associated subject-related raw data or where applicable, authorized copies of raw data.
- Clinical photographs stored on CD-ROM or similar electronic media.
- Histopathology slides and molecular assay results.
- The subjects' signed Informed Consent forms.

10.11 Site Monitoring

The investigator has the responsibility for monitoring the study according to a monitoring plan.

10.12 Reporting Requirements

The investigator bears reporting responsibility per local regulations.

10.13 Confidentiality

This study is confidential. All reports, communications and public information relating to study subjects will identify the subject only by his/her trial ID code. The study personnel will complete subject identification on a confidential subject log, which will be used for purposes of subject tracking and follow-up. This will be treated in accordance with strict adherence to professional standards of confidentiality, and will be filed with adequate security and restricted accessibility.

11 Abbreviations and Terms

AE	Adverse Event
SAE	Serious Adverse Event
EC	Ethical Committee
IRB	Institutional Review Board
CRF	Case Report Form
VAS	Visual Analogue Scale

12 Appendixes

12.1 Appendix A - Study Flow Chart

Study Flow Chart

Study Activities	**Visit #1**	**Visit #2** 4 weeks after Visit #1	**Visit #3** 4 weeks after Visit #2	**Visit #4** 4 weeks after Visit #3
	Screening &Tx1	FU1 and Tx2	FU2 and Tx3	FU3
Qualify for study: Informed Consent, Eligibility assessment, Demographic information, Medical history & treatment related medical examination	X			
Photographs	X	X	X	X
PH measurement	X	X	X	X
Histology and Molecular Studies	X	X	X	X
Treatment	X	X	X	
Immediate and short term responses (assessment by investigator)	X	X	X	
Subject Pain assessment (VAS)	X	X	X	
Subject Duration of Post-Treatment Adverse Events Questionnaire	X	X	X	X
Subject Treatment Evaluation Questionnaire (v. 4)	X	X	X	X
Subject's improvement/satisfaction (GAIS)				X
Concomitant medication	X	X	X	X
Adverse events recording	X	X	X	X
Skin improvement assessment by independent evaluators using photographs				X

12.2 Appendix B - GAI Scale

Table 1 - Global Aesthetic Improvement (GAI) scale to be used for both investigator and subject evaluation:

(3)	Very Much Improved
(2)	Much Improved
(1)	Improved
(0)	No Change
(-1)	Worse
(-2)	Much Worse
(-3)	Very Much Worse

12.3 Appendix C - Photographs Assessment Log

Independent Evaluators' Form

Subject ID (initials)	Treated Area	Slide Set #	GAI score
	☐Mons Pubis ☐Labia	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	

12.4 Appendix D - Histopathology Molecular Assay Assessment log

Principal Investigator's Form

Subject ID (initials)	Treated Area	Slide Set #	Assay Result
	☐Mons Pubis ☐Labia ☐Introitus	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia ☐Introitus	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia ☐Introitus	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia ☐Introitus	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia ☐Introitus	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia ☐Introitus	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia ☐Introitus	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia ☐Introitus	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia ☐Introitus	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia ☐Introitus	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia ☐Introitus	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia ☐Introitus	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia ☐Introitus	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia ☐Introitus	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia ☐Introitus	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia ☐Introitus	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia ☐Introitus	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia ☐Introitus	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia ☐Introitus	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	
	☐Mons Pubis ☐Labia ☐Introitus	☐Baseline + ☐FU1/☐ FU2/ ☐FU3	

12.5 Appendix E - VAS (Visual Analog Scale)

Check one of the following boxes to indicate today's Treatment Visit:

Tx1 □ Tx2□ Tx3□

Immediate Pain Assessment for the Venus Freeze (MP)^2 Mons Pubis and Labia procedures:

Pain assessment of Mons Pubis
Please make a mark on the line below to indicate how much discomfort or pain you experienced when you were administered the treatment:

No Pain — Pain as bad as it can be

Pain assessment of Labia

Please make a mark on the line below to indicate how much discomfort or pain you experienced when you were administered the treatment:

