December 26, 2024

Pacira Biosciences, Inc.
Niloufa Insanally
Director, Regulatory Affairs Clinical Strategy
10410 Science Center Drive, Building A
San Diego, California 92121

Re: K243677
Trade/Device Name: iovera System
Regulation Number: 21 CFR 882.4250
Regulation Name: Cryogenic Surgical Device
Regulatory Class: Class II
Product Code: GXH, ETN
Dated: November 27, 2024
Received: November 27, 2024

Dear Niloufa Insanally:

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 (the 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 available 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.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

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 Part 803) for devices or postmarketing safety reporting (21 CFR Part 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 Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 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,

Adam D. Pierce -S
Digitally signed by Adam D. Pierce -S
Date: 2024.12.26 11:48:31 -05'00'

Adam D. Pierce, Ph.D.
Assistant Director
DHT5A: Division of Neurosurgical, Neurointerventional, and Neurodiagnostic Devices
OHT5: Office of Neurological and Physical Medicine 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: 07/31/2026
*See PRA Statement below.*

Submission Number *(if known)*

K243677

Device Name

iovera° System

Indications for Use *(Describe)*

The iovera° System is used to destroy tissue during surgical procedures by applying freezing cold. It can also be used to produce lesions in peripheral nervous tissue by the application of cold to the selected site for the blocking of pain. It is also indicated for the relief of pain and symptoms associated with osteoarthritis of the knee for up to 90 days. The iovera° System is not indicated for treatment of central nervous system tissue.

When stimulation compatible components are used, the iovera° System can also facilitate target nerve location by conducting electrical nerve stimulation from a compatible 3rd party nerve stimulator.

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.**

# 510(k) SUMMARY - K243677

| | |
|---|---|
| **Device Trade Name:** | iovera° System |
| **Device Common Name** | Cryogenic Surgical Device |
| **Device Class:** | II |
| **Classification Name:** | Cryosurgical Unit and Accessories Device<br>Surgical Nerve Stimulator |
| **Regulation No.:** | 21 CFR Part 882.4250 and 874.1820 |
| **Product Code:** | GXH, ETN |
| **Predicate Device:** | iovera° System K220656 and K211334 |
| **Owner/Submitter:** | Pacira Pharmaceuticals, Inc.<br>10410 Science Center Drive, Building A,<br>San Diego, California 92121 |
| **Regulatory Contact:** | Niloufa Insanally, Ph.D., RAC<br>Director, Regulatory Affairs Clinical Strategy<br>Tel: 858 220 3761<br>Email: niloufa.insanally@pacira.com |
| **Date:** | December 26, 2024 |

## DEVICE DESCRIPTION

The iovera° System is a portable cryogenic surgical device used to destroy tissue and/or produce lesions in nervous tissue through application of extreme cold to the selected site. The device is based on introduction of a Smart Tip internally cooled by the cryogenic fluid (nitrous oxide, $N_2O$) to a selected area. The Smart Tip is cooled by the Joule-Thomson Effect and/or latent heat of vaporization. The iovera° System may be used in conjunction with standard of-the-shelf nerve stimulator device in applications where precise nerve location is desired.

Device Design

The device is comprised of four main components:

- A reusable Handpiece
- A Charging Dock
- An assortment of single-patient-use Smart Tips
- A Cartridge containing nitrous oxide

The iovera° System Handpiece is battery powered and provides feedback to the user during device preparation and use. The Handpiece connects to both the Cartridge and to the Smart Tip. The user activates a treatment cycle through a control on the Handpiece, which starts and stops the treatment. The Handpiece contains an LCD display for providing feedback to the user when the device is ready to use. The Charging Dock stores the Handpiece between uses and provides power for charging the battery.

An assortment of Smart Tips is available for the iovera° system. All Smart Tip needles are made of stainless steel and have a closed-end design that fully contains the cryogen so that it does not enter the target tissue. The Smart Tip is the only patient contacting component of the iovera° System. The user removes the Smart Tip from its sterile packaging and attaches it to the Handpiece immediately before use. Certain Smart Tip designs provide a connection to an external nerve stimulator to facilitate nerve location prior to treatment.

The iovera° System uses a commercially available nitrous oxide cylinder. The Cartridge is filled with pure $N_2O$.

