SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Stimulator, Spinal-Cord, Totally Implanted for Pain Relief

Device Trade Name: Prospera Spinal Cord Stimulation (SCS) System, Resilience Percutaneous Lead, HomeStream Remote Management

Device Procode: LGW

Applicant's Name and Address: BIOTRONIK NRO, INC.
6024 Jean Road
Lake Oswego, OR 97035

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P210037

Date of FDA Notice of Approval: March 31, 2023

II. INDICATIONS FOR USE

The Prospera Spinal Cord Stimulation (SCS) system is indicated as an aid in the management of chronic, intractable pain in the trunk and/or limbs, which may include unilateral or bilateral pain, resulting from any of the following:

- Failed Back Syndrome (FBS) or low back syndrome or failed back
- Radicular pain syndrome or radiculopathies resulting in pain secondary to FBS or herniated disk
- Postlaminectomy pain
- Multiple back operations
- Unsuccessful disk surgery
- Degenerative Disk Disease (DDD)/herniated disk pain refractory to conservative and surgical interventions
- Peripheral causalgia
- Epidural fibrosis
- Arachnoiditis or lumbar adhesive arachnoiditis
- Complex Regional Pain Syndrome (CRPS), Reflex Sympathetic Dystrophy (RSD), or causalgia.

III. CONTRAINDICATIONS

Implantation of a spinal cord stimulator may be contraindicated in patients with the following characteristics:

- Are unable to operate the SCS system
- Have failed to receive effective pain relief during SCS trial stimulation

- Patients who are poor SCS surgical candidates based on presentation and underlying pathology

Note: The safety and effectiveness of Prospera SCS system has not been established in pediatric patients or pregnant or nursing patients.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Prospera Spinal Cord Stimulator System's labeling.

V. DEVICE DESCRIPTION

The Prospera SCS System with HomeStream Remote Management is a rechargeable, 16-electrode, MRI conditional spinal cord stimulation system that delivers electrical stimulation to the dorsal column of the spinal cord for the management of chronic intractable pain of the trunk and/or limbs.

The Prospera SCS System includes a rechargeable Implantable Pulse Generator (IPG), one or more percutaneously implantable leads, a clinician programmer, a trial stimulator, a patient programmer, a charger, the Neuro Service Center, and other accessories that are standard in other commercially available SCS products. Figure 1 displays the main system components.

Figure 1: Prospera SCS System with HomeStream Remote Management

The implanted components of the BIOTRONIK Prospera SCS System include the following:

Implanted Pulse Generator

The Prospera IPG is an active implantable therapy device with a Li-Ion rechargeable battery and 16 output channels. The IPG enclosure consists of biocompatible materials, with a titanium housing and epoxy header. It is hermetically sealed. The battery of the IPG can be wirelessly charged using the IPG charger. The physical specifications of the Prospera IPG are depicted in

Table 1.

Table 1: Physical Specifications of Prospera IPG

Parameter	Prospera IPG
Size (H x W x D)	59 x 44 x 11mm
Volume	20 cc
Weight	31.6g

The Prospera IPG is capable of stimulating the neural tissue of the spinal cord through two 8-contact lead port connections. Any combination of up to 4 cathodes and 4 anodes can be used to deliver stimulation. One or two implanted percutaneous leads will be connected to the lead ports. The electrical characteristics and stimulation parameters of the Prospera IPG are depicted in Table 2.

Table 2: Electrical Characteristics and Stimulation Parameters of Prospera IPG

Parameter	Prospera IPG
Number of Channels	16 (2 lead ports, 8 electrodes each)
Waveform (monophasic, biphasic)	Biphasic
Pulse Shape (e.g. rectangular, sinusoidal)	Rectangular, current control
Maximum output current (500 Ohms)	20.0 mA
Pulse width	30 – 1000 µs
Frequency	2 – 1400 Hz
Electrode selection	Bipolar, Multipolar
Pulse delivery modes	Continuous, Interleaved pulse trains
Number of programs	Up to 12

Percutaneous Leads

The leads are attached to a trial stimulator or IPG and are implanted within the epidural space to deliver therapy to the target region. The system is MRI conditional: the leads, when used in combination with the Prospera IPG under specific conditions, are MRI conditional for 1.5T and 3T full body MRI scans. The lead specifications are listed in Table 3.

Table 3: Resilience Percutaneous Lead Specifications

Parameter	Resilience Percutaneous Leads
Lead Length (cm)	55 and 75
Lead Diameter (French)	4
Number of Electrodes	8
Electrode material	Platinum-Iridium

Electrode spacing (edge to edge) (mm)	4
Electrode Span (mm)	52
Electrode Surface area (mm2)	12.53 each
Conductor Resistance (Ohm) @ Room Temperature	< 20
Conductor material	MP35N jacket with silver core
Lead body insulation	Polyurethane

Lead Anchors and Port Plugs

- **Suture Anchors:** Used to fixate the lead near the epidural insertion point. Basic Anchors remain permanently implanted.

- **Active Anchors:** An alternative method of fixating the lead near the epidural insertion point. It uses an internal mechanical fixation method for tightening the anchor onto the lead. Active Anchors remain permanently implanted.

- **Port Plug:** Used to seal any unused IPG Lead port.

External Components

- **Trial Stimulator:** Also known as the external pulse generator (EPG). Provides stimulation during the stimulation trial period and used to perform intraoperative testing. The trial stimulator's output parameters are identical to those available for the IPG.

- **Trial Accessories Kit:** For use during the trial procedure. Consists of the following devices:

    - **Trial Header:** Contains the lead contacts used to connect the leads to the EPG. When in use, the trial stimulator can be used for therapy delivery.

    - **EPG Cap:** Used to cover the EPG contacts when not in use.

    - **Affixation Pouch:** Encloses the EPG and has adhesive backing which is used to adhere to the patient's skin. The pouch protects the EPG from water and secures the EPG to the patient's body.

- **Intraoperative Test Cable (IOC):** Connects the leads to the EPG during implantation for intraoperative testing. The IOC consists of the lead connection and the header, which are connected through a cable.

- **Clinician Programmer (CP):** Used within clinical setting or from a remote location to program output stimulation parameters of the implanted IPG or EPG. It is an off-the-shelf tablet installed with proprietary BIOTRONIK *HomeStreamCP* programmer software to provide multiple stimulation programs, available to the patient to select from on the Patient

Programmer. The CP is also used to set the program settings that will be available on the Patient Programmer.

- **Charger:** Used by the patient to transcutaneously recharge the IPG battery. The charger itself is a rechargeable device with an optional affixation belt to secure the charger position directly over the IPG location while charging.

- **Patient Programmer:** Allows patient to make system adjustments to stimulation on/off, stimulation program, and intensity of the therapy within clinician programmed limits, and to receive remotely transmitted programs. The Patient Programmer is an off-the-shelf smart phone installed with proprietary BIOTRONIK *MyHomeStream* programmer software that communicates with the IPG or EPG.

- **M50 Magnet:** Used to pair the IPG and EPG with the clinician programmer and patient programmer. The magnet can also be used to suspend IPG or EPG stimulation

- **Neuro Service Center:** Provides secure data connectivity between the Clinician Programmer and Patient Programmer for enabling the HomeStream Remote Management functionality. The HomeStream Remote Management functionality allows for authorized users to remotely access patient system status information and securely send new or updated program options to the patient. The NSC is also a repository for technical data.

Implantation Accessories

Implantation accessories provided with the Prospera SCS system include the following:

- **Torque Wrench:** Used to tighten the set screws that lock the Lead into the IPG and associated Active Anchors.

- **Lead Stylets:** Used to steer the Lead through the epidural space to the desired location. Available in two options: curved and straight.

- **Insertion Needle:** Spoon-billed needle used during Lead implant procedure to introduce Lead into the epidural space. A Needle Stylet is used to prevent coring of tissue and assist with proper needle puncturing.

- **Clearing Wire:** Inserted through Insertion Needle during implantation to clear path for the introduction of the Lead into the epidural space.

- **IPG Pocket Template:** Optional aid during implantation for proper sizing of the IPG implantation pocket.

- **Tunneling Tool:** Used during implant procedure to create a tunnel for the Leads from the incision to the IPG site.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the treatment of chronic intractable pain of the trunk and/or limbs. Patients are typically treated on a treatment continuum with less invasive therapies prescribed first. Established non-surgical treatment options include, but are not limited to oral medications, massage therapy, physical/occupational/exercise therapy, psychological therapies (e.g., behavior modification, hypnosis), Transcutaneous Electrical Nerve Stimulation (TENS), acupuncture, sympathetic nerve blocks, epidural blocks, intrathecal blocks, and facet joint blocks. The surgical treatment options for these patients include sympathectomy, implantable intrathecal drug delivery systems, partially implanted SCS systems (power source is external) and commercially available fully implantable SCS systems. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The Prospera Spinal Cord Stimulation (SCS) System, Resilience Percutaneous Lead, and HomeStream Remote Management has not been marketed in the United States or any foreign country.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of potential adverse effects (e.g., complications) associated with the use of SCS systems. The adverse effects include: (1) those associated with any surgical procedure, (2) those associated with the SCS system placement procedures, and (3) those associated with having an implanted SCS system to treat pain, including the Prospera SCS System. In addition to the risks listed below, there is the risk that the SCS therapy may not be effective in relieving symptoms, or may cause worsening of symptoms. Additional intervention may be required to correct some of the adverse effects.

