June 12, 2019

Viveve Inc.
Suzon Lommel
Sr. VP, Regulatory and Quality Affairs
345 Inverness Drive South, Building B, Suite 250
Englewood, Colorado 80109

Re: K190422
Trade/Device Name: Viveve 2.0 System
Regulation Number: 21 CFR 878.4400
Regulation Name: Electrosurgical Cutting and Coagulation Device and Accessories
Regulatory Class: Class II
Product Code: GEI
Dated: February 15, 2019
Received: February 21, 2019

Dear Suzon Lommel:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's

requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

for

Jennifer R. Stevenson
Acting Division Director
DHT4A: Division of General Surgery Devices
OHT4: Office of Surgical
and Infection Control Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K190422

Device Name
Viveve® 2.0 System

Indications for Use *(Describe)*
The Viveve® 2.0 System is indicated for use in general surgical procedures for electrocoagulation and hemostasis.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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SECTION 5

510(k) SUMMARY

5.1 REGULATORY AUTHORITY

Safe Medical Devices Act of 1990, 21 CFR 807.92

5.2 APPLICANT INFORMATION

Applicant: Viveve® Inc.
345 Inverness Drive South
Suite: B-250
Englewood, CO 80112

Contact: Suzon Lommel
Sr. VP, Regulatory and Quality Affairs
slommel@viveve.com
C: 408-645-4979
F: 720-696-8199

Date Prepared: February 15, 2019

5.3 SUBJECT DEVICE INFORMATION

Trade Name: Viveve® 2.0 System
Common Name: Electrosurgical System
Product Code: GEI
Classification Name: Electrosurgical Cutting and Coagulation Device and Accessories (21 CFR 878.4400)
Device Panel: General Surgery/Restorative Device
Device Classification: Class II

5.4 PREDICATE DEVICE

Viveve® System (K180584)

5.5 DEVICE DESCRIPTION

The Viveve 2.0 System utilizes monopolar radiofrequency (RF) energy to selectively heat a given volume of tissue beneath the surface, while cryogen is delivered to the inside of the treatment tip to cool the surface tissue. The generator delivers energy to the treatment tip to create an electric field under the treatment tip (electrode). The mechanism of action is the application of RF energy to the tissue causing coagulation and/or hemostasis.

The Viveve 2.0 System consists of four (4) primary components:

- An RF Generator to provide the heating energy. The Generator incorporates the Cooling Module to supply coolant which provides the cooling energy.
- A hand piece that couples the cooling and heating energy to the tissue through the treatment tip.
- A footswitch that allows the user to turn the RF Energy on or off.
- 5cm or 8cm Sterile Disposable Treatment Tips.

Accessories include:

- Coupling Fluid
- Cryogen
- Return Cable
- Return Pad
- Power Cord

5.6 INDICATIONS FOR USE

The Viveve 2.0 System is indicated for use in general surgical procedures for electrocoagulation and hemostasis.

5.7 COMPARISON OF TECHNOLOGICAL CHARACTERISTICS WITH THE PREDICATE DEVICE

The technological characteristics of the subject device Viveve 2.0 System are substantially equivalent to the predicate device, Viveve System (K180584). The Viveve 2.0 System is an electrosurgical device that delivers radiofrequency (RF) energy to selectively heat a given area of tissue, while cryogen is delivered to the inside of the treatment tip to cool the surface tissue at the end of energy deposition. The application of RF energy causes the tissue to coagulate and/or become hemostatic.

This submission application confirms the continued conformance to applicable technical design specifications and performance requirements, including requirements associated with industry safety and performance standards.

5.8 BASIS FOR DETERMINATION OF SUBSTANTIAL EQUIVALENCE

The Viveve 2.0 System is substantially equivalent to the predicate device listed in K180584. The principle of operation between the predicate device and the subject device remain the same as do all output parameters to tissue, however the subject device includes the following design and technological/environmental specification modifications:

5.8.1 DESIGN MODIFICATIONS

5.8.1.1 RF Console (Generator)

- Overall footprint of the RF Console and corresponding case (weight, shape and size) is changed to allow for the upgrade to a touchscreen display panel
- RF Console Display screen is updated from standard display to touchscreen display
- RF Console Display incorporates an optical power switch
- RF Console Display has modified user interface screens and display graphics for ease of use
- RF Console connector panel is now located in the back to minimize inadvertent damage over the use life

5.8.1.2 Footswitch

- Cover is added to the unit
- Stylistic changes are incorporated in the overall design

5.8.1.3 Handpiece

- Color is changed from purple to white for brand alignment
- Connector is changed from female to male to prevent connection to Predicate system

5.8.1.4 Cryogen

- R134a (1,1,1,2 tetrafluoroethane) or 1234ze (trans-1, 3, 3, 3-Tetrafluoroprop-1-ene) cryogen can be used in the Viveve 2.0 System. 1234ze has been developed as a more environmentally friendly option.