No Pain — Pain as bad as it can be

Subject Initials/ID Number:_____

Date (mm/dd/yy):_____

Study Personnel Transcribing V.A.S. Assessment Scores to Final CRF:_____

12.6 Appendix F - Investigator Immediate and Short Term Response

Check one of the following boxes to indicate today's Treatment Visit:

Tx1 □ Tx2□ Tx3□

Circle one of the scores below that best presents the **IMMEDIATE** tissue response to the treatment

1=none
2=trace
3=moderate
4=marked
5=severe

Circle one of the scores below that best presents the **SHORT TERM** (~30mins post treatment) tissue response to the treatment

1=none
2=trace
3=moderate
4=marked
5=severe

12.7 Appendix G – Subject Duration of Post Treatment Adverse Events Questionnaire

Check one of the following boxes to indicate today's Treatment/Follow up Visit:
Tx2 □ Tx3□ FU3□.

Please check the box that correlates with the duration of possible post treatment side effects by checking the box that corresponds to the day your symptoms resolved:

	Day of the Treatment	1 day after	2 day after	3 day after	4 day after	7 day after
Redness						
Swelling						
Crusting						
Blistering						

12.6 Appendix H - Treatment Evaluation: Follow-Up Visit Client's Questionnaire (version 4)

Subject Initials:	Subject ID #:
Have you delivered vaginally?	Yes / No, if yes, how many_
Are you sexually active (vaginal intercourse)?	Yes / No, if yes, Av. frequency?
Question regarding the treatments:	**Answers:**
1. Was the treatment duration tolerable for you?	Yes / No | Too long / Too short
2. Which of the applicators was most comfortable for you?	External / Internal / Both / None/ None Applicable
3. How would you describe any sensations you experienced during the treatment? i.e., tingling, warm, hot, burning, itching, etc.	Open answer:
4. Did you feel intimidated by any of the devices used during the procedure (the treatment equipment / probes/ thermometer etc.)?	Open answer:
General questions:	**Answers:**
5. Did you feel uncomfortable during the procedure (type of treatment, intimacy etc.)? Were you ever alone with your gynecologist?	Yes / No / uncertain / Not applicable Please specify: Yes / No / uncertain
6. How frequently would you be willing to have Fiore treatments?	Open answer:
7. What feminine areas for rejuvenation and skin tightening (mons pubis/labia)?	Open answer:
8. Have you ever experienced similar treatment/s?	Yes / No / uncertain / Not applicable If yes, please specify:
9. Have you suffered from any of these listed conditions?	Please mark the relevant box/s: ☐ Pelvic prolapse ☐ Orgasmic disorders ☐ Labia sagging ☐ hyperplastic dystrophy Lichen sclerosus and vulvar vestibulitis ☐ Stress urinary incontinence ☐ Dyspareunia (painful sexual intercourse) Vaginal dryness (atrophic vulva Vaginitis) ☐
10. How long have you experienced any of the above condition/s?	Open answer:
11. Do you feel that the quality of your sex life is negatively affected by the conditions described above?	Open answer:
12. Would you consider receiving hormonal therapy to address the above conditions?	Yes / No / uncertain / Not applicable
13. Have you sought a solution, on your own initiative, to address any of the condition/s described above?	Yes / No / uncertain / Not applicable
14. Have you spoken with your friends about any of the above condition(s)?	Yes / No / uncertain / Not applicable
15. Have you considered in the past, or would consider, appropriate surgical solultions for the above medical conditions?	Yes / No / uncertain / Not applicable
16. In your opinion, what would be the best way to increase awareness for Fiore types of treatments (e.g. TV or radio commercials, Facebook/Internet, magazines ads, news articles, information at physician offices, etc.)	Open answer:
17. Would you recommend this treatment to your friends?	Yes / No / uncertain / Not applicable

SUBJECT GLOBAL RESPONSE ASSESSMENT SCALE

Vaginal Tightness

PLEASE CIRCLE THE SCORE THAT BEST DESCRIBES YOUR LEVEL OF VAGINAL TIGHTNESS.	
Score	
1	Very loose
2	Moderately loose
3	Slightly loose
4	Neither tight nor loose
5	Slightly tight
6	Moderately tight
7	Very tight