Risks associated with Implant Procedures

- Risks associated with anesthesia, including cardiac arrest
- Surgical complications, such as infection, cellulitis, abscess, fever, sepsis, bleeding
- Cerebrospinal fluid leak
- Intracranial hypotension
- Hematoma, seroma or thrombosis
- Epidural hemorrhage
- Impaired or inadequate wound healing, wound dehiscence
- Temporary or persistent tenderness or pain at implant site
- Lead migration leading to ineffective pain control or other undesirable changes in stimulation
- Suboptimal lead or IPG placement or migration requiring revision or explant
- Spinal cord compression; nerve, nerve root, or spinal cord injury
- Weakness, lack of coordination, or numbness
- Paralysis
- Death

Risks associated with SCS Stimulation

- Loss of pain relief, loss of paresthesia, unpleasant paresthesia
- Increased pain
- Undesirable stimulation due to cellular changes over time in tissue around electrodes, changes in electrode position, loose electrical connections, or lead failure
- Uncomfortable stimulation of tissue around the leads including skin and muscle
- Other undesirable sensation such as tingling or prickling

Risks associated with Implanted Device Components

- Tissue reaction or allergy to implanted materials
- Persistent pain at implant site (lead or IPG)
- Failure of device components or the battery including lead breakage or movement (migration), hardware malfunctions, loose connections, electrical shorts or open circuits, and lead insulation breaches
- Failure or malfunction resulting in ineffective pain control or other undesirable changes in stimulation, and possibly requiring explant and re-implantation
- Skin erosion or seroma at the lead or IPG site
- Pressure sores
- External sources of electromagnetic interference that cause the device to malfunction and could affect stimulation
- Exposure to magnetic resonance imaging (MRI) can result in heating of tissue, image artifacts, induced voltages in the IPG and/or leads, and lead dislodgement

Risk associated with External Device Components

- Tissue reaction or allergy to external materials
- Uncomfortable heating effects, discomfort or burn

For the specific adverse events that occurred in the clinical studies, please see Section X below.

IX. SUMMARY OF NONCLINICAL STUDIES

A. Laboratory Studies

Testing was conducted to provide adequate data to support the intended use of the Prospera SCS system. Testing was performed according to commonly recognized test methods, FDA guidance documents, and standards, such as International Standards Organization (ISO), European Standards (EN), and American Society and Materials (ASTM).

i. IPG

The IPG system verification consists of electrical and mechanical elements. Both mechanical and electrical tests were conducted in accordance with ISO 14708-3:2017 *Implants for surgery – Active implantable medical devices – Part 3: Implantable neurostimulators*. Key testing on the IPG is summarized in the Table 4 below. All test acceptance criteria were met, and all tests passed.

Table 4: Summary of IPG Testing

Test	Test Purpose	Acceptance Criteria
IPG Mechanical Design	Evaluate IPG size, shape, visual condition, and high-level functional requirements.	Mechanical Design: IPG units shall meet specifications for thickness, volume, mass, and radius. Functional Features: IPG units shall have two lead ports with lead securing mechanisms. Two suture holes for securement in the implant pocket.
Hermetic Leak Test	This test demonstrates that the IPG maintains hermeticity after exposure to mechanical forces. Complete IPG units are punctured through the titanium housing and the gas within is analyzed with a mass spectrometer.	Residual moisture <1640 ppm. No critical foreign gasses compared to filling gas.
IPG-Lead Interface	This test evaluates: • The insertion, withdraw, and retention forces that occur when the lead is introduced to the IPG connector cavities. • Stimulation impedance is evaluated before and after a 10-Day soak of the system in saline solution.	Insertion, withdraw, retention force: • Maximum lead insertion and withdraw forces shall be equal to or less than 10N. • After deploying the set screw, lead does not release from IPG connector cavity when 10N is applied. Stimulation impedance: • After retention testing impedance values are within specification indicating a viable electrical path.

Mechanical Forces	<u>Shock Test:</u> This test simulates mechanical shock effects such as suddenly applied forces or abrupt movements that can occur during incorrect use or transport. <u>Random Vibration:</u> Vibration tests with variable frequency.	Test specification in accordance with ISO 14708-3:2017 section 23. Afterwards: Visual: no damage or cracks. Electrical: no change of parameters.
Stimulation Parameter Test	This test verifies stimulation output conforms to system requirements.	Pulse amplitude, pulse width, stimulation frequency, and therapy modes are within output specifications.
Electrical Neutrality	Maximum leakage current of each electrode shall be less than 7.5 $\mu A/mm^2$.	Test specification in accordance with ISO 14708-3:2017.
Thermal Overdose Charging Lockout	Verify IPG disables charging prior to a CEM43 dose of 40 as measured on external device housing and charging will not resume for 60 minutes after a thermal overdose is detected.	Test specification in accordance with ISO 14708-3: 2017 Cl 17. CEM43 dosage should be less than or equal to 40 when thermal overdose event occurred.Quantity of thermal overdose events should be one. Charger will not resume charging for 60 minutes after thermal overdose event occurred.
Pressure Test	Evaluation of visual condition and electrical function after exposure to changes in pressure expected during normal use (not less than 150 kPa).	14708-3:2017 section 25. Afterwards: Visual: no cracks or rupture of IPG housing. Electrical: no change of parameters.
IPG Recharging Intervals	This test verifies the IPG battery can be recharged from Low Power Threshold (LPT) to End Charge Voltage (ECV) within the specified time.	Charge time $\leq$ 2.5 hours at coaxial and boundary alignment conditions between charger and IPG.

ii. Percutaneous Lead Testing

Resilience percutaneous leads underwent verification and validation testing to establish safety and effectiveness. Key tests of the leads are summarized in Table 5 below. All the specified test acceptance criteria were met, and all tests passed.

Table 5: Summary of Resilience Percutaneous Lead Testing

Test	Test Purpose	Acceptance Criteria
Dimensional	To ensure the leads meet the dimensional measurements for: • Lead length • Diameter of the lead body, electrode, and connector regions • Connector length and spacing • Electrode length and spacing	Meets dimensional specifications.
DC Resistance	To ensure intended therapy (targeted current delivery) is not affected by lead design.	Lead DC resistance from each electrode to its connector contact shall be less than 25 Q at 37°C.
Lead-stylet Interactions	To evaluate the handling force required to insert and withdraw the stylet from the lead. During handling stylet must remain contained within the lead body.	The maximum allowable force required to insert or remove the stylet through the lad center lumen shall be 2 N. Stylet shall remain within the lead body after application of a 5N force to the stylet handle relative to the lead.
Lead-Anchor interaction	Demonstrate the Anchors can slide on the lead and restrain the lead within the patient.	The specification is met if: • The maximum measured sliding forces are ≤ 1.0N. • The minimum retention force after suturing is 3.1N.
Tensile strength	Demonstrate the lead remains mechanically and electrically intact after exposure to tensile loads that can occur during or after implantation. Lead is pulled to 5N or experience 20% elongation, whichever happens first.	1. Permanent elongation is ≤ 5%. 2. The Lead shall not have any cracking or tearing of any functional electrical insulation. 3. Lead remains electrically sound.
Lead Insulation Integrity Test	Demonstrate the safety of the electrical insulation.	Leads shall not have current leakage over 160μA when tested to a minimum of 32.0VDC.

Connector Flex Test	Demonstrate that lead conductors at the exit of the IPG maintain electrical continuity after flexural fatigue stressors.	Leads shall survive a minimum of 164,000 test cycles when bent to 45° ± 2° in each direction. The measured DC resistance of each electrode and its connector contact shall meet the required maximum limit.
Distal Electrode Flex Test	Demonstrate that the distal electrode region maintains electrical continuity after flexural fatigue stressors.	Leads shall survive a minimum of 1,020,000 test cycles when bent to 18.6° +2°/-0° in each direction. The measured DC resistance of each electrode and its connector contact shall meet the required maximum limit.
Lead Body Flex test	Demonstrate that the conductors in the lead body region maintain electrical continuity after flexural fatigue stressors	Leads shall survive a minimum of 94,000 test cycles when bent to 90° +0°/-5° in each direction. The measured DC resistance of each electrode and its connector contact shall meet the required maximum limit.

iii. Charger and Trial Stimulator (EPG)

Prospera Charger and EPG was subjected to design verification testing for the following aspects: electrical/firmware, mechanical features and interactions, packaging testing (environmental and distribution), product safety testing (IEC 60601-1), EMC testing. All the specified test acceptance criteria were met, and all tests passed.

iv. Clinician Programmer and Patient Programmer

The Software associated with the Clinician Programmer and Patient Programmer was developed based on guidance from the FDA document "Guidance for the Content of Pre-market Submission for Software Contained in Medical Devices" (May 11, 2005).

v. Electromagnetic compatibility testing

EMC testing for the implanted components per 14708-3: 2017: Implants for surgery – Active implantable medical devices – Part 3: Implantable neurostimulators," on the following clauses:

- 20: Protection from Damage by External Defibrillator,
- 21: Protection from Damage Caused by High Frequency Surgical Exposure
- 24: Protection from Damage Caused by Electrostatic Discharge
- 27: Protection from Damage Caused by Electromagnetic Non-ionizing Radiation

In addition, the device was tested for compatibility with Electronic Article Surveillance Systems and external components were tested per IEC 60601-1-2. All test articles met defined acceptance criteria for the defined tests.

vi. Wireless Coexistence

Wireless coexistence and wireless quality of service testing was performed in accordance with the IEEE/ANSI C63.27-2017, AAMI TIR69: 2017, and section 5.101 of ISO 14708-3:2017. Testing of the BLE RF telemetry and near-field coil telemetry were also performed. All acceptance criteria were met.

vii. IPG Medical Compatibility testing

The Prospera IPG was tested for protection from damage by external defibrillators, high frequency surgical exposure, diagnostic ultrasound, EMI disturbances, AC magnetic field exposure. All samples met all functional requirements of the testing after exposure to medical therapy conditions.

viii. System Testing

To confirm that the system-level design and performance requirements were met, interactions between Prospera SCS System components were performed. All test articles met the acceptance criteria. Additionally, system level validation testing was performed to confirm compatibility, functional interaction of the components when used together as a system. All validation testing was successfully passed confirming the safety and effectiveness of the Prospera SCS system.

B. Biocompatibility

Biocompatibility was evaluated for all tissue-contacting components of the Prospera SCS System in accordance with ISO 10993-1:2018 *Biological evaluation of medical devices – Part 1: evaluation and testing within a risk management process*. FDA's 2020 Biocompatibility Guidance "Use of International Standard ISO 10993-1, 'Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process'" was also followed. All biocompatibility studies were conducted in compliance with Good Laboratory Practices (GLP), 21 CFR Part 58, on finished, sterilized devices or representative samples reflecting all materials and manufacturing processes. The implanted components of the Prospera SCS System are considered long-term (> 30 days) implants in contact with tissue/bone. The Prospera SCS System also contains external communicating components with limited (≤ 24 hours) tissue/bone contact and intact skin-contacting components with limited to long-term (≤ 24 hours to over 30 days) contact. The biocompatibility test data are summarized in Table 6 below.