5.8.2 SOFTWARE MODIFICATIONS

5.8.2.1 Viveve RF Console Software

- Updated to most recent version for incorporation of changes impacting the RF Console

5.8.2.2 Viveve RF Display Module Software

- Updated to most recent version for incorporation of changes impacting the RF Display Module

5.8.2.3 Viveve RF Handpiece Software

- Updated to most recent version for incorporation of changes impacting the RF Handpiece

5.8.3 HARDWARE MODIFICATIONS

5.8.3.1 Operating System

- Viveve 2.0 System operates on a PAL platform instead of PC/104 to allow for most up-to-date technology. The PAL is a Platform Abstraction Layer that is used in a variety of projects. The PAL allows for easy compatibility between many different flavors of UNIX/Linux, including AIX 6.1 and later, HP/UX 11.31 and later, Solaris 5.10 and later, and most versions of Linux as far back as RedHat 5.0, SuSE 10.1, and Debian 5.0.

5.8.4 LABELING MODIFICATIONS

5.8.4.1 Technical User Manual

- Updates include but are not limited to modified user interface graphics and nomenclature relative to the Viveve 2.0 System

5.8.4.2 Instructions for Use

- Updates include but are not limited to nomenclature relative to the Viveve 2.0 System There have been no changes related to clinical use other than the differences in the GUI

5.8.5 TECHNICAL/ENVIRONMENTAL SPECIFICATION MODIFICATIONS

5.8.5.1 Environmental and Packaging Specifications

- IEC60601, Electrostatic Discharge (ESD) and Voltage Dip are aligned with CMO's Quality Management System (QMS) Requirements

5.8.5.2 RF Frequency

- Is modified to 6.78 MHz to allow for the appropriate function due to updated internal components (many predicate components are at end of life per the manufacturers) of the updated system with the same output to tissue

5.8.5.3 Operation temperature

The operational temperature in 2.0 System is decreased to allow for increased product longevity while maintaining the same heat profile to tissue in the clinical environment.

5.8.5.4 Storage pressure

- Range is now aligned with that outlined in packaging and environmental testing

5.8.6 CONTRACT MANUFACTURER MODIFICATIONS (CMO)

- Sparton Medical Systems is added for closer proximity to Viveve headquarters to allow for increased engineering involvement

- Cirtec Medical is now added for increased treatment tip sourcing options and the only manufacturer of the Viveve 2.0 Treatment Tip

All previously outlined modifications to the Viveve 2.0 System are discussed in further detailed in **Section 12: Substantial Equivalence Discussion** of this Premarket Notification. A comparison of the technical characteristics of Viveve 2.0 System are compared to those of the predicate device, Viveve System, in **Table 5-1** below.

Table 5-1: Comparison of Technological Characteristics of Viveve 2.0 System and Viveve System (K180584)

Item	Viveve 2.0 System (Subject Device)	Viveve System (Predicate Device K180584)
510(k) Number	Subject device	K180584
Legal Manufacturer	Viveve, Inc.	Viveve, Inc.
Contract Manufacturer	• Sparton Medical Systems (Generator and Handpiece) • Cirtec Medical (Treatment Tips)	• Stellartech Research Corporation (All 3 system components)
Indication for Use	The Viveve 2.0 System is indicated for use in general	The Viveve System is indicated for use in general surgical