PLEASE CIRCLE THE SCORE THAT BEST DESCRIBES HOW YOU NOW FIND YOUR LEVEL OF VAGINAL TIGHTNESS COMPARED TO BEFORE TREATMENTS.	
Score	
1	Markedly Worse
2	Moderately Worse
3	Slightly Worse
4	No Change
5	Slightly Improved
6	Moderately Improved
7	Markedly Improved

Sexual Satisfaction

PLEASE CIRCLE THE SCORE THAT BEST DESCRIBES YOUR LEVEL OF SEXUAL SATISFACTION.	
Score	
1	None
2	Poor
3	Fair
4	Good
5	Very good
6	Excellent

PLEASE CIRCLE THE SCORE THAT BEST DESCRIBES HOW YOU NOW FIND YOUR LEVEL OF SEXUAL SATISFACTION COMPARED TO BEFORE TREATMENTS.	
Score	
1	Markedly Worse
2	Moderately Worse
3	Slightly Worse
4	No Change
5	Slightly Improved
6	Moderately Improved
7	Markedly Improved

Vaginal Dryness

PLEASE CIRCLE THE SCORE THAT BEST DESCRIBES YOUR LEVEL OF VAGINAL DRYNESS.	
Score	
1	Markedly dry
2	Moderately dry
3	Slightly dry
4	No Change
5	Slightly moist
6	Moderately moist
7	Markedly moist

PLEASE CIRCLE THE SCORE THAT BEST DESCRIBES HOW YOU NOW FIND YOUR LEVEL OF VAGINAL DRYNESS COMPARED TO BEFORE TREATMENTS.	
Score	
1	Markedly Worse
2	Moderately Worse
3	Slightly Worse
4	No Change
5	Slightly Improved
6	Moderately Improved
7	Markedly Improved

_____ _____

Patient Initials Date (dd/MM/YYYY)

12.7 Appendix I – Additional Safety Background Data

Non-ablative or non-burning RF therapy has been used for vaginal tightening previously within human vaginal mucosa at 75-90 J/m2. (J Sex Med 2010 Sep; 7(9): 3088). For the purpose of this study premenopausal patients will be treated at 90J/m2, whereas the post menopausal patients will be treated with less cumulative heat. We have calculated that the thickness of vagina epithelium (the most susceptible tissue to thermal injury) is decreased 16% in menopause. (This has been calculated by the percent change seen in human vaginal epithelium of menopausal versus non-menopausal on histomorphometry measurements -J. Sex Med 2009 Nov 6(11): 3097.) Reducing energy delivery by 16% yields a safe basement level of 75.6 J/m2 for menopausal patients. Again it is important to emphasize the proposed study device has thermal feedback safety settings and real-time multipolar thermal control to virtually eliminate the possibility of tissue burns. Additionally, now over 3 patients have been treated in Geneva Switzerland with Dr. Stevan Jovanovich, using the proposed study device (Venus Versa) both internally intravaginal and externally. No burns or off target damage was appreciated.

On advisement from the IRB committee and combined with the above information update; for further patient protection we will modify the protocol to perform initial safety parameters on the first 10 patients using 75J/m2 for premenopausal patients and 90J/m2 for premenopausal patients. If these safety parameters are consistent with the preliminary safety studies in Europe, the IRB will review these results, at which time we will submit an expanded study of up to 300 for review.

SAFETY SOP FOR POTENTIAL BURNS:

The following SOP shall be conformed to at all study facilities if a patient experienced any first, second or third degree burn or pain beyond narcotics:

1. The event will be reported to the study Director within 24 hours of occurrence.
2. A copy of the patient chart and treatment parameters are to be forwarded to the study Director within 24 hours.
3. Immediate triage and treatment of the patient shall be determined by the treating physician and based upon severity and type of burn identified.
4. The study Director will be responsible for issuing a written report to the company and the IRB Chairman no later than 7 days from the incident.
5. Long term follow up and care shall continue at the discretion of the treating physician.
6. All patients experiencing a complication of the device will be followed a minimum of 2 years following the initial injury. Longer care and observation will be at the discretion of the treating physician.
7. All minor complications such as appearance or altered sensation, except for pain, can be reported within 30 days of patient complaint. Both chart and treatment parameters are to be provided to the study Director and shared with the company and IRB chairman.

13 Bibliography

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