Table 6: Biocompatibility Test Data on the Implantable, External Communicating, and Intact Skin-contacting Components of the Prospera SCS System

Biological Effect (Applicable Standard)	Test Method	Results
Implanted[a], External Communicating[b], and Intact Skin-contacting[c] Components:		
Cytotoxicity (ISO 10993-5)	Neutral Red Uptake (NRU) Cytotoxicity Test (implants, external communicating components, and intact skin-contacting component with prolonged contact**)	Non - cytotoxic
Sensitization (ISO 10993-10)	Guinea Pig Maximization Test (implants, external communicating components, and intact skin-contacting component with prolonged contact**)	Non-sensitizing
Irritation or Intracutaneous Reactivity (ISO 10993-10, ISO 10993-23)	Intracutaneous Reactivity Test (implants, external communicating components, and intact skin-contacting component with prolonged contact**)	Non-irritant
Implanted[a] and External Communicating[b] Components		
Systemic Toxicity (ISO 10993-11) Material-Mediated Pyrogenicity USP <151>	Material-Mediated Pyrogenicity Test	Non-pyrogenic
External Communicating[b] Components		
Systemic Toxicity (ISO 10993-11) Acute	Acute Systemic Toxicity Test	No acute systemic toxicity
Implanted[a] Components		
Systemic Toxicity (ISO 10993-11) Acute Subacute	Analytical chemical characterization (IPG, Percutaneous Lead, Port Plug, Active Anchor) and Toxicological Risk Assessment	Acceptable systemic toxicity risks
	13-week Rabbit Subcutaneous Implantation / Systemic Toxicity Study (IPG, Port Plug)	

Biological Effect (Applicable Standard)	Test Method	Results
Subchronic Chronic	13-week Rabbit Intramuscular-subcutaneous Implantation / Systemic Toxicity Study (Percutaneous Lead)	
Genotoxicity (ISO 10993-3)	Bacterial Reverse Mutation Assay (Ames Test) (IPG, Percutaneous Lead)	Non-genotoxic
	In Vitro Mouse Lymphoma Assay (IPG, Percutaneous Lead)	
	Analytical chemical characterization (IPG, Percutaneous Lead, Port Plug, Active Anchor) and Toxicological Risk Assessment	
Local Effects after Implantation (ISO 10993-6)	4-week Rabbit Subcutaneous Implantation Study (IPG, Port Plug, Active Anchor)	Acceptable implantation risks
	13-week Rabbit Subcutaneous Implantation Study (IPG, Port Plug, Active Anchor)	
	4-week Rabbit Intramuscular Implantation Study (Percutaneous Lead)	
	13-week Rabbit Intramuscular Implantation Study (Percutaneous Lead)	
Carcinogenicity (ISO 10993-3)	Analytical chemical characterization (IPG, Percutaneous Lead, Port Plug, Active Anchor) and Toxicological Risk Assessment	Non-carcinogenic

[a] Components tested: IPG, Percutaneous Lead, Port Plugs, Active Anchor*
*(*Biocompatibility data on the Active Anchor are leveraged to support the biocompatibility of the Suture Anchor)*
[b] Components tested: Tunneling Tool, Insertion Needle, Clearing Wire
[c] Component tested: Adhesive Pouch
** For assessment of cytotoxicity, sensitization, and irritation risks from the intact skin-contacting components with limited and long-term contact, the use of the identical materials in US legally marketed devices and the manufacturer's compliance with quality system requirements and other post market controls (related to 21 CFR 820.50, 21 CFR 820.70, 21 CFR 820.80, 21 CFR 820.100, 21 CFR 820.198, and 21 CFR 803) were considered.

C. Sterility

The Prospera SCS System devices which are provided sterile are terminally sterilized with ethylene oxide (EtO) sterilization process to provide a minimum sterility assurance level (SAL) of 10-6. The sterilization processes are in compliance with ISO 11135 1:2014+AMD1:2018.
Sterilant residuals conform to the maximum allowable limits of EO and Ethylene Chlorohydrin (ECH) residuals specified in ISO 10993-7: 2008+TC1:2009+AMD1:2019. *Biological Evaluation of Medical Devices – Part 7: Ethylene Oxide Sterilization Residuals*. and AAMI TIR19-1998.

The product has also been shown to meet the bacterial endotoxin limit of 20 EU/device as described in the FDA's *Guidance for Industry - Pyrogen and Endotoxins Testing: Questions and Answers (June 2012)* and are verified using Limulus Amebocyte Lysate (LAL) testing.

D. Packaging and Product Shelf Life

Packaging shelf life has been demonstrated in compliance with ISO 11607-1: 2019 *Packaging for terminally sterilized medical devices — Part 1: Requirements for materials, sterile barrier systems and packaging systems.*

Shelf-life of one year has been established for sterile devices of the Prospera SCS System.

E. Additional Studies

i. Usability Testing

Implantation and patient-facing interfaces usability testing of the Prospera SCS System was performed in accordance with *IEC 62366-1 Medical devices – Part 1: Application of usability engineering to medical devices* and the FDA guidance document *Applying Human Factors and Usability Engineering to Medical Devices,* issued on February 3, 2016. Usability testing was completed successfully in the intended use environments. The Prospera SCS user interfaces were found to be safe and effective for the intended users, uses, and use environments. No residual use-related risks have been identified during the product development process, in particular the usability engineering process.

ii. MRI-compatibility testing

MRI compatibility testing of the Prospera SCS system was performed according to the ISO/TS 10974:2018 *Assessment of the safety of magnetic resonance imaging for patients with an active implantable medical device*. The requirements of the Technical Specification were derived from the known or foreseeable potential hazards to patients with an AIMD undergoing an MR scan.

All the tests were successfully passed to demonstrate a MR Conditional Labeling.

X. SUMMARY OF PRIMARY CLINICAL STUDIES

A. Study Design

The safety and effectiveness of the Prospera SCS System were based on a systematic review and meta-analysis (for safety outcomes) of published clinical studies that evaluated the safety and/or effectiveness of commercially available, fully implantable SCS systems in treating chronic intractable pain of the trunk and/or limbs, which may

include unilateral or bilateral pain. The Prospera SCS System is similar in design, technology, performance, intended use, and patient population to the SCS systems evaluated in these studies. The literature review strategy was conducted according to the guidelines outlined in the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) Statement.

A total of 19 studies (23 articles) were identified for inclusion in the systematic review. A total of 13 studies (16 articles) (see references in Section XV below) representing a total of 626 patients were identified for inclusion in the safety analysis. A total of 18 studies (22 articles) representing 864 patients were identified for inclusion in the effectiveness analysis.

The Prospera SCS System is similar to the SCS systems reported in the published literature in intended use, target patient population, device design and output characteristics. Based on these similarities the primary objective of the literature search was to provide clinical evidence of the safety and effectiveness of the Prospera device, for the relief of chronic, intractable pain in the trunk and/or limbs (unilateral or bilateral pain) resulting from any of the indications for use listed in Section II.

Effectiveness was demonstrated by the following

- A reduction of pain as demonstrated by a clinically significant reduction in a validated patient-reported assessment of pain (e.g., Visual Analog Scale [VAS], Numerical Rating Scale [NRS], Patient- reported Pain Relief [PRP])
- A 50% reduction in pain when compared to ??? using a validated patient-reported assessment of pain (e.g., VAS, NRS, PRP) in at least 30% of patients included in the study
- A clinically significant difference in pain reduction as measured by a validated patient-reported assessment of pain (e.g., VAS, NRS, PRP) when compared to a control group

Safety of the Prospera SCS System was established using literature articles by examining the incidence of complications of the SCS systems used in each study. The articles report data for patient populations implanted with SCS systems to treat chronic, intractable pain in the trunk and/or limbs (unilateral or bilateral pain) resulting from pain diagnoses/etiologies consistent with the indications for use listed in Section II.

B. Literature Search Strategy

The literature review strategy was conducted according to the guidelines outlined in the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) Statement.

The literature search was conducted on October 25, 2021 utilizing two databases:

- PubMed, which is the online version of Index Medicus produced by the US National Library of Medicine (NLM). It provides (among other resources) free access to MEDLINE, NLM's database of citations and abstracts in the fields of biomedicine and life sciences.
- To ensure the literature search was thorough and extensive, a second well-established database was searched: EMBASE, a comprehensive biomedical research database.

Eligibility Criteria

The participants, interventions, comparators, and outcomes (PICO) used as criteria for eligibility for this systematic review are described in Table 7.

Table 3: Study Characteristics: PICO

Participant(s) / disease(s) or condition(s)	Patients suffering from chronic pain in the trunk and/or limbs resulting from any of the following: • Failed Back Syndrome (FBS) or low back syndrome or failed back • Radicular pain syndrome or radiculopathies resulting in pain secondary to FBSS or herniated disk • Postlaminectomy pain • Multiple back operations • Unsuccessful disk surgery • Degenerative Disk Disease (DDD) / herniated disk pain refractory to conservative and surgical therapies • Peripheral causalgia • Epidural fibrosis • Arachnoiditis or lumbar adhesive arachnoiditis • Complex Regional Pain Syndrome (CRPS), Reflex Sympathetic Dystrophy (RSD), or Causalgia
Intervention(s)	Spinal cord stimulation from commercially available implanted SCS Systems (IPGs and leads) of similar design to the Prospera SCS system.
Comparator(s) / control(s)	Studies with comparator(s)/control (s) may include patients treated with spinal cord stimulation from other devices / systems, surgery/reoperation, placebo/sham stimulation, other medical treatment or conventional medical management. Uncontrolled studies without comparator(s)/controls (s) may be included.

Outcome(s) / endpoint(s)	Primary effectiveness outcomes will focus on reductions in pain / pain-relief following permanent SCS system implantation and will include validated patient-reported assessments of pain (e.g. visual analog scale (VAS) for pain, numeric rating scale (NRS) for pain, patient-reported pain relief (PRP), etc.). Primary safety outcomes will include assessment of SCS-related adverse events (AEs) and/or device-related complications associated with permanent SCS system implantation.

Participants

- Studies that do not include participant populations with one or more conditions or etiologies consistent with the proposed indications for use for the Prospera SCS system listed in Table 7 will be excluded.
- This review will target adult patients (age ≥ 18 years); studies conducted in pediatric populations will be excluded.