Device Functionality/Scientific Concepts:

The device functionality is based on the user introducing the Smart Tip into the selected treatment area or the target nervous tissue. The user then initiates the flow of cryogen by pressing the on/off button. Liquid cryogen flows from the Handpiece into the closed-end Smart Tip. The Smart Tip is cooled by the Joule-Thomson Effect and/or latent heat of vaporization; as the liquid cryogen expands into a gas, the temperature drops around the external surface of the Smart Tip, causing the surrounding tissue to freeze. The treatment is completed after a pre-programmed amount of time, at which time the user can safely remove the Smart Tip from the treatment site.

**INTENDED USE/INDICATIONS FOR USE**

*The iovera° System is used to destroy tissue during surgical procedures by applying freezing cold. It can also be used to produce lesions in peripheral nervous tissue by the application of cold to the selected site for the blocking of pain. It is also indicated for the relief of pain and symptoms associated with osteoarthritis of the knee for up to 90 days. The iovera System is not indicated for treatment of central nervous system tissue.*

*When stimulation compatible components are used, the iovera° System can also facilitate target nerve location by conducting electrical nerve stimulation from a compatible 3rd party nerve stimulator.*

**Subject Device**

The iovera° System's "1x180" Smart Tip configuration (indicating one needle which is 180 mm long) can also facilitate target nerve location by conducting electrical nerve stimulation from a separate nerve stimulator.

## SUMMARY/COMPARISON OF IOVERA° SYSTEM DEVICE CHARACTERISTICS

The iovera° System is substantially equivalent in intended use, technology, design, and materials to the listed legally marketed predicate devices.

**Table 1. Substantial Equivalence Comparison Table**

| Parameter | Proposed<br>iovera° System<br>**STT21180STIM**<br>**Subject of this Special 510(k)** | Predicate 1<br>iovera° System<br>**K220656** | Predicate 2<br>iovera° System<br>**K211334** |
|---|---|---|---|
| **Intended Use** | Destroy tissue through freezing | Same | Same |
| **Indications for Use** | The iovera° System is used to destroy tissue during surgical procedures by applying freezing cold. It can also be used to produce lesions in peripheral nervous tissue by the application of cold to the selected site for the blocking of pain. It is also indicated for the relief of pain and symptoms associated with osteoarthritis of the knee for up to 90 days. The iovera System is not indicated for treatment of central nervous system tissue.<br>When stimulation compatible components are used, the iovera° System can also facilitate target nerve location by conducting electrical nerve stimulation from a compatible 3rd party nerve stimulator. | The over° System is used to destroy tissue during surgical procedures by applying freezing cold. It can also be used to produce lesions in peripheral nervous tissue by the application of cold to the selected site for the blocking of pain. It is also indicated for the relief of pain and symptoms associated with osteoarthritis of the knee for up to 90 days. The iovera° system is not indicated for treatment of central nervous system tissue. When stimulation compatible components are used, the iovera° System can also facilitate target nerve location by conducting electrical nerve stimulation from a compatible 3rd party nerve stimulator. | The iovera° System is used to destroy tissue during surgical procedures by applying freezing cold. It can also be used to produce lesions in peripheral nervous tissue by the application of cold to the selected site for the blocking of pain. It is also indicated for the relief of pain and symptoms associated with osteoarthritis of the knee for up to 90 days. The iovera° system is not indicated for treatment of central nervous system tissue. |
| **Anatomical Sites** | Peripheral nerves | Same | Same |
| **Intended Users** | Qualified medical personnel (doctors, specialists) | Same | Same |
| **Where used? Clinical Setting** | Hospital or medical environment (professional clinical setting) | Same | Same |
| **Technology** | Cryogenic surgical device with needle which penetrates treatmen area | Same | Same |
| **Energy used/or delivered** | Cryotherapy removes energy from the body.<br>Cryogen used: Nitrous Oxide | Same | Same |