Item	Viveve 2.0 System (Subject Device)	Viveve System (Predicate Device K180584)
	surgical procedures for electrocoagulation and hemostasis.	procedures for electrocoagulation and hemostasis.
FDA Classification	Class II	Class II
CFR/Product Code	21 CFR 878.4400/GEI	21 CFR 878.4400/GEI
Invasiveness of Treatment	Non-invasive. Device applies to the surface.	Non-invasive. Device applies to the surface.
Principles of Operation	Radiofrequency (RF) energy selectively heats a given volume of tissue beneath the surface, while cryogen is delivered to the inside of the Treatment Tip to cool the surface tissue. The Treatment Tip is placed on the surface of the skin and the internal tissues are heated while the surface tissue is protected. (Reverse thermal gradient)	Radiofrequency (RF) energy selectively heats a given volume of tissue beneath the surface, while cryogen is delivered to the inside of the Treatment Tip to cool the surface tissue. The Treatment Tip is placed on the surface of the skin and the internal tissues are heated while the surface tissue is protected. (Reverse thermal gradient)
Energy	RF	RF
Treatment Type	Monopolar	Monopolar
Main Input (Input voltage/Current/Frequency)	100 - 120 Vac / 10A / 50/60 Hz 220 - 240 Vac / 5A / 50/60 Hz	100 - 120 Vac / 10A / 50/60 Hz 220 - 240 Vac / 5A / 50/60 Hz
Maximum Power (generator)	240 Watts	240 Watts
Operating Frequency	6.78 MHz ±15%.	6 MHz ±2%.
Voltage Waveform	6.78 MHz continuous sinusoidal waveforms	6.0 MHz continuous sinusoidal waveforms
Electrode Probe	Monopolar	Monopolar
Impedance Range	25 – 120 Ω	25 – 120 Ω
Tip	5cm and 8cm Treatment Tips	5cm and 8cm Treatment Tips
Packaging	Tyvek pouch	Tyvek pouch
Sterility	ETO	ETO
Cooling Solution	Cryogen	Cryogen

5.9 PERFORMANCE DATA

Design verification testing, including bench performance, electrical safety/electromagnetic compatibility, software verification/validation, packaging and shelf-life studies, provided in

the subject premarket notification demonstrate that the Viveve 2.0 System is substantially equivalent to the predicate device, Viveve System.

5.9.1 Performance Data

Design development and control is conducted in phases as described in the Sparton Medical Design Control Procedure 120924. Coordination of project activities is assigned to a Project Leader. A Design Development team is formed and includes members from appropriate groups in the organization. Team members are assigned responsibilities as appropriate for completion of the project. The design of the product is verified and validated to ensure design inputs are met. Copies of the Design Verification and Validation Test Reports are maintained in the Design History File and further detailed in Section 18.

The following are the documents to support the Design Verification and Validation testing of the Viveve 2.0 System.

Document Title	Document Number
Design Control Procedure	Sparton 120924
Animal Study Reports	Study Group C: 15 Dec 2010 Study Group D: 16 Dec 2010 Study Group E: 18 Jan 2011 Study Group F: 20 Jan 2011 Study Group G: 26 Jan 2011 Study Group H: 26 Apr 2011 Study Group I: 21 Apr 2011

5.9.1 Pre-Clinical Performance Data

Viveve conducted the following Animal Studies to prove safety and efficacy of the device:

- GLP Study IV0311g
- GLP Study VI-OV-SAF-04 (VIV-1702)
- Non-GLP Study VI-OV-SAF-05 (VIV-1801)

Study summaries are below:

GLP STUDY IV0311g

The objective of GLP study IV0311g was to evaluate the safety of and tissue response after the use of a radiofrequency (RF) device intended to treat vaginal laxity in humans. Using an in-vivo ovine vaginal model, this study demonstrated how the Viveve System preserves the surface vaginal mucosal viability while raising the temperature of the submucosal tissues to approximately 50°C. The various means of heating tissue include laser, ultrasound, electrosurgical tools, and conduction of radio frequency (RF) electrical current through the tissue. Of these methods, the conduction of RF electrical current

through tissue was the most benign and practical means of gently heating the tissue to a temperature low enough to disrupt the tissue, but not destroy/denature the collagen or elastin.

A summary of the GLP animal study IV0311g is listed below.