Interventions: SCS System Characteristics and Clinical Use in Publication

- The SCS systems used to treat the patient populations in the analyzed published clinical studies will be similar with the Prospera SCS system in terms of design, technology, performance, output characteristics, intended use and target patient population.
- To make this determination the approved labeling of the commercially available SCS Systems from the referenced publications will be compared with the Prospera SCS System.
- Studies exclusively evaluating commercially available SCS systems with fundamental differences in design (e.g. surgical/paddle leads, etc.) will be excluded.
- Studies exclusively evaluating stimulation modalities that are not similar to the stimulation delivered by the Prospera SCS system will be excluded.
- Studies of commercially available SCS systems with other significant differences from the Prospera SCS System will be excluded.
- Studies that do not provide sufficient information regarding the manufacturer/model of the SCS system under investigation to enable the comparisons with the Prospera SCS system noted in the above three criteria will be excluded.

An assessment of the clinical use of the device in the published studies was carried out. Factors assessed included an assessment of the use of the SCS System in

accordance to the approved indications for use (etiologies, conditions, implant indications), anatomical locations and surgical approach/technique.

- Publications exclusively investigating the use of an SCS System in a manner significantly deviating from the approved labeling will be excluded. Studies with such a treatment group, but with an applicable comparator group may be utilized, however, only data reported for the patients treated with SCS consistent with the approved labeling will be used for evaluation of the BIOTRONIK SCS System.

Comparators/controls

- There will be no restrictions based on study comparators or controls.

Outcomes/endpoints

- Publications that do not include investigation of any of the applicable safety or effectiveness outcomes will be excluded.

Study Designs

The following types of studies will be included

- Randomized controlled trials
- Non-randomized controlled clinical trials
- Non-randomized uncontrolled clinical trials
- Prospective, ambispective, and retrospective cohort studies
- Case-control or nested case-control studies
- Systematic reviews or meta-analyses

Setting

- There will be no restrictions by type of setting.

Timeframe

- Studies with data reported only for the SCS trial period, or that do not have a patient follow-up time of at least 3 months following permanent SCS implant for one or more of the outcomes/endpoints described in Table 3 will be excluded.

Report characteristics

- Publications in languages other than English will be excluded

- Publications on animal studies will be excluded
- Publications on case reports or case series will be excluded
- Publications with no clinical data (e.g. protocol, commentary, letter, response, narrative summary without data analysis) will be excluded
- Search terms used in other contexts than the given indications (e.g., angina, headache or cancer-related treatment) will be excluded
- Search terms used in contexts other than SCS therapy (e.g., deep brain stimulation, experimental surgical or stimulation techniques) will be excluded
- Years considered: the literature search will be limited to studies published within the last 25 years. Studies published prior to this cutoff will be excluded

Publications that do not meet the eligibility criteria may still be used for extracting relevant background information. Any modifications to these eligibility criteria made during the conduct of this systematic review will be described in the Summary of Primary Clinical Studies report, including the reasons for modification.

The PubMed and EMBASE searches were designed to identify publications providing evidence of the safety and effectiveness of SCS systems that are interchangeable with the Prospera SCS system.

Terms were searched as keywords within all fields (not only titles) and explored where possible in both PubMed and EMBASE. The PubMed database was searched first, and subsequently the EMBASE database search was carried out, including a secondary step to eliminate potential duplication of records obtained from the PubMed search.

The initial search of the two databases resulted in a total of 1713 records (Embase: 607, PubMed: 1106). After removal of duplicate records (N=23), 1690 records remained. Following the execution of the initial database searches and removal of duplicates, detailed screening of the 1690 articles against the protocol eligibility criteria was carried out in the following steps:

1. Screening of the article information from the 1690 records yielded by the PubMed and EMBASE searches (e.g. information present in titles, abstracts, etc.) against the eligibility criteria was carried out independently by the two reviewing authors. Results from the independent classification were reviewed, and any differences between reviewers was resolved through discussion. Full publications were sought for all articles that appeared to meet the eligibility criteria or where there was any uncertainty,

and one of these reports could not be obtained (N=207/1690 records selected).

2. Clinical review for inclusion of the remaining publications was carried out independently by the two reviewing authors for the full text reports to further assess whether the article satisfied all pre-defined protocol eligibility criteria. The results of this independent classification were reviewed, and any differences were resolved through discussion.
3. Final appraisal and selection of eligible articles by the two independent clinical reviewers and a statistical reviewer (N= 23/207 reports selected).
4. Determination of studies meeting all protocol eligibility criteria including reporting of safety data/endpoints appropriate to evaluate the safety of the Prospera SCS system (N= 16 reports)
5. Determination of studies meeting all eligibility criteria including reporting of effectiveness outcomes data/endpoints appropriate to evaluate the effectiveness of the Prospera SCS system (N= 22 reports).

C. Safety and Effectiveness Results

1. Safety Results

The evaluation of safety is based on the incidence of adverse events (AE)s, device-related complications and/or surgical interventions reported from a total of 13 study populations representing a total of 626 patients implanted with SCS systems of interchangeable design to the Prospera SCS System. The median sample size was 42 (range, 15 to 97) patients, and 386 (61.7%) of the patients were female. The median average age was 52 (range, 39.0 to 56.3) years. The median follow-up time was 12.1 (range, 3.0 to 60.0) months. The studies were published between 1999 and 2020, and 4/13 (30.8%) studies were conducted in the United States, representing 225 (35.9%) of the patients in the safety analysis. The primary treated pain diagnoses were Failed back surgery syndrome (FBSS): N=427 (68.2%), Complex regional pain syndrome (CRPS): N=153 (24.4%), radiculopathy/radicular pain syndrome: N=69 (11.0%) and Degenerative disc disease (DDD): N=49 (7.8%). These characteristics are consistent with the patient population for which the Prospera SCS System is indicated

The safety profile was based on adverse events (AEs) device-related complications, and surgical interventions reported for patient populations with characteristics that are consistent with the Prospera SCS System indications, following treatment with a totally implantable SCS system of interchangeable design to the Prospera SCS system

Adverse effects that occurred in the literature review:

Standard summary statistics are provided for each adverse event type and surgical intervention. In cases where data for a particular event was reported in at least 4 studies, a random-effects model was used to estimate a pooled rate. Two models stratified by follow-up time post- implant (≥3 and <12 months, ≥12 months) were conducted for adverse event and complications reported in at least 4 studies for their respective time periods. If the number of events was reported in the article rather than the number of participants experiencing an event, it was assumed that each event was experienced by a unique participant.

Ten adverse event/complication types/surgical interventions reported in at least four studies were formally meta-analyzed: pain at the implant site (e.g., IPG, electrode), infection, hematoma, cerebrospinal fluid leak, ineffective pain control (permanent implant), device malfunction (e.g., mechanical or technical failure of IPG, lead, etc.), uncomfortable stimulation (target or non-target area), lead migration, lead fracture/failure, and surgical intervention (e.g., revision, explant, replacement).

Table 7 provides a summary of all meta-analyzed adverse events, device-related complications and surgical interventions

Table 7: Summary of Meta-Analyzed Adverse Events

Event Type	N Studies (N Patients)*	Median (Range) Follow-up (months)	Pooled Rate (95% CI)	Median Rate (IQR) [Range]
Adverse Events				
Pain at the implant site (e.g. IPG, electrode)	8 (479)	11.5 (3.0 to 32.0)	. % (1.7-6.2)	.7% (2.7 to 7.8) [2.2 to 16.7]
Infection	9 (469)	12.1 (3.0 to 32.0)	2.7% (0.8-4.7)	4.8% (2.2 to 6.7) [1.0 to 10.0]
Hematoma	4 (261)	9.8 (3.0 to 32.0)	2. % (0-5.2) †	2.1% (2.1 to .4) [2.1 to 8.7]
Cerebrospinal Fluid (CSF) Leak	5 (345)	10.9 (3.0 to 12.1)	1.7 % (0.1-3.4) †	2.4% (2.1 to 4.2) [1.1 to 4.6]
Device-related complications				
Ineffective pain control (permanent implant)	6 (320)	13.3 (8.6 to 32.0)	12.6% (0-27.5)	7.4% (3.2 to 22.0) [0.2 to 53.3]
Device malfunction (e.g. mechanical or technical failure of IPG, lead, etc.)	7 (322)	12.1 (3.0 to 32.0)	8.2 % (3.1-13.3)	8.7% (4.8 to 14.6) [1.1 to 16.7]
Uncomfortable stimulation, target or non-target area	5 (339)	10.9 (3.0 to 24.0)	7. % (0.6-15.3)	.2% (8.3 to 11.3) [1.1 to 14.6]

Lead Migration	9 (510)	12.0 (8.6 to 32.0	7.4% (4.7-10.0) †	7.1% (6.4 to 13.0) [5.2 to 16.7]
Lead Fracture/Failure	4 (130)	22.7 (12.1 to 32.0)	3.5% (0-8.6)	4.2% (3.2 to 5.5) [2.4 to 6.7]
Surgical intervention				
Surgical intervention (e.g. revision, explant, replacement)	12 (578)	12.1 (8.6 to 60.0)	31.4% (16.6-46.2)	27.1% (13.1 to 44.7) [5.3 to 75.0]

*Refers to the number of study populations and patients for which each outcome measure was assessed. †To permit estimation, the variance matrix was forced to allow negative values in the restricted maximum likelihood (REML).

All other adverse event and device-related complications were reported in fewer than 4 studies and were not meta-analyzed. Table 8 provides an overall summary of non-meta-analyzed events, including summary statistics.