| Parameter | Proposed<br>iovera° System<br>**STT21180STIM**<br>**Subject of this Special 510(k)** | Predicate 1<br>iovera° System<br>**K220656** | Predicate 2<br>iovera° System<br>**K211334** |
|---|---|---|---|
| **Cryogen cartridge size** | 21ml (14.3 gram fill) nitrous oxide cartridge | Same | Same |
| **Cryogen cartridge loading** | Cartridge is loaded via a hinged door on the side of the device. Closing the door provides the force necessary to pierce the cartridge. | Same | Same |
| **Cryogen cartridge piercing point/filter** | In-line piercing point and filter assembly resides in a replaceable assembly within the device. | Same | Same |
| **Cartridge status/detection** | Measurement of cryogen pressure; detection switch. | Same | Same |
| **Cartridge heating** | Resistive flex circuit with redundant monitoring thermistors. | Same | Same |
| **Human Factors** | Hand-held device containing cryogen. Detachable cryoprobes (Smart Tips). | Same | Same |
| **Information display** | Color graphic LCD on rear of device. Additional information regarding failure mode is also displayed. | Same | Same |
| **Charging Dock display** | LED light bar indicating Charging Dock is receiving power from AC-DC adapter (Power Supply). Light bar changes color when Charging Dock is charging current to Handpiece. | Same | Same |
| **Digital Interfaces** | USB Type B Port and SD Card Slot. The SD Card slot is inactive; the USB Port is not for customer use and is for log retrieval by company staff. Cybersecurity aspects of both the SD Card Slot and USP Port are covered and tested in the Software Development Life Cycle activities. | Same | Same |
| **Method of Smart Tip attachment** | Push-on / pull-off design | Same | Same |
| **Skin-warmer heating** | Semiconductor device used as heating element – this element is thermally connected to skin warmer (heating block) and monitored with redundant thermistors. | Same | Same |
| **Cryogen valve** | Valve comprises needle valve in | Same | Same |

| Parameter | Proposed<br>iovera° System<br>**STT21180STIM**<br>**Subject of this Special 510(k)** | Predicate 1<br>iovera° System<br>**K220656** | Predicate 2<br>iovera° System<br>**K211334** |
|---|---|---|---|
| | compliant sealing element. Valve is controlled by stepper-motor-based linear actuator. Switch detects valve open position. | | |
| **Power Source** | Battery powered<br>Battery type: Single cell Lithium Ion, 3100mAh<br>Battery voltage: 3.6Volts Mains powered Charging Dock with Manufacturer- supplied, medical grade power supply (5V DC). | Same | Same |
| **Operating Principle** | Joule-Thomson Effect / Latent Heat (enthalpy) of Vaporization | Same | Same |
| **Patient contacting materials** | Closed tip stainless steel needle | Same | Same |
| **Biocompatibility** | Biocompatible patient contacting materials, tested to "ISO 10993-1:2018, Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process." | Same | Same |
| **Needle Sizes** | 27G (STT2309)<br>20G (STT2190)<br>20G (STT2190STIM)<br>25G (**STT21180STIM**) | 27G (STT2309)<br>20G (STT2190)<br>20G (STT2190STIM) | 27G (STT2309)<br>20G (STT2190) |
| **Catalog Numbers** | STT2309, STT2190, STT2190STIM and STT21180STIM | STT2309, STT2190, and STT2190STIM | STT2309 and STT2190 |
| **Working Length** | 8.5 mm (STT2309)<br>90mm (STT2190, and STT2190STIM)<br>180 mm (**STT21180STIM**) | 8.5 mm (STT2309)<br>90mm (STT2190, and STT2190STIM) | 8.5 mm (STT2309)<br>90mm (STT2190) |
| **Nerve Stimulation** | Yes (for STT21180STIM) | Yes (for STT2190STIM) | No |
| **Nu ber of Needles/Smart Tip** | 1 x 25G (180mm) (**STT21180STIM**)<br>1 x 20G (90mm) (STT2190, and STT2190STIM)<br>3 x 27G (8.5mm) (STT2309) | 1 x 20G (90mm) (STT2190, and STT2190STIM))<br>3 x 27G (8.5mm) (STT2309) | 1 x 20G (90mm) (STT2190)<br>3 x 27G (8.5mm) (STT2309) |