- Study Design: Blinded vaginal introitus study conducted at a single test facility.
- Objective: The Good Laboratory Practices ovine vaginal introitus study was performed to evaluate the Viveve Vaginal Laxity RF Treatment and Accessories in a fashion that emulated its future clinical use.
- Animal Number and Species: 25 non-nulliparous female ovine (*Ovisaries*)
- Purebred or black-faced Suffolk crossbreeds of various strains: This animal model was selected based on the similar anatomical structure as compared to the human.
- Test System: *In-vivo* Suffolk ovine vaginal introitus model.
- Control Treatment: Untreated (*Group A, n=3*) and surface cryogen delivery only (*Group B, n=3*) ovine.
    - Group A consisted of 3 untreated sheep that were anesthetized for a time period comparable to the treatment groups in this study. Group A sheep served as observational and biopsy controls. Biopsy samples were taken at post–treatment intervals of 7, 30, and 90 days.
    - Group B consisted of 3 sheep serving as a sham control that were treated with a minimum of RF energy (1-2 J/cm^2) and cryogen cooling. Biopsy samples were taken at post-treatment intervals of 7, 30, and 90 days.
- Active Treatment: Viveve Vaginal Laxity RF Treatment and Accessories. Delivering 60, 90, 120, or 160 J/cm^2 with surface cryogen cooling and 5 treatment passes. (*Groups C, F, & G, n=19*). Group C consisted of 4 different treatment levels of 16 total sheep, with each group receiving an escalated treatment dose of RF energy starting at the 1:00 o'clock position and finishing at the 11:00 o'clock position with 5 repetitive treatments. Biopsy samples were taken at post-treatment intervals of 7, 30 and 90 days.
    - 60 J/cm^2: 4 sheep
    - 90 J/cm^2: 4 sheep [These 4 sheep were transitioned over to Group F, see below.]
    - 120 J/cm^2: 5 sheep
    - 160 J/cm^2: 3 sheep

Group F consisted of the 4 sheep from Group C that were treated with 90 J/cm^2. Of these 4 sheep, 3 sheep were necropsied at 90 days and 1 sheep necropsied at 180 days. This was updated in Amendment 12.

Group G consisted of 3 acute sheep treated with 90 J/cm^2 while monitoring temperature at 3 depth levels below the vaginal mucosa. The placement of the thermistors to monitor temperature were at depths of 3, 6 and 9 mm from the surface of the vaginal mucosa and within the 2 cm area of the treatment probe when placed on the vaginal mucosa.

Non-overlapping vaginal introitus biopsies were obtained on Days 7, 30, and 90. These biopsies were formalin-fixed, routine processed, and hematoxylin and eosin (H&E) and

Gömöri trichrome stained. In total, 96 *in vivo* treated and 15 control vaginal introitus biopsies were evaluated between 7- and 90-days post-treatment. Using routine light microscopy, the slides were evaluated by two blinded board-certified pathologists. The vaginal tissues were histologically evaluated for signs of thermal tissue injury, fibroblast activation, and qualitative collagen increases.

The study's pathology-based criteria for success were defined as the presence of increased submucosal fibroblast activation over control levels with:

- No mucosal epithelial erosion and/or ulceration;
- No tissue necrosis regions;
- No granulation tissue foci; and/or
- No extensive or hypertrophic scar-like collagen increases.

The submucosa was assessed for the cytologic features of fibroblast activation. Fibroblasts were considered quiescent when they had condensed nuclear chromatin and scant cytoplasm. Fibroblasts were considered stimulated/activated when they had open chromatin and more abundant cytoplasm. Based on their prominence and cellular density, the stimulated fibroblasts were graded along the following spectrum:

- Minimal, if activated, fibroblasts were rare;
- Mild, if activated, fibroblasts were frequent, scattered and without clustering;
- Moderate, if activated, fibroblasts were frequent, focally clustered and with increased cellular density; or
- Extensive, if activated, fibroblasts were frequent with multifocal clustering and increased cellular density.

The submucosa was also qualitatively assessed for increases in collagen content. If the collagen appeared increased, it was graded along the following spectrum:

- Minimal, if collagen appeared to have a slightly increased fiber density, maintained a fibrillary architecture, and had a normal cellular density;
- Mild, if collagen fibers appeared slightly courser or compact without a decrease in regional cellularity;
- Moderate, if collagen fibers appeared moderately courser or compact with mild regional hypocellularity; or
- Extensive, if collagen fibers appeared densely compacted or hyalinized (hypertrophic scar-like) with regional hypocellularity.