Table 8: Summary of Non-meta-analyzed Events: Adverse Events, Device-related Complications

Event Type	N studies (N patients)	Median (Range) Follow-up (months)	Median Rate (Range)
Adverse Events			
Inflammation at implant site	2 (90)	7.6 (3.0-12.1)	11.2% (10.4 to 11.9)
Spinal tap	1 (36)	24.0	8.3%
Death (non-device related)	2 (126)	23.3 (11.0-35.6)	.4% (1.0 to 13.8)
Recurrent rejection ascribed to SCS system	1 (24)	60.0	4.2%
Seroma	2 (107)	21.6 (12.1-31.0)	3.9% (3.1 to 4.8)
herpes zoster	1 (29)	12.0	3.5%
Ulcerative colitis	2 (60)	42 (24.0-60.0)	3.5% (2.8 to 4.2)
Implant site irritation (e.g. dermatitis, rash, pruritus)	3 (210)	7.0 (3.0-11.0)	3.1% (1.5 to 8.3)
Pain	3 (210)	10.9 (3.0-11.0)	3.1% (1.0 to 1 .)
Other postoperative pain	2 (139)	11.5 (11.0-12.1)	2.9% (1.0 to 4.8)
Cellulitis	1 (48)	3.0	2.1%
Hypoesthesia	1 (48)	3.0	2.1%
Muscle spasms	2 (97)	7.0 (3.0-11.0)	2.1% (2.1 to 2.1)
Nausea	1 (65)	11.0	1.5%
Abstinence syndrome	1 (65)	10.9	1.5%
Headache	3 (198)	11.0 (10.9-24)	1.5% (1.0 to 2.8)
Seizure	1 (65)	10.9	1.5%
Skin erosion	1 (93)	8.6	1.1%
Micturition urgency	1 (97)	11.0	1.0%
Anxiety	1 (97)	11.0	1.0%
Arrhythmia	1 (97)	11.0	1.0%
Cardiac arrest	1 (97)	11.0	1.0%
Extradural abscess	1 (97)	11.0	1.0%
Implant site effusion	1 (97)	11.0	1.0%
Stitch abscess	1 (97)	11.0	1.0%
Tinnitus	1 (97)	11.0	1.0%
Urinary retention	1 (97)	11.0	1.0%
Dehiscence	1 (97)	11.0	0.0%
Impaired healing at implant site	1 (97)	11.0	0.0%
Motor dysfunction	1 (97)	11.0	0.0%

Other wound complication at implant site	1 (97)	11.0	0.0%
Paresis	1 (97)	11.0	0.0%
Suture removal	1 (97)	11.0	0.0%
Device-related complications			
SCS system explant (cessation of treatment)	1 (36)	24.0	11.1%
Over/under-stimulation	3 (107)	24.0 (12.1-35.6)	9.5% (2.8 to 20.7)
Recharging issue	2 (90)	7.6 (3-12.1)	7.6% (4.8 to 10.4)
IPG/lead heating	1 (15)	31.0	6.7%
Device connection issue (e.g. lead, lead connection)	2 (65)	22.1 (12.1-32.0)	5.7% (4.4 to 7.1)
Inability to place lead	1 (42)	12.1	4.8%
Damage to device	2 (135)	10.4 (8.6-12.1)	. % (2.4 to 1 .8)
Device use error	2 (90)	7.6 (3.0-12.1)	. % (2.4 to 4.2)
Other stimulation issue	3 (181)	11.0 (3.0-24.0)	2.8% (1.0 to 4.2)
Technical procedure problems during the implantation	1 (36)	24.0	2.8%
Premature generator battery depletion	3 (219)	11.0 (8.6-35.6)	1.6% (1.0 to 2.2)
Stimulation-related neurologic deficit	2 (126)	11.5 (11.0-12.0)	0.0%

Manufacturer and User Facility Device Experience (MAUDE) Database Search Results for SCS Systems used in Publications Selected to Evaluate the Safety and Effectiveness of the Prospera SCS System

To supplement the evaluation of safety in the systematic review, an analysis of MAUDE database event information was carried out for the commercial SCS systems implanted in the patient populations for all 19 selected studies. The MAUDE search included the overall time period from 1988 (date of approval of the earliest device PMA) through June 30, 2021. Search criteria included the product code: LGW (Stimulator, Spinal-Cord, Totally Implanted For Pain Relief), and the IPG and lead model information obtained from the selected studies. The search identified a total of 117888 MDRs reporting a total of 128950 patient problems and 190562 device problems. Table 9 and Table 10 provide summaries of the reported patient problems and device problems.

Table 9: MAUDE Database: Reported Patient Problems

Patient Problems	N Events (% Total Events)
Inadequate Pain Relief	21545 (16.708%)
Pain	19931 (15.456%)
Therapeutic Effects, Unexpected	18501 (14.347%)
Therapeutic Response, Decreased	7647 (5.930%)
Discomfort	7299 (5.660%)
Electric Shock	5152 (3.995%)
Complaint, Ill-Defined	5077 (3.937%)
Undesired Nerve Stimulation	4492 (3.484%)
Burning Sensation	4066 (3.153%)
Unspecified Infection	3803 (2.949%)
Device Overstimulation of Tissue	2808 (2.178%)
Patient Problems	N Events (% Total Events)
Ambulation Difficulties	1516 (1.176%)
Swelling	1322 (1.025%)
Fall	1256 (0.974%)
Bacterial Infection	926 (0.718%)
Post Operative Wound Infection	837 (0.649%)
Numbness	824 (0.639%)

Tingling	767 (0.595%)
Scar Tissue	661 (0.513%)
Muscle Spasm(s)	633 (0.491%)
Fluid Discharge	628 (0.487%)
Headache	626 (0.485%)
Erythema	597 (0.463%)
Wound Dehiscence	590 (0.458%)
Staphylococcus Aureus	572 (0.444%)
Weight Changes	521 (0.404%)
Sleep Dysfunction	518 (0.402%)
Erosion	513 (0.398%)
Fever	480 (0.372%)
Irritation	424 (0.329%)
Impaired Healing	401 (0.311%)
Cerebrospinal Fluid Leakage	388 (0.301%)
Burn(s)	328 (0.254%)
Purulent Discharge	307 (0.238%)
Nausea	306 (0.237%)
Inflammation	305 (0.237%)
Pocket Erosion	297 (0.230%)
Bruise/Contusion	287 (0.223%)
Seroma	287 (0.223%)
Muscle Weakness	285 (0.221%)
Hematoma	279 (0.216%)
Discharge	278 (0.216%)
Alteration In Body Temperature	257 (0.199%)
Hypersensitivity/Allergic reaction	252 (0.195%)
Malaise	245 (0.190%)
Weakness	245 (0.190%)
Skin Erosion	237 (0.184%)
Seizures	231 (0.179%)
Paralysis	212 (0.164%)
Cramp(s)	201 (0.156%)
Itching Sensation	199 (0.154%)
Device Embedded In Tissue or Plaque	197 (0.153%)
Shaking/Tremors	197 (0.153%)
Death	194 (0.150%)
Anxiety	185 (0.143%)
Muscular Rigidity	181 (0.140%)
Distress	174 (0.135%)
Neuropathy	174 (0.135%)
Shock	171 (0.133%)
Neck Pain	165 (0.128%)
Abdominal Pain	160 (0.124%)
Cognitive Changes	156 (0.121%)
Vomiting	155 (0.120%)
Neurological Deficit/Dysfunction	153 (0.119%)
Skin Irritation	149 (0.116%)
Rash	145 (0.112%)
Failure of Implant	144 (0.112%)
Incontinence	138 (0.107%)
Nerve Damage	135 (0.105%)
Foreign Body Reaction	134 (0.104%)
Other events (313 event types with individual incidence <0.1%)	5484 (4.253%)
Total	128950 (100.0%)

Table 10: MAUDE Database: Reported Device Problems

Device Problem	N Events (% Total Events)
Device Operates Differently Than Expected	14742 (7.736%)
High impedance	11695 (6.137%)
Charging Problem	11514 (6.042%)
Failure to Deliver Energy	9417 (4.942%)
Battery Problem	8185 (4.295%)
Charging issue	6740 (3.537%)
Migration	5782 (3.034%)
Improper or Incorrect Procedure or Method	5261 (2.761%)
Unintended Collision	4893 (2.568%)
Therapeutic or Diagnostic Output Failure	4802 (2.520%)
Inappropriate Shock	4718 (2.476%)
Communication or transmission issue	4563 (2.394%)
Failure to Interrogate	4423 (2.321%)
Communication or Transmission Problem	4375 (2.296%)
Migration of device or device component	4133 (2.169%)
Migration or Expulsion of Device	3964 (2.080%)
Energy Output Problem	3714 (1.949%)
Intermittent Continuity	3513 (1.843%)
Device displays error message	3472 (1.822%)
Unexpected Therapeutic Results	3401 (1.785%)
Low Battery	3372 (1.770%)
Delayed Charge Time	3202 (1.680%)
Battery issue	3189 (1.673%)
Therapy Delivered to Incorrect Body Area	2892 (1.518%)
No Device Output	2531 (1.328%)
Use of Device Problem	2197 (1.153%)
Malposition of Device	1991 (1.045%)
Inappropriate/Inadequate Shock/Stimulation	1987 (1.043%)
Premature Discharge of Battery	1832 (0.961%)
Fracture	1829 (0.960%)
Device Displays Incorrect Message	1824 (0.957%)
Patient Device Interaction Problem	1803 (0.946%)
Overheating of Device	1687 (0.885%)
Break	1664 (0.873%)
Impedance Problem	1640 (0.861%)
Use of Device Issue	1515 (0.795%)
Failure to Charge	1430 (0.750%)
Positioning Issue	1351 (0.709%)
Wireless Communication Problem	1329 (0.697%)
Low impedance	1254 (0.658%)

Device Inoperable	1222 (0.641%)
Unstable	1108 (0.581%)
Impedance issue	1105 (0.580%)
Electromagnetic Compatibility Problem	1066 (0.559%)
Connection Problem	975 (0.512%)
Temperature issue	931 (0.489%)
Connection issue	840 (0.441%)
Overheating of device or device component	793 (0.416%)
Electromagnetic Interference	708 (0.372%)
Electro-magnetic interference (EMI)	691 (0.363%)
Positioning Problem	681 (0.357%)
Electromagnetic compatibility issue	677 (0.355%)
Replace	661 (0.347%)
Explanted	630 (0.331%)
Material Integrity Problem	615 (0.323%)
Material integrity issue	597 (0.313%)
Display or Visual Feedback Problem	542 (0.284%)
Device remains implanted	510 (0.268%)
Energy Output To Patient Tissue Incorrect	495 (0.260%)
Data Problem	473 (0.248%)
Implant, reprogramming of	450 (0.236%)
Disconnection	446 (0.234%)
Defective Device	398 (0.209%)
Pocket Stimulation	396 (0.208%)
Unknown (for use when the device problem is not known)	376 (0.197%)
Device Or Device Fragments Location Unknown	361 (0.189%)
Device Stops Intermittently	325 (0.171%)
Improper Device Output	303 (0.159%)
Patient-Device Incompatibility	285 (0.150%)
Electronic property issue	248 (0.130%)
Unintended Movement	248 (0.130%)
Device Remains Activated	219 (0.115%)
Material Deformation	212 (0.111%)
Loss of Data	209 (0.110%)
Incorrect display	194 (0.102%)
Other events (323 event types with individual incidence <0.1%)	6746 (3.540%)
Total	190562 (100.0%)

2. Effectiveness Results

The evaluation of effectiveness is based on data reported from a total of 18 studies (22 articles) representing a total of 864 patients implanted with an SCS systems. The median sample size was 37 (range, 8 to 117) patients, and 600 (69.4%) of the patients were female.The median average age was 53.3 (range, 40.0 to 63.5) years. The median follow-up time was 12.0 (range, 3.0 to 60.0) months. The studies were published between 2000 and 2021, and 6/18 (33.3%) studies were conducted in the United States, representing 338 (39.1%) of the patients in the effectiveness analysis. The primary treated pain diagnoses were FBSS: N=638 (73.8%), CRPS: N=222 (25.7%), radiculopathy/radicular pain syndrome: N=137 (15.9%) and DDD: N=63 (7.3%). These characteristics are consistent with the patient population for which the Prospera SCS System is indicated.