| Parameter | Proposed<br>iovera° System<br>**STT21180STIM**<br>**Subject of this Special 510(k)** | Predicate 1<br>iovera° System<br>**K220656** | Predicate 2<br>iovera° System<br>**K211334** |
|---|---|---|---|
| | | | |
| **Silica ID** | 32 µm (8.5mm)<br>65µm (STT2190, STT2190STIM, and **STT21180STIM**) | Same | Same |
| **Applet** | 11876 | Same | Same |
| **Pre-heat time (min)** | 12-seconds (STT2309)<br>1-second (STT2190, STT2190STIM, and **STT21180STIM**) | 12-seconds (STT2309)<br>1-second (STT2190, and STT2190STIM) | 12-seconds (STT2309)<br>1-second (STT2190) |
| **Cooling Time (max)** | 33-seconds (STT2309)<br>60-seconds (STT2190, and STT2190STIM)<br>70-seconds (**STT21180STIM**) | 33-seconds (STT2309)<br>60-seconds (STT2190, and STT2190STIM) | 33-seconds (STT2309)<br>60-seconds (STT2190) |
| **Post -heat Time** | 20-seconds (STT2309)<br>45-seconds (STT2190, and STT2190STIM)<br>15-seconds (**STT21180STIM**) | 20-seconds (STT2309)<br>45-seconds (STT2190, and STT2190STIM) | 20-seconds (STT2309)<br>45-seconds (STT2190) |
| **Skin Warmer Set Point** | 30°C (STT2309, STT2190, and STT2190STIM)<br>15°C (**STT21180STIM)** | 30°C (STT2309, STT2190, and STT2190STIM) | 30°C (STT2309, and STT2190) |
| **Clinical Effect** | Cellular death through cryoneurolysis and Wallerian degeneration.<br>Second degree nerve injury (axonotmesis) | Same | Same |
| **Treatment Temperature** | -55° C to -88°C (-88°C is the boiling point of $N_2O$). | Same | Same |
| **Treatment Time** | Preprogrammed into the Smart Tip. | Same | Same |
| **Treatment Options** | Multiple Smart Tip options are available for producing different cryozone (ice ball) sizes. | Same | Same |
| **Single-patient Use?** | Smart Tips are single-use. Handpiece is reusable. | Same | Same |
| **Sterilization (cryoprobes)** | EO (provided sterile by manufacturer) | Same | Same |
| **Sterility Assurance level** | Smart Tip individually packages and sterile with a SAL of $10^{-6}$ | Same | Same |

| Parameter | Proposed<br>iovera° System<br>**STT21180STIM**<br>**Subject of this Special 510(k)** | **Predicate 1**<br>iovera° System<br>**K220656** | **Predicate 2**<br>iovera° System<br>**K211334** |
|---|---|---|---|
| **Shelf Life** | 37 months | Same | Same |
| **Compatibility with intended environments** | Verified for operation in a professional clinical setting. | Same | Same |
| **Electrical, Mechanical and Thermal safety** | Conforms to IEC 60601-1 Electrical Safety | Same | Same |
| **EMC** | Conforms to IEC 60601-1 Ed. 3.2, Medical electrical equipment - Part 1: General requirements for basic safety and essential performance. | Same | Same |

| **Differences** | **Predicate 1**<br>iovera° System<br>**K220656** | **Predicate 2**<br>iovera° System<br>**K211334** |
|---|---|---|
| 1. The needle gauge for the 1 x 180mm STIM Smart Tip differs from the devices in K211334 [25G (**STT21180STIM**)]. It is in between the 20G and 27G gauge. The gauge size for the STT21180 STIM needle was changed to provide compatibility with the off-the-shelf introducer. | | 27G (STT2309)<br>20G (STT2190) |
| 2. The needle working length for the 1 x 180mm STIM Smart Tip differs from the devices in K211334 [180 mm (STT21180STIM)]. It is longer than the 8.5mm and 90 mm Smart Tips. **Topological change** to STT21180 STIM needle: the needle is longer to enable ice ball formation at deeper peripheral nerves, and gauge size changed to provide compatibility with the off-the-shelf introducer. | | 8.5 mm (STT2309)<br><br>90mm (STT2190) |
| 3. The number of needles differs from one of the devices in K211334 (i.e., 8.5mm STT2309 has 3 needles) while the 1 x 180 mm STT21180STIM has one needle. | | 8.5 mm (STT2309) – has 3 needles. |
| 4. The stimulation feature for the 1 x 180mm STIM Smart Tip differs from the devices in K211334 which have no stimulation feature. | | 8.5 mm (STT2309) – no STIM feature<br><br>90mm (STT2190) - no STIM feature |
| 5. No masking or coating is present on the STT21180 STIM needle. Parylene coating was removed since all Off-the-shelf RF introducers have insulation coating except around the distal end of needle. This is the same for the predicate devices which have no masking. | | 8.5 mm (STT2309) – no masking/coating<br><br>90mm (STT2190) – no masking/coating |