To facilitate statistical comparison of the Viveve Treatment doses with the controls, the descriptive fibroblast activation and collagen categories for each biopsy were converted to an ordinal, approximately interval type, scaled score as follows:

- Score 0 = Not identified
- Score 0.3 = Minimal
- Score 0.5 = Minimal to Mild
- Score 1 = Mild or Minimal with focal mild
- Score 1.5 = Mild to Moderate

- Score 2 = Moderate or Mild with focal moderate
- Score 2.5 = Moderate to Extensive
- Score 3 = Extensive or Moderate with focal extensive

The individual biopsy results were used to calculate composite group means, standard deviations, medians, minimums and maximums for both the treated and control groups. Fibroblast activation and qualitative collagen scores were statistically compared using the non-parametric Wilcoxon rank sums method with significance of $p \leq 0.05$.

Results: In this study, the 90 J/cm^2 and 120 J/cm^2 Viveve Treatments significantly increased fibroblast activation over the baseline activation identified in the controls. This fibroblast activation was associated with an increase in submucosal collagen in Days 30 and 90 biopsies. In these biopsies, the mean collagen increase was approximately twice that of the controls. At Days 30 and 90, some controls showed focal minimal-mild qualitative collagen increases, consistent with background changes related to their prior vaginal manipulation and biopsies.

In support of the Viveve Vaginal Laxity RF Treatment mode of action and efficacy, the 90 J/cm^2 and 120 J/cm^2 treatments met the Criteria for Success with increased submucosal fibroblast activation and reasonable collagen increases. Mucosal erosion-ulceration, tissue necrosis, granulation tissue and excessive collagen increases (hypertrophic scar-like) were not identified in this study, consistent with an appropriate safety profile.

Summary: A series of ninety-six (96) treated and fifteen (15) control ovine vaginal introitus biopsies have been evaluated 7 to 90 days post-treatment. Over the 90-day study period, the 90 J/cm^2 and 120 J/cm^2 treatments met the pathology-based Criteria for Success with:

- Significantly increased submucosal fibroblast activation without mucosal erosion-ulceration, tissue necrosis;
- No granulation tissue or extensively increased (hypertrophic scar-like) collagen.

The 160 J/cm^2 energy level treatment showed similar changes that approached significantly increased fibroblast activation over time. The 60 J/cm^2 energy level treatment lacked sufficient fibroblast activation to meet the criteria.

GLP Study VI-OV-SAF-04 (VIV-1702)

The objective of this acute GLP study was to evaluate the temperature-time profile and histopathology of vaginal tissue following radiofrequency (RF) energy administration in the ovine model. Using an in-vivo ovine vaginal model, this study demonstrated how the Viveve System preserves the surface vaginal mucosal viability while raising the temperature of the submucosal tissues to approximately 50°C. The various means of heating tissue include laser, ultrasound, electrosurgical tools, and conduction of radio frequency (RF) electrical current through the tissue. Of these methods, the conduction of RF electrical current through tissue was the most benign and practical means of gently heating the tissue to a temperature low enough to disrupt the tissue, but not destroy/denature the collagen or elastin.

A summary of the GLP animal study VI-OV-SAF-04 is provided below.

- Study Design: Vaginal introitus study conducted at a single test facility.

- Animal Number and Species: Six parous female ovine (*Ovisaries*)
- Test System: *In-vivo* Suffolk ovine vaginal introitus model.
- Treatments: Two treatments were employed in this study.

The Clinical Treatment Protocol consisted of 4 sheep that were treated according to the standard clinical protocol (110 pulses, 5 passes around the vaginal introitus. Prior to treatment, fluoroptic temperature probes were placed at four positions in the in the introital region of the vaginal canal in the plane of energy flow (at the mucosal surface, two submucosal positions and one probe in the muscularis). Once the temperature probes were placed, baseline local tissue temperatures were taken for 3-5 minutes. While still under general anesthesia, each sheep was treated with the Viveve device at the introitus in a manner similar to the clinical setting and tissue temperatures measured over time during and after treatment (1-hour post-treatment or until temperature returned to baseline). Baseline temperature was defined as the tissue temperatures just prior to treatment. The core body temperature was also recorded prior to, during and post treatment, and changes were noted in the assessment of potential local tissue temperature baseline changes. Each sheep was euthanized, and necropsy performed.