A summary of effectiveness results in the selected studies is provided in Table 11. The number of patients with demographic data and pain diagnoses/etiologies reported in the publications is provided, as well as the total number of patients included in the effectiveness analysis. Reasons for differences between the total number of patients analyzed for effectiveness outcomes and the total number of patients with demographic/pain diagnoses include:

- For some articles, not all patients reported in the demographic summaries were assessed for the effectiveness outcomes at the respective time intervals (e.g., demographic data was reported for all enrolled patients, and not all enrolled patients were implanted and/or completed the respective follow-up).

- For some articles where sufficient outcomes data was reported separately for different SCS system types, treatments, pain etiologies, etc., the sub-set of patients meeting all systematic review protocol eligibility criteria were sub-selected for analysis (e.g., excluding patients not meeting all systematic review eligibility criteria)

Success percentages (e.g., responder rates) were determined by dividing the number of patients meeting one or more definitions of effectiveness listed above in Section X.A. by the total number of patients that were evaluated for each respective time interval. The specific success criterion and time point for which the criteria was assessed is provided. If outcomes were reported for specific pain locations (e.g., overall, back, leg) and/or pain etiologies (e.g., FBSS, CRPS, etc.), outcomes results are provided for the respective pain areas and etiologies. For articles where a clinically significant change in the pain outcome measure was reported, summary statistics for the outcome measure at the assessed time points,

along with the number of participants assessed and results of any statistical tests are provided.

Publication	**Study Design**	**Demographic Data** (N patients, age, gender)	**Diagnoses** (Etiology, Condition, Implant Indications)	**Timeframe**	**Effectiveness Outcomes** Endpoint Duration: Success % (N of Patients) or clinically significant change in primary outcome measure
Villavicencio et al. 2000	Retrospective, non-randomized, single-center study	27 (implanted): 44.4% female Cylindrical percutaneous leads (used for analysis): 15/27, mean age (range): 53 (24-74) years	FBSS: 60%, N=9 Causalgia I and II: 13%, N=2 Neuropathic pain: 7%, N=1 Other: 20%, N=3	Follow-up duration (percutaneous): mean: 10.3 months Follow-up time points: all patients followed at least 6 months	Responder rate % (Criterion: PRP ≥ 50%): Mean follow-up: 10.3 months: 80% (12/15)
Forouzanfar et al. 2004	Prospective, non-randomized, single-center study	36 (implanted): mean age (± SD): 40 (± 10.1) years, range: 26-59 years; 66.7% female	CRPS I: 100%, N=36	Follow-up duration: Median (range): 24 months (12 to 24 months) Follow-up time points (n patients completing): baseline (36/36), 6 months (36/36), 12 months (36/36), 24 months (31/36) post implantation	Responder rate % (Criterion: ≥ 50% reduction in VAS): 6 months: 63.9% (23/36) 12 months: 61.1% (22/36) 24 months: 45.2% (14/31)

Harke et al. 2005	Prospective, non-randomized, single-center study	29 (implanted): mean age (± SD): 49.8 (± 14.5) years, range: 27-86 years; 55.2% female	CRPS I: 100%, N=29	Follow-up duration: mean: 35.6 ± 21 months. Follow-up time points: all patients followed at least 12 months	Responder rate % (Criterion: ≥ 50% reduction in VAS): 12 months: Deep pain: 96.6% (28/29) Allodynia: 100.0% (22/22) Last follow-up: 35.6 ± 21 months Deep pain: 100.0% (29/29) Allodynia: 100.0% (22/22)
Oakley et al. 2007 Supplement al articles: Krames et al. 2008	Prospective, non-randomized, multi-center study	65 (trialed): mean age (range): 52.0 (28-84) years; 40.0% female	FBSS: 61.5%, N=40 CRPS: 13.9%, N=9 Radiculopathy/neuropathy: 6.2%, N=4 Other: 4.6%, N=3 UnNnown: 13.9%, N=9	Follow-up duration: mean: 10.9 months Follow-up time points: baseline, 2 weeks, 3 months, 6 months, and every six months thereafter until study closure	Responder rate % (Criterion: ≥ 50% VAS reduction, stim ON vs. Off): 3 months: 63% (24/38) 6 months: 55% (18/33)
Kemler et al. 2008 Supplemental articles: Kemler et al. 2000, 2004	Prospective, single-center, RCT (2:1)	36 (trialed): mean age (± SD): 40 (± 12) years; 61.1% female	CRPS I: 100%, N=24	Follow-up duration: Median: 60 months Follow-up time points (n patients completing): baseline, 3, 6, 12, 24 (24/24), 36, 48, 60 months (20/24)	Criterion: significant reduction in mean VAS 24 months: mean reduction in VAS (SCS+PT group): 3.0 cm (N=24) mean reduction in VAS (PT alone): 0.0 cm (N=16) p=0.001 60 months:

					mean reduction in VAS (SCS+PT group): 2.5 cm (N=20) mean reduction in VAS (PT alone): 1.0 cm (N=13) p=0.06
Van Buyten et al. 2008	Prospective, non-randomized, multi-center study	45 (trialed): mean age: 51.3 years, range: 31.1 to 69.4 years; 66.7% female	Post-operative back or leg pain: 55%, N=25 Radicular pain: 27%, N=12 CRPS I: 7%, N=3 CRPS II: 7%, N=3 Other: 4%, N=2	Follow-up duration: mean (range) 12 months (8 to 13 months) Follow-up time points: baseline, 6, 12 months post-implant	Responder rate % (Criterion: PRP ≥ 50%): 12 0onths: 80.5% (33/41)
Moriyama et al. 2012	Prospective, non-randomized, multi-center study	34 (implanted): mean age (± SD): 53.5 (± 16.9) years; 52.9% female	FBSS: 50.0%, N=17 CRPS: 41.2%, N=14 Other: 8.8%, N=3	Follow-up duration: median: 6 months Follow-up time points (n patients completing): baseline, 1, 6 months (29/34)	Responder rate % (Criterion: ≥ 50% reduction in VAS): 6 0onths: Total Population: 65.5% (19/29), CRPS: 83.3% (10/12), FBSS: 46.7% (7/15), Other: 100% (2/2)
Kinfe et al. 2014	Prospective, non-randomized, single-center study	100 (trialed): mean age (range): 56.3 (27-89) years; 57.0% female Cylindrical percutaneous leads (used for analysis): N=50	FBSS: 100%, N=100	Follow-up duration: mean 1.2 ± 0.3 years (range: 0.4-2.0 years): Follow-up time points: all patients followed at least 4 months	Responder rate % (Criterion: ≥ 50% reduction in VAS): 1.2 ± 0.3 years (range: 0.4-2.0 years): 70% (35/50) (cylindrical percutaneous leads) Percentage pain relief (SD): 69.6% (11.2%)(cylindrical percutaneous leads)

Kapural et al. 2016 (primary source for effectiveness analysis) Supplemental articles: Kapural et al. 2015 (primary source for safety analysis)	Prospective, multi-center RCT	87 (per protocol population): mean age (± SD): 55.2 (± 13.4) years, range: 19.2 to 82.3 years; 58.6% female	FBSS: 74.7%, N=65 Radiculopathy: 60.9%, N=53 Degenerative disc disease: 57.5%, N=49 Spondylosis: 36.8%, N=32 Mild/moderate spinal stenosis: 19.5%, N=17 Sacroiliac dysfunction: 16.1%, N=14 Lumbar facet-mediated pain: 16.1%, N=14 Spondylolisthesis: 2.3%, N=2 Other chronic pain: 20.7%, N=18 Other neuropathic pain: 12.6%, N=11	Follow-up duration: median: 24 months Follow-up time points (n patients completing): baseline, 3, 6, 12 (80/81), 18, and 24 (71/81) months	Responder rate % (Criterion: ≥ 50% reduction in VAS): Leg pain 12 months: 50.0% (40/80) 24 months: 49.3% (35/71) Back pain 12 months: 51.3% (41/80) 24 months: 49.3% (35/71)
Denisova et al. 2016	Prospective, non-randomized, single-center study	75 (implanted): median age (range): 51.6 (26 to 83) years; 62.7% female	FBSS: 70.7%, N=53 CRPS II: 12.0%, N=9 Other: 17.3%, N=13	Follow-up duration: Range: 6-18 months Follow-up timepoints: baseline, 3, 6, 12 months	Criterion: significant reduction in mean VAS N=75 Baseline (mean (range) VAS): 6.5 (5-10) cm 3 months (mean VAS): 3.1 cm, Difference in means: -3.4 cm 6 months (mean VAS): 3.1 cm, Difference in means: -3.4 cm