| Parameter | Proposed<br>iovera° System<br>**STT21180STIM**<br>**Subject of this Special 510(k)** | **Predicate 1**<br>iovera° System<br>**K220656** | **Predicate 2**<br>iovera° System<br>**K211334** |
|---|---|---|---|
| **Differences** | | **Predicate 1**<br>**iovera° System**<br>**K220656** | **Predicate 2**<br>**iovera° System**<br>**K211334** |
| 6. The needle geometry for the 1 x 180mm STIM Smart Tip differs from the devices in K211334 [Blunt tip (**STT21180STIM**)]. The 8.5 mm (STT2309) & 90 mm (STT2190) Smart Tips are sharp. The STT21180 STIM Smart Tip is first placed inside the introducer and the use of the introducer (cannula) allows the STT21180 STIM Smart Tip to perform in the same manner as the 8.5mm and 90mm Smart Tips, since the introducer has a sharp tip. | | | 8.5 mm (STT2309) – sharp tip<br><br>90mm (STT2190) – sharp tip |
| 7. The cycle times (i.e. pre-heat time, cooling time, post-heat time) for each predicate device (STT2309 and STT2190 & STT2190STIM) remain the same for each device type. The STT21180STIM Smart Tip differs in that the cooling time is 70 seconds and the post-heat time is 15 seconds. | | | STT2309:<br>Pre-heat: 12 sec<br>Cooling: 33 sec<br>Post-heat: 20 sec<br><br>STT2190:<br>Pre-heat: 1 sec<br>Cooling: 60 sec<br>Post-heat: 45 sec |
| | | | |
| **Differences** | | **Predicate 1**<br>**iovera° System**<br>**K220656** | **Predicate 2**<br>**iovera° System**<br>**K211334** |
| 1. The needle gauge for the 1 x 180mm STIM Smart Tip differs from the devices in K220656 [25G (**STT21180STIM**)] | | 20G (STT2190STIM) | |
| 2. The needle working length for the 1 x 180mm STIM Smart Tip differs from the devices in K220656 [180 mm (STT21180STIM)]. The 180mm Smart Tip is longer than the 90 mm Smart Tips (as well as the 8.5mm Smart Tip). | | 90mm (STT2190, and STT2190STIM) | |
| 3. The stimulation feature for the 1 x 180mm STIM Smart Tip is the same as that for the 90mm STIM Smart Tip described in K220656. No difference in stimulation capability of STT2190 STIM and STT21180 STIM Smart Tips. | | 90mm (STT2190STIM) – has the stimulation feature | |

| Parameter | Proposed<br>iovera° System<br>**STT21180STIM**<br>**Subject of this Special 510(k)** | **Predicate 1**<br>iovera° System<br>**K220656** | **Predicate 2**<br>iovera° System<br>**K211334** |
|---|---|---|---|
| **Differences** | | **Predicate 1**<br>**iovera° System**<br>**K220656** | **Predicate 2**<br>**iovera° System**<br>**K211334** |
| 4. | The needle geometry for the 1 x 180mm STIM Smart Tip differs from the devices in K220656 [Blunt tip (**STT21180STIM**)]. The 90 mm (STT2190) and 90 mm STIM Smart Tip (STT21190 STIM) are sharp. The STT21180 STIM Smart Tip is first placed inside the introducer and the use of the introducer (cannula) allows the STT21180 STIM Smart Tip to perform in exactly the same manner as the 90mm Smart Tips (as well as the STT2309) since the introducer has a sharp tip. | STT2309, STT2190, and STT2190STIM – all have sharp tips. | |
| 5. | No masking or coating is present on the STT21180 STIM needle. Parylene coating was removed since all Off-the-shelf RF introducers have insulation coating except around the distal end of needle. This differs for the predicate device STT2190STIM which has masking. | 90mm (STT2190STIM) – has the masking feature | |
| 6. | The cycle times (i.e. pre-heat time, cooling time, post-heat time) for the predicate device STT2190STIM is the same as for the STT2190 Smart Tip, but the STT21180STIM Smart Tip differs in that the cooling time is 70 seconds and the post-heat time is 15 seconds. | STT2190STIM:<br>Pre-heat: 1 sec<br>Cooling: 60 sec<br>Post-heat: 45 sec | |

**SUMMARY OF PERFORMANCE TESTING**

Design Verification testing was previously performed for the iovera° System to demonstrate that the device meets product specifications and is safe and effective for its intended clinical use. Design verification testing was performed according to recognized standards which define the test methods and is consistent with the predicate devices (K220656 and K211334) (refer to Table 2, below). The verification methods used and applied have not changed since the previous submission. The verification and validation testing assured the subject device meets design input requirements, product specifications and relevant standards.

