SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

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

Device Trade Name: Precision™ Spinal Cord Stimulator System
Precision Spectra™ Spinal Cord Stimulator System
Precision Novi™ Spinal Cord Stimulator System
Precision™ Montage™ MRI Spinal Cord Stimulator System
Precision™ Montage™ Spinal Cord Stