May 20, 2022

Pacira Biosciences, Inc.
Danny Rivera
Sr. Director, Quality and Regulatory Affairs
10450 Science Center Drive
San Diego, California 92121

Re: K220656
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: April 20, 2022
Received: April 21, 2022

Dear Danny Rivera:

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,

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: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K220656

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.

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510(k) SUMMARY

Device Trade Name:	iovera^{o} System
Device Common Name	Cryogenic Surgical Device
Device Class:	II
Classification Name:	Cryosurgical Unit and Accessories Device Surgical Nerve Stimulator
Regulation No.:	21 CFR Part 882.4250 and 874.1820
Product Code:	GXH, ETN
Predicate Device:	iovera^{o} System K173763 and K211334
Owner/Submitter:	Pacira Biosciences, Inc. 10450 Science Center Drive San Diego, California 92121
Regulatory Contact:	Danny Rivera Senior Director, Quality and Regulatory Affairs Tel: 8586252414 Ext 3175 Email: Danny.Rivera@Pacira.com
Date:	May 20, 2022

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 comprises 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.

SUMMARY/COMPARISON OF IOVERA^{O} SYSTEM DEVICE CHARACTERISTICS

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

Substantial Equivalence Comparison Table

Parameter	**Proposed** iovera° System	**Predicate 1** iovera° System K211334	**Predicate 2** iovera° System K173763
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. When stimulation compatible components are used, the iovera° System can also facilitate target nerve location by conducting electrical nerve stimulation from a 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.	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. The iovera° System's "1x90" Smart Tip configuration (indicating one needle which is 90 mm long) can also facilitate target nerve location by conducting electrical nerve stimulation from a separate nerve stimulator.
Anatomical Sites	Peripheral nerves	Same	Same

Parameter	Proposed iovera° System	Predicate 1 iovera° System K211334	Predicate 2 iovera° System K173763
Technology	Cryogenic surgical device with needle which penetrates treatment area	Same	Same
Cryogen cartridge size	21ml (14.3 gram fill) nitrous oxide cartridge	Same	10ml (7.5 gram fill) nitrous oxide cartridge
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	Same	Cartridge is loaded from the back of the device. Screwing on the cap provides the force necessary to pierce the cartridge.
Cryogen cartridge piercing point/filter	In-line piercing point and filter assembly resides in a replaceable assembly within the device.	Same	In-line piercing point and filter are part of cryogen cartridge assembly.
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	Same	Array of different colored LEDs located around the device.
Charging Dock display	LED light bar indicating Charging Dock is receiving power from AC-DC adapter. Light bar changes color when Charging Dock is supply charging current to Handpiece.	Same	LED indicating Charging Dock is receiving power from AC-DC adapter.
Digital Interfaces	USB and SD card. The SD card is not part of the product offering to the customer. This tool is used for troubleshooting during in-house failure investigation. The SD card has no impact on	Same	USB
Method of Smart Tip attachment	Push-on/pull-off design	Same	Screw-on tip attachment
Skin-warmer heating	Semiconductor device used as heating element – this element is thermally connected to heating block and monitored with redundant thermistors.	Same	Resistors used as heating element – this element is thermally connected to heating block and monitored with redundant thermistors.

Parameter	Proposed iovera° System	Predicate 1 iovera° System K211334	Predicate 2 iovera° System K173763
Cryogen valve	Valve comprises needle valve in compliant sealing element. Valve is controlled by stepper-motor-based linear actuator. Switch detects valve open position.	Same	Valve comprises face-to-face seal against compliant sealing element. Valve is controlled by stepper-motor-based linear actuator.
Power Source	Battery powered Battery type: Single cell Lithium Ion, 3100mAh Battery voltage: 3.6Volts Main powered Charging Dock	Same	Same
Operating Principle	Joule-Thomson Effect / Latent Heat of Vaporization	Same	Same
Needle Size	20G, 27G	Same	20G
Catalog Numbers	STT2309, STT2190, and STT2190STIM	STT2309 and STT2190	STT0811
Needle Working Length	8.5mm, 90mm	Same	90mm length
Needles/Tip	1 x 20G (90mm) 3 x 27G (8.5mm)	Same	1 x 20G (90mm)
Nerve Stimulation Support	Yes[1]	N/A	Yes
Pre-heat time (min)	12 seconds (8.5mm) 1 second (90mm)	Same	1 second (90mm)
Cooling Time (max)	33 seconds (8.5mm) 60 seconds (90mm)	Same	60 seconds (90mm)
Post -heat Time	20 seconds (8.5mm) 45 seconds (90mm)	Same	45 seconds (90mm)
Skin Warmer Set Point	30°C	Same	Same
Clinical Effect	Cellular death through cryoneurolysis and Wallerian degeneration Second degree nerve injury (axonotmesis)	Same	Same
Treatment Temperature	-55° C to -75°C (-67°F to -103°F)	Same	Same

[1] Nerve-stim tips have a thin, electrically insulating coating (Parylene C) over most of the needle and include an electrical connection between the needle and an external, off-the-shelf PENS device. All other aspects of the design are identical to the non-nerve-stim version of the tip.

Parameter	Proposed iovera° System	Predicate 1 iovera° System K211334	Predicate 2 iovera° System K173763
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-patient use. Handpiece is reusable.	Same	Same
Sterility Assurance Level	Smart Tip individually packaged and sterile with a SAL of $10^{-6.}$	Same	Same
Shelf Life	37-month	Same	Same
Biocompatible	Biocompatible. All patient contacting materials, tested to ISO 10993-1	Same	Same

SUMMARY OF PERFORMANCE TESTING

Design Verification testing was performed for the iovera° System to demonstrate that the device meets product specifications for its intended clinical use. Using a risk-based approach for the modifications, design verification testing was performed according to recognized standards, and is consistent with the predicate device and test methods described in previous 510(k) submissions for the iovera° system. The verification methods used and applied are appropriate for the changes. The verification and validation testing assures the modified subject device meet design input requirements, product specifications and relevant standards.

- Functional and Product Performance Testing of the Handpiece and Cartridge
- Smart Tip Functional Testing
- User Interface Testing: IEC 62366-1:2015
- Software Testing: Conforms to IEC 62304:2006/A
- Electrical and EMC Safety Testing: Conforms to IEC-60601-1: A1 2012 and 60601-1-2:2014
- Mechanical and Thermal Safety Testing: Conforms to IEC 60601-1: A1:2012
- Sterility Testing: Conforms to ASTM F1980-16 and ISO 11135:2014/A
- Packaging Testing: Conforms to ASTM D4332-14.
- Biocompatibility Testing: Conforms to ISO 10993-1

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, indications for use, design, materials, technological features, and principles of operation as the cleared iovera° Systems (K211334 and K173763), is substantially equivalent to these predicate devices. The modification to the Indications for Use proposed in this 510(k) 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.

The modification described, and the information presented, in this special premarket notification demonstrates that 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.