- Functional and Product Performance Testing, including the Handpiece, stim cable, cartridges, etc.
- Smart Tip STT21180STIM Functional Testing
- Usability Engineering/ User Interface Testing: to IEC 62366-1 Ed. 1.1
- Software Development Lifecycle Testing: Conforms to IEC 62304 Ed. 1.1
- Basic Safety and Essential Performance/Mechanical and Thermal Safety Testing: Conforms to IEC 60601-1 Ed. 3.2
- Electromagnetic Compatibility (EMC) Testing: Conforms to IEC 60601-1-2 Ed. 4.1

- Sterility Assurance: Conforms to ASTM F1980-21 and ISO 11135:2014
- Packaging Evaluation Testing: Conforms to ASTM D4332-22
- Biological Evaluation/Biocompatibility Testing: Conforms to ISO 10993-1:2022

**Table 2.** Reference Standards

| Document Number | Description |
|---|---|
| EN ISO 10993-7:2008+A1:2022 | Biological evaluation of medical devices-Ethylene oxide sterilization residuals |
| EN 60601-1 Edition 3.2 | Medical Electrical Equipment Part 1: General Requirements For Basic Safety And Essential Performance |
| EN60601-1-2 Edition 4.1 | Medical Electrical Equipment - Part 1-2: Collateral Standard: Electromagnetic Disturbances. Requirements and Tests |
| IEC 62366-1 Ed. 1.1 b:2020 | Medical devices — Part 1: Application of Usability Engineering to Medical Devices |
| AAMI TIR28:2016 (R)2024 | Product adoption and process equivalency for ethylene oxide sterilization. |
| BS EN ISO 11135:2014 + A1:2019 | Sterilization of health-care products - Ethylene oxide - Requirements for the development, validation and routine control of a sterilization process for medical devices - Amendment 1 |
| BS EN ISO 11737-1:2018+A1:2021 | Sterilization of health care products. Microbiological methods-Determination of a population of microorganisms on products |
| AAMI/IEC 62304:2006 & A1:2016 | Medical device software - Software life cycle processes - Consolidated Text |
| IEC 62304 Ed. 1.1 b:2015 | Medical device software - Software life cycle processes CONSOLIDATED EDITION |
| ISO 11607-1:2019/Amd1:2023 | Packaging for terminally sterilized medical devices - Part 1: Requirements for materials, sterile barrier systems and packaging systems |
| ISO 11607-2:2019/Amd1:2023 | Packaging for terminally sterilized medical devices - Part 2: Validation requirements for forming, sealing and assembly processes |
| BS EN ISO 11607-1:2020+A11:2023 | Packaging for terminally sterilized medical devices |
| BS EN ISO 11607-2:2020+A1:2023 | Packaging for terminally sterilized medical devices |
| ASTM F1886/F1886M-16 | Standard Test Method for Determining Integrity of Seals for Flexible Packaging by Visual Inspection |
| ASTM F88/F88M-23 | Standard Test Method for Seal Strength of Flexible Barrier Materials |
| BS EN ISO 10993-1:2022 | Biological evaluation of medical devices, Part 1: Evaluation and testing within a risk management process |

The iovera° System Smart Tip (STT21180STIM) underwent thorough evaluation using standardized test methods to ensure compliance, safety, and usability, including:

- ASTM Standards (D4332, D4169, F88/F88M, F1980, F2096): Validated packaging integrity and compliance with ISO 11607 requirements for sterile barrier systems.
- IEC 60601-1 and IEC 60601-1-2: Confirmed Ensuring Basic Safety and Essential Performance, and Electromagnetic Compatibility (EMC).
- IEC 62366: Assessed usability by identifying hazards and hazardous situations associated with the user interface, ensuring the device's safety features are intuitive and support proper usage.
- ISO 10993-1: Verified the biocompatibility of patient-contacting materials, ensuring safety for clinical use.