					12 months (mean VAS): 3.6 cm, Difference in means: -2.9 cm
De Andres et al. 2017	Prospective, randomized, single-blinded (evaluators collecting pain ratings), single- center study	29 (implanted): mean age: 53.8 years; 62.1% female	FBSS: 100%, N=29	Follow-up duration: 12 months (all implanted participants) Follow-up time points (n patients completing): baseline (29/29), 3 (29/29), 6 (29/29), 12 months (29/29) post-implant	Criterion: significant reduction in mean NRS Conventional frequency group (excluding HF10) (N=29): 6 months: mean of the difference (SD): -1.67 (2.69), P.000 12 months: mean of the difference (SD) -1.44 (2.28), P.000
Deer et al. 2017	Prospective, multi-center, RCT	76 (trialed): mean age (± SD): 52.5 (± 11.5) years; 51.3% female	CRPS: 56.6%, N=43 Causalgia: 43.4%, N=33	Follow-up duration: median (implanted): 12 months (range: 3-12 months) Follow-up time points (n patients completing): baseline, 3 (54/54), 6 (52/54), 12 months (50/54)	Responder rate % (Criterion: ≥ 50% reduction in VAS in the primary area of pain with no incidence of stimulation- induced neurological deficits): SCS arm: 3 months: 55.7% (39/70)* 6 months: 60.3% (41/68)* 12 months: 53.0% (35/66)* *Randomized subjects who did not proceed to permanent implant were considered treatment failures for this

					endpoint at each study visit.
Gatzinsky et al. 2017	Prospective, non-randomized, multi-center study	93 (trialed): mean age (± SD): 52 (± 12) years; 52.7% female	FBSS: 100.0%, N=93	Follow-up duration: median: 12 months Follow-up time points (n patients completing): baseline, 6 (68/81), 12 months (65/81) post implant	Responder rate % (Criterion: ≥50% reduction in VAS): 6 months: Leg pain: 63.3% (38/60) Back pain: 34.0% (22/65) 12 months: Leg pain: 63.1% (41/65) Back pain: 40.3% (25/62)
Tanei et al. 2018	Retrospective, non-randomized, single-center study	8 (implanted): mean age (± SD): 63.5 (± 15.1) years, range: 40-78 years; 44.4% female	FBSS: 62.5%, N=5 Peripheral neuropathy: 25.0%, N=2 CRPS I: 12.5%, N=1	Follow-up duration: mean (± SD): 29.5 (± 16.8) months, range: 12-63 months Follow-up time points: baseline, 1, 6, 12 months, last follow-up	Responder rate % (Criterion: ≥50% reduction in VAS): 6 Months: Total population: 50.0% (4/8), FBSS: 40.0% (2/5), CRPS I: 100.0% (1/1), PNP: 50.0% (1/2) 12 Months: Total population: 50.0% (4/8), FBSS: 40.0% (2/5), CRPS I: 100.0% (1/1), PNP: 50.0% (1/2) Last Follow-up (mean: 29.5 months): Total population: 50.0% (4/8), FBSS: 40.0% (2/5), CRPS I: 100.0% (1/1),

					PNP: 50.0% (1/2)
Benyamin et al. 2020	Prospective, non-randomized, multi-center study	32 (implanted): mean age (± SD): 56.0 (± 11.9) years; 59.4% female	FBSS: 100.0%, N=32	Follow-up duration: median: 3 months Follow-up time points (n patients completing): baseline, 1, 2, and 3 months (29/32) post-implant	Responder rate % (Criterion: ≥ 3 point reduction in NRS) Overall pain 3 months: 69.0% (22/32), mean reduction of 3.7 points from baseline (P < 0.01)
Graziano et al. 2020	Prospective, non-randomized, single-center	23 (implanted): mean age (± SD): 61.6 (± 11.5) years, range: 38-79 years; 47.8% female	FBSS: 100.0%, N=23	Follow-up duration: mean (±SD): 12.9 (± 8.2) months, range: 1- 25 months Follow-up time points: all patients followed at least 1 month.	Responder rate % (Criterion: VAS ≥ 3): 12.9 months (range: 1 to 25 months)*: 87.0% (20/23) *Patients meeting success criteria in the publication but with < 3 months follow-up are excluded from the analysis. Patients not meeting success criteria are included independent of follow-up time and counted as failures.
Hatheway et al. 2021	Prospective, non-randomized, single-arm, multi-center study	103 (implanted): mean age (range) 60.8 (29-93) years; 54.4% female	FBSS: 44.7%, N=46 Radicular pain syndrome: 27.2%, N=28	Follow-up duration: median: 12 months Follow-up time points (n patients completing):	Responder rate % (95% CI) (Criterion: ≥ 50% reduction in VAS): Overall pain, Low back pain, Leg pain

			Degenerative disc disease: 13.6%, N=14 CRPS I: 1.0%, N=1 Other: 13.6%, N=14	baseline, 3 months (98/103), 6 months (96/103), 12 months (91/103) post- activation	3 months (N=103): 68.3% (59.0–77.5%) 59.8% (49.9–69.7%) 77.4% (69.1–85.7%) 6 months (N=103): 66.2% (56.9–75.5%) 58.4% (48.8–68.1%) 72.2% (63.1–81.3%) 12 months (N=103): 59.1% (49.0–69.2%) 57.1% (47.1–67.1%) 67.9% (58.5–77.2%)
Kallewaard et al. 2021	Retrospective, multi-center observational cohort study	188 (implanted): mean age (± SD): 60.0 (± 12.3) years; 53.7% female	FBSS: 64%, N=120 Lumbosacral radiculopathy: 21%, N=40 Compressive myelopathy from spinal stenosis: 9%, N=17 Other: 6%, N=11	Follow-up duration: mean (± SD): 9.73 (±6.81) months Follow-up time points: baseline, 3 months, 12 months.	Responder rate % (Criterion: ≥ 50% reduction in NRS for overall pain): 3 mo: 68.4% (80/117) 12 mo: 70.0% (63/90)

Collectively, the data in Table 11 were obtained from a total of 638 (73.8%) patients diagnosed with FBSS, 222 (25.7%) patients diagnosed with CRPS I, CRPS II, or CRPS (unspecified), 137 (15.9%) patients diagnosed with radiculopathy/radicular pain syndrome, 63 (7.3%) patients diagnosed with degenerative disc disease, and patients with other less frequently occurring diagnoses. Overall, the population is consistent with the Prospera SCS System indications.

The improvement in pain across all conditions/etiologies/pain locations for the 15/18 studies with response rates reported based on success percentage ≥ 50% reduction and/or clinically significant reductions in a validated patient-reported assessment of pain (e.g., VAS, NRS, PRP)) ranged from:

- All study follow-up durations (range: 3.0 to 35.6 months) (15 studies): success rates ranged from 34% to 100%, with 10/15 studies reporting success rates ≥ 50%, and 7/15 studies reporting success rates ≥ 68%

- Long term pain relief (≥12 months) (range: 12.0 to 35.6 months) (11 studies): success rates ranged from 40% to 100%, with 8/11 studies reporting success rates ≥ 50%, and 5/11 studies reporting success rates ≥ 70%

The improvement in pain across all conditions/etiologies/pain locations for the 3/18 studies reporting clinically significant reductions in a validated patient-reported assessment of pain (e.g., VAS, NRS, PRP) ranged from:

- All study follow-up durations (range: 3.0 to 60 months) (3 studies): mean improvement in pain at follow-up compared to baseline ranged from 1.44 unit mean reduction (NRS) to 3.4 unit mean reduction (VAS). All results were considered clinically and/or statistically significant by the publication physician authors

3. Pediatric Extrapolation
   In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population.

D. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. None of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

XI. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Neurological Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The evaluation of effectiveness is based on data reported from a total of 18 studies (22 articles) representing a total of 864 patients implanted with an SCS systems. The median sample size was 37 (range, 8 to 117) patients, and 600 (69.4%) of the patients were female. The median average age was 53.3 (range, 40.0 to 63.5) years. The median follow-up time was 12.0 (range, 3.0 to 60.0) months. The studies were published between 2000 and 2021, and 6/18 (33.3%) studies were conducted in the United States, representing 338 (39.1%) of the patients in the effectiveness analysis. The primary treated pain diagnoses were FBSS: N=638 (73.8%), CRPS: N=222 (25.7%), radiculopathy/radicular pain syndrome: N=137 (15.9%) and DDD: N=63 (7.3%). These characteristics are consistent with the patient population for which the Prospera SCS System is indicated.

The improvement in pain across all conditions/etiologies/pain locations for the 15/18 studies with response rates reported based on success percentage ≥ 50% reduction and/or clinically significant reductions in a validated patient-reported assessment of pain (e.g., VAS, NRS, PRP)) ranged from:

- 34% to 100%, with 10/15 studies reporting success rates ≥ 50%, and 7/15 studies reporting success rates ≥ 68% (all follow-up durations)

- 40% to 100%, with 8/11 studies reporting success rates ≥ 50%, and 5/11 studies reporting success rates ≥ 70% (follow-up ≥ 12 months)

The results of the systematic literature review of similar devices support the effectiveness of SCS therapy in treating patients who suffer from chronic, intractable pain in the trunk and/or limbs which may include unilateral or bilateral pain resulting from the indications for use listed in Section II.

B. Safety Conclusions

The risks of the device are based on incidence of adverse events (AE)s, device-related complications and/or surgical interventions reported from a total of 13 study populations representing a total of 626 patients implanted with SCS systems of interchangeable design to the Prospera SCS System. The median sample size was 42 (range, 15 to 97) patients, and 386 (61.7%) of the patients were female. The median average age was 52 (range, 39.0 to 56.3) years. The median follow-up time was 12.1 (range, 3.0 to 60.0) months. The studies were published between 1999 and 2020, and 4/13 (30.8%) studies were conducted in the United States, representing 225 (35.9%) of the patients in the safety analysis. The primary treated pain diagnoses were FBSS:

N=427 (68.2%), CRPS: N=153 (24.4%), radiculopathy/radicular pain syndrome: N=69 (11.0%) and DDD: N=49 (7.8%). These characteristics are consistent with the patient population for which the Prospera SCS System is indicated.

The clinical evidence provided to support the safety of the Prospera SCS System includes:

- A systematic literature review, safety summary results and meta-analysis of study populations implanted with SCS systems of interchangeable design to the Prospera SCS System.

- Analysis of Manufacturer and User Facility Device Experience (MAUDE) Database search results for the SCS systems of interchangeable design to the Prospera SCS System utilized in the studies selected in the systematic review.

Summary information for the adverse events, device-related complications and surgical interventions reported in the 13 study populations:

- A total of 135 AEs were reported in the safety population of 626 patients. Pain at the implant site was the most frequently occurring individual AE reported (30 events [5.9%]), followed by infection (19 events [3.2%]), pain (12 events [5.7%]) and inflammation at implant site (10 events [5.3%]).