Collection of vaginal wall segments (one section on the side of the vagina where the probes were located and one 180 degrees across the vagina in the treatment site) and peri-vaginal tissue (urethra, rectum, and bladder samples) were conducted. Tissues were preserved in 10% formalin and the vaginal/peri-vaginal tissues sent for histological analysis to assess any potential effects of treatment. Prior to treatment, fluoroptic temperature probes were placed at four positions in the in the introital region of the vaginal canal in the plane of energy flow (at the mucosal surface, two submucosal positions and one probe in the muscularis). Once the temperature probes were placed, baseline local tissue temperatures were taken for 3-5 minutes.

While still under general anesthesia, each sheep was treated with the Viveve device at the introitus in a manner similar to the clinical setting and tissue temperatures measured over time during and after treatment (1-hour post-treatment or until temperature returned to baseline). Baseline temperature was defined as the tissue temperatures just prior to treatment. The core body temperature was also recorded prior to, during and post treatment, and changes were noted in the assessment of potential local tissue temperature baseline changes. Each sheep was euthanized, and necropsy performed. Collection of vaginal walls (one section on the side of the vagina where the probes were located and one 180 degrees across the vagina in the treatment site) and peri-vaginal tissue (urethra, rectum, and bladder samples) were conducted. Tissues were preserved in 10% formalin and the vaginal/peri-vaginal tissues sent for histological analysis to assess any potential effects of treatment.

The Supra-Therapeutic Protocol consisted of 2 sheep that were treated with 110 pulses, but with 15 passes which is three times the clinical dose with no time lag between pulses. This treatment constituted a worst-case scenario in that more energy was delivered in a short duration due to no lag time between pulses which would be expected to cause the tissue temperature to rise to higher levels since the tissue would not have time to return to basal temperature before another pulse was delivered at the same location.

Results: Neither the Clinical Protocol nor the Supra-Therapeutic Protocol with the Viveve RF device resulted in temperatures that would be expected to cause cellular damage. This was confirmed by the histological evaluation. Maximum temperatures were well below temperatures that would pose safety concerns and were within the range that

could result in the desired cellular changes. Administration of radiofrequency from the Viveve system resulted in tissue temperature increases in deep tissue layers, with approximately 3-8 mm seeming to be the target area. Heating did appear in the muscularis, but there was not deposition of heat in this area and the heat dissipated rapidly. Variations in temperature-time profiles appeared to be a result of body-type/tissue characteristics that are unique to each ewe; but in all cases, there were no profile differences that would indicate a safety concern.

Conclusion: The objective of this acute GLP study was to evaluate the temperature-time profile and histopathology of vaginal tissue following radiofrequency (RF) energy administration in the ovine model. A total of 6 parous ewes were divided into 2 groups of 4 sheep in one and 2 sheep in the other; one group (N=4) receiving the Clinical Treatment protocol energy level and the other group (N=2) receiving the Supra-therapeutic energy administration protocol. Tissues were preserved in 10% formalin and the vaginal/perivaginal tissues sent for histological analysis to assess any potential effects of treatment. Tissue temperature data were reported in a sub-report which included graphical and tabular summaries for each location and treatment protocol.

Tissue temperature results demonstrated that during both the Clinical and Supra-therapeutic procedures, treatment with the Viveve RF device did not result in temperatures that would be expected to cause cellular damage. This was confirmed by the histological evaluation. Maximum temperatures were well below temperatures that would pose safety concerns and yet were within the range that could result in the desired cellular changes. Administration of radiofrequency from the Viveve system resulted in tissue temperature increases in deep tissue layers, with approximately 3-8 mm seeming to be the target area. Heating did appear in the muscularis, but there was not deposition of heat in this area and the heat dissipated rapidly. Variations in temperature-time profiles appeared to be a result of body-type/tissue characteristics that are unique to each ewe; but in all cases, there were no profile differences that would indicate a safety concern. Under the conditions of this study, there were no histopathologic findings associated with radiofrequency (RF) energy administration at either planned Clinical levels or Supra-therapeutic levels of RF treatment.