A brief discussion of the nonclinical tests submitted, referenced, or relied on in this premarket notification submission for a determination of substantial equivalence is provided below:

**1) Biocompatibility testing**

The biocompatibility evaluation for the iovera System device was conducted in accordance with the International Standard ISO 10993-1 "Biological Evaluation of Medical Devices − Part 1: Evaluation and Testing Within a Risk Management Process," as recognized by FDA. The battery of testing included the following tests:

- Cytotoxicity
- Sensitization
- Irritation
- Systemic toxicity
- Pyrogen Testing

The comprehensive biocompatibility and chemical characterization studies confirmed the safety of the STT21180STIM Smart Tip. Testing showed no signs of acute systemic toxicity and pyrogenic response, sensitization, skin irritation, , meeting all ISO10993-1 and USP acceptance criteria. Chemical analysis verified that all extractables were below the Analytical Evaluation Threshold (AET), with no unexpected contaminants or material degradation. The toxicological risk assessment reinforced these findings, demonstrating negligible toxicological risk with a significant margin of safety for detected elements and no hazardous compounds identified. These results validate the device's compliance with biocompatibility requirements, ensuring patient safety.

**2) Electrical safety and electromagnetic compatibility (EMC)**

Electrical safety and EMC testing were conducted on the iovera System device, consisting of the handpiece, docking station, cryogen cartridge and Smart Tip needle. The system complies with the IEC 60601-1 and IEC 60601-1-2 standards for safety and the IEC 60601-1-2 standard for EMC. The device complied with IEC 60601-1:2005+AMD1:2012+AMD2:2020 Edition 3.2, IEC 60601-1-6:2010+AMD1:2013 +AMD2:2020 Edition 3.2, and IEC 60601-1-8:2006+AMD1:2012+AMD2:2020 Edition 2.2 standards for safety (e.g. electric shock), usability, and alarms.

Additionally, the iovera System device met all EMC requirements per IEC TS 60601-4-2:2024 specifically the following clauses: 1.3, 4.2.1, 5.1, 5.2.2, 5.2.4, 6, 6.1, 6.2, 8.4, 8.7, 8.9, 8.10, 8.11, 8.12, 8.13 and 8.14.

**3) Software Verification and Validation Testing**

Software verification and validation testing were conducted and documentation was provided as recommended by FDA's Guidance for Industry and FDA Staff, "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices." The software for this device was considered as a "Class B" level of concern, since a failure or latent flaw in the software could directly result in non-serious injury to the patient or operator.

The references used for the software development, including the application of risk management (software architecture and dFMEA), the software life cycle processes and the cybersecurity requirements, followed the guidance and conditions set forth in the following references:

1. IEC 62304:2006/AMD1:2015: Medical Device Software – Software Life Cycle Processes

2. FDA Guidance Document: Guidance for Industry, FDA Reviewers, and Compliance on Off-the-Shelf Software Use in Medical Devices, issued September 9, 1999.
3. FDA Guidance Document: General Principles for Software Validation; Final Guidance for Industry and FDA Staff, issued January 11, 2002
4. FDA Guidance Document: Content of Premarket Submissions for Device Software Functions, issued June 14, 2023
5. FDA Guidance Document: Cybersecurity in Medical Devices: Quality System Considerations and Content of Premarket Submissions, issued September 27, 2023

**4) Mechanical and Resistance Testing**

Additional testing was conducted to ensure mechanical strength and reliability and package integrity (no breach of sterility):

- Resistance Testing – test of difficulty in securing connection between needle and PCBA
- Flex Introducer and Leak Test – to ensure needle dose not break
- Heater Block-to-Needle Bond Strength Test
- Simulated use testing - Human Factors Study - Introducer with the Smart Tip and Stim cable assembly attached
- Package Integrity - Peel Strength Testing – Sterilization validation
- Package Integrity - Package Visual Inspection and bubble

Verification and validation testing performed on the subject device supports the substantial equivalence of the modified iovera° System to the predicate device. The subject iovera° System device met the design verification and validation inputs, passing all predetermined acceptance criteria. No new issues of safety or effectiveness were identified during design verification and validation testing.

**CONCLUSION**

The subject iovera° System, with the same intended use, same indications for use, design, materials, technological features, and principles of operation as the cleared iovera° Systems (K220656 and K211334), is substantially equivalent to these predicate devices. The new Smart Tip STT21180STIM does not affect the safety and effectiveness of the device as the intended therapeutic use for the creation of lesions with the application of cold in peripheral nerves to block pain has not changed.

In conclusion, the new Smart Tip STT21180STIM described, and the information presented in this special premarket notification demonstrated that the iovera° System is safe and effective, does not introduce or raise new questions of safety and effectiveness, and is substantially equivalent in intended use, technology, design, and materials to the legally marketed predicate devices.