- A total of 211 device-related complications were reported in the safety population of 626 patients. Lead migration was the most frequently occurring device-related complication (49 events [9.6%]), followed by ineffective pain control (31 events [9.7%]), uncomfortable stimulation (30 events [8.8%]), device malfunction
- (28 events [8.7%]), premature generator battery depletion (19 events [8.7%]) and over/under-stimulation (17 events [15.9%]).

- A total of 205 surgical interventions (e.g., IPG/lead revision, explant, replacement) were reported in the safety population of 626 patients, resulting in an overall rate of 32.7%.

Summary information for the meta-analyzed events reported in at least 4 studies, includined stimated pooled rates of occurrence:

- Four adverse event types: pain at the implant site (3.9%) infection (2.7%), hematoma (2.3%) and CSF leak (1.7%)
- Five device-related complication event types: ineffective pain control

(permanent implant) (12.6%), device malfunction (8.2%), uncomfortable stimulation (7.9%), lead migration (7.4%), and lead fracture/failure (3.5%)

- Surgical intervention: any device-related intervention (e.g., IPG/lead revision, explant, replacement) (31.4%)

Summary information for the meta-analyzed events reported in at least 4 studies, including estimated pooled rates of occurrence:

- Four adverse event types: pain at the implant site (3.9%) infection (2.7%), hematoma (2.3%) and CSF leak (1.7%)
- Five device-related complication event types: ineffective pain control (permanent implant) (12.6%), device malfunction (8.2%), uncomfortable stimulation (7.9%), lead migration (7.4%), and lead fracture/failure (3.5%)
- Surgical intervention: any device-related intervention (e.g., IPG/lead revision, explant, replacement) (31.4%)

The reported event rates including the estimated pooled rates of occurrence of these events that were appropriate for meta-analysis are consistent with trends reported in the literature and in other similarly designed evaluations of SCS system safety based on large- scale systematic reviews.[1–5] Additionally, the results reported for non-meta-analyzed event types, and the results of the MAUDE Database analysis of patient and device problems are consistent with the results above, and indicate relatively stable reporting of well- known, previously identified risks associated with SCS.

The results of the systematic literature review support the safety of SCS therapy (delivered by legally marketed, fully implantable SCS systems with interchangeable designs to the Prospera SCS system) in treating patients who suffer from chronic, intractable pain in the trunk and/or limbs which may include unilateral or bilateral pain resulting from for the indications for use listed in Section II.

C. Benefit-Risk Determination

The probable benefits of the device are also based on data collected collected in this systematic literature review. The primary treated pain diagnoses were failed back surgery syndrome (FBSS): N=638 (57.5%), complex regional pain syndrome (CRPS): N=245 (22.1%), radiculopathy/radicular pain syndrome: N=137 (12.4%) and degenerative disc disease (DDD): N=96 (8.7%). These characteristics are consistent with the patient population for which the Prospera SCS System is indicated.

The improvement in pain across all conditions/etiologies/pain locations for the 15/18 studies with response rates reported ranged from:

- 34% to 100%, with 10/15 studies reporting success rates ≥50%, and 7/15 studies reporting success rates ≥ 68% (all follow-up durations)

- 40% to 100%, with 8/11 studies reporting success rates ≥ 50%, and 5/11 studies reporting success rates ≥ 70% (follow- up ≥12 months)

The probable risks of the device are also based on data collected in this systematic literature review. The adverse events that were reported were consistent with the safety profile of SCS systems. Rates of study related AEs, device-related complications, abd surgical interventions reported in this systematic literature review are consistent with this device type. There are no new risks or new adverse events identified in this subset of the patient population.

1. Patient Perspective
   This submission either did not include specific information on patient perspectives or the information did not serve as part of the basis of the decision to approve or deny the PMA for this device.

In conclusion, given the available information above, the data support that for the indication for use of the devicethe probable benefits outweigh the probable risks.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The results from the clinical evaluation support reasonable assurance of the safety and effectiveness of the Prospera SCS System, as well its long-term performance, when used in a manner consistent with its labeling and intended use. The evidence supporting the safety and effectiveness of the Prospera SCS System is based on a foundation of 22 years of clinical research and experience reported in the published studies of patient populations (with characteristics that are consistent with the Prospera SCS System indications) implanted with SCS systems of similar design to the Prospera SCS System. The analyses also support a clinical benefit to risk determination that is favorable.

XIII. CDRH DECISION

CDRH issued an approval order on April 3, 2023

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.

XV. REFERENCES

Benyamin R, Galan V, Hatheway J, et al. Options: A Prospective, Open- Label Study of High-Dose Spinal Cord Stimulation in Patients with Chronic Back and Leg Pain. Pain Physician. 2020;23(1):87-98.

De Andres J, Monsalve-Dolz V, Fabregat-Cid G, et al. Prospective, Randomized Blind Effect-on-Outcome Study of Conventional vs High- Frequency Spinal Cord Stimulation in Patients with Pain and Disability Due to Failed Back Surgery Syndrome. Pain Med. 2017;18(12):2401- 2421.

Deer TR, Levy RM, Kramer J, et al. Dorsal root ganglion stimulation yielded higher treatment success rate for complex regional pain syndrome and causalgia at 3 and 12 months: a randomized comparative trial. Pain. 2017;158(4):669-681.

Denisova NP, Rogov DY, Rzaev DA, Khabarova EA, Dmitriev AB. [Spinal cord stimulation in the treatment of chronic pain syndromes]. Zh Vopr Neirokhir Im N N Burdenko. 2016;80(2):47-52.

Forouzanfar T, Kemler MA, Weber WE, Kessels AG, van Kleef M. Spinal cord stimulation in complex regional pain syndrome: cervical and lumbar devices are comparably effective. Br J Anaesth. 2004;92(3):348-353.

Gatzinsky K, Baardsen R, Buschman HP. Evaluation of the Effectiveness of Percutaneous Octapolar Leads in Pain Treatment with Spinal Cord Stimulation of Patients with Failed Back Surgery Syndrome During a 1-Year Follow-Up: A Prospective Multicenter International Study. Pain Pract. 2017;17(4):428-437.

Graziano F, Gerardi RM, Lo Bue E, et al. Surgical Back Risk Syndrome and Spinal Cord Stimulation: Better Safe Than Sorry. World Neurosurg. 2020;133:e658-e665.

Harke H, Gretenkort P, Ladleif HU, Rahman S. Spinal cord stimulation in sympathetically maintained complex regional pain syndrome type I with severe disability. A prospective clinical study. Eur J Pain. 2005;9(4):363-373.

Hatheway JA, Mangal V, Fishman MA, et al. Long-Term Efficacy of a Novel Spinal Cord Stimulation Clinical Workflow Using Kilohertz Stimulation: Twelve-Month Results From the Vectors Study. Neuromodulation. 2021;24(3):556-565.

Kallewaard JW, Paz-Solis JF, De Negri P, et al. Real-World Outcomes Using a Spinal Cord Stimulation Device Capable of Combination Therapy for Chronic Pain: A European, Multicenter Experience. J Clin Med. 2021;10(18).

Kapural L, Yu C, Doust MW, et al. Novel 10-kHz High-frequency Therapy (HF10 Therapy) Is Superior to Traditional Low-frequency Spinal Cord Stimulation for the Treatment of Chronic Back and Leg Pain: The SENZA- RCT Randomized Controlled Trial. Anesthesiology. 2015;123(4):851- 860.

Kapural L, Yu C, Doust MW, et al. Comparison of 10-kHz High-Frequency and Traditional Low-Frequency Spinal Cord Stimulation for the Treatment of Chronic Back and Leg Pain: 24-Month Results From a Multicenter, Randomized, Controlled Pivotal Trial. Neurosurgery. 2016;79(5):667-677.

Kemler MA, Barendse GA, van Kleef M, et al. Spinal cord stimulation in patients with chronic reflex sympathetic dystrophy. N Engl J Med. 2000;343(9):618-624.

Kemler MA, Barendse GA, Van Kleef M, Van Den Wildenberg FA, Weber WE. Electrical spinal cord stimulation in reflex sympathetic dystrophy: retrospective analysis of 23 patients. J Neurosurg. 1999;90(1 Suppl):79-83.

Kemler MA, De Vet HC, Barendse GA, Van Den Wildenberg FA, Van Kleef M. The effect of spinal cord stimulation in patients with chronic reflex sympathetic dystrophy: two years' follow-up of the randomized controlled trial. Ann Neurol. 2004;55(1):13-18.

Kemler MA, de Vet HC, Barendse GA, van den Wildenberg FA, van Kleef M. Effect of spinal cord stimulation for chronic complex regional pain syndrome Type I: five-year final follow-up of patients in a randomized controlled trial. J Neurosurg. 2008;108(2):292-298.

Kinfe TM, Quack F, Wille C, Schu S, Vesper J. Paddle versus cylindrical leads for percutaneous implantation in spinal cord stimulation for failed back surgery syndrome:

a single-center trial. J Neurol Surg A Cent Eur Neurosurg. 2014;75(6):467-473.

Krames ES, Oakley JC, Foster AM, et al. Spinal cord stimulation has comparable efficacy in common pain etiologies. Neuromodulation. 2008;11(3):171-181.

Moriyama K, Murakawa K, Uno T, et al. A prospective, open-label, multicenter study to assess the efficacy of spinal cord stimulation and identify patients who would benefit. Neuromodulation. 2012;15(1):7- 11; discussion 12.

Oakley JC, Krames ES, Prager JP, et al. A new spinal cord stimulation system effectively relieves chronic, intractable pain: a multicenter prospective clinical study. Neuromodulation. 2007;10(3):262-278.

Tanei T, Kajita Y, Maesawa S, et al. Long-term Effect and Predictive Factors of Motor Cortex and Spinal Cord Stimulation for Chronic Neuropathic Pain. Neurol Med Chir (Tokyo). 2018;58(10):422-434.

Van Buyten JP, Fowo S, Spincemaille GH, et al. The restore rechargeable, implantable neurostimulator: handling and clinical results of a multicenter study. Clin J Pain. 2008;24(4):325-334.

Villavicencio AT, Leveque JC, Rubin L, Bulsara K, Gorecki JP. Laminectomy versus percutaneous electrode placement for spinal cord stimulation. Neurosurgery. 2000;46(2):399-405; discussion 405-396.