Non-GLP Study VI-OV-SAF-05 (VIV-1801)

The objective of this acute non-GLP study was to evaluate the temperature-time profile of vaginal tissue following radiofrequency (RF) energy administration in the ovine model to validate the Viveve 2.0 System. Using an in-vivo ovine vaginal model, this study demonstrated how the Viveve 2.0 System preserves the surface vaginal mucosal viability while raising the temperature of the submucosal tissues to≤50°C. This study also demonstrates substantial equivalency between the Viveve 2.0 System and the currently cleared Viveve System. The various means of heating tissue include laser, ultrasound, electrosurgical tools, and conduction of radio frequency (RF) electrical current through the tissue. Of these methods, the conduction of RF electrical current through tissue was the most benign and practical means of gently heating the tissue to a temperature low enough to disrupt the tissue, but not destroy/denature the collagen or elastin.

A summary of the non-GLP animal study VI-OV-SAF-05 is provided below.

- Study Design: Vaginal introitus study conducted at a single test facility.

- Animal Number and Species: Three parous female ovine (*Ovisaries*)
- Test System: *In-vivo* Suffolk ovine vaginal introitus model.
- Treatments: One treatment was employed in this study.

The Clinical Treatment Protocol consisted of 3 sheep that were treated according to the standard clinical protocol (110 pulses, 5 passes around the vaginal introitus). Prior to treatment, fluoroptic temperature probes were placed at four positions in the in the introital region of the vaginal canal in the plane of energy flow (at the mucosal surface, two submucosal positions and one probe in the muscularis), as per similar procedures used for Study VI-OV-SAF-04. Once the temperature probes were placed, baseline local tissue temperatures were taken for 3-5 minutes. While still under general anesthesia, each sheep was treated with the Viveve 2.0 System at the introitus in a manner similar to the clinical setting and tissue temperatures measured over time during and after treatment (30-min post-treatment or until temperature returned to baseline). Baseline temperature was defined as the tissue temperatures just prior to treatment. The core body temperature was also recorded prior to, during and post treatment, and changes were noted in the assessment of potential local tissue temperature baseline changes. Each sheep was euthanized post treatment.

Results: The Clinical Protocol with the Viveve 2.0 System resulted in temperatures that would not be expected to cause cellular damage and were substantially equivalent to the currently cleared Viveve System; temperature values were compared to the values measured in the VIV-OV-SAF-04 to determine substantial equivalency. Maximum temperatures were well below temperatures that would pose safety concerns and were within the range that could result in the desired cellular changes. Administration of radiofrequency from the Viveve 2.0 System resulted in tissue temperature increases in deep tissue layers, with approximately 3-8 mm seeming to be the target area. Heating did appear in the muscularis, but there was not deposition of heat in this area and the heat dissipated rapidly. Variations in temperature-time profiles appeared to be a result of body-type/tissue characteristics that are unique to each ewe; but in all cases, there were no profile differences that would indicate a safety concern.

Conclusion: The objective of this acute non-GLP study was to evaluate the temperature-time profile and demonstrate substantial equivalency between the Viveve 2.0 System and the currently cleared Viveve System when treating vaginal tissue following radiofrequency (RF) energy administration in the ovine model. A total of 3 parous ewes were treated with the Clinical Treatment protocol energy level. Tissue temperature data were reported in a sub-report which included graphical and tabular summaries for each location and treatment protocol.

Tissue temperature results demonstrated that during the Clinical procedure, treatment with the Viveve 2.0 System did not result in temperatures that would be expected to cause cellular damage and were substantially equivalent to the Viveve System. Maximum temperatures were well below temperatures that would pose safety concerns and yet were within the range that could result in the desired cellular changes. Administration of radiofrequency from the Viveve 2.0 System resulted in tissue temperature increases in deep tissue layers, with approximately 3-8 mm seeming to be the target area. Heating did appear in the muscularis, but there was not deposition of heat in this area and the heat dissipated rapidly. Variations in

temperature-time profiles appeared to be a result of body-type/tissue characteristics that are unique to each ewe; but in all cases, there were no profile differences that would indicate a safety concern.

The studies serve two purposes:
1. Prove equivalency to the predicate device and
2. Support future equivalency to an indication under evaluation (VI-15-01)

Study summaries are submitted in Section 19. The full studies are available in Attachment 1.

5.10 CONCLUSION

The design, technical characteristics, functionality, indications for use, and principle operation of the subject device Viveve 2.0 System remains unchanged from that of the predicate device, Viveve System (K180584). The proposed design modifications do not raise new questions of the safety or efficacy of the device and the intended use of the Viveve 2.0 System remains unchanged from that of the cleared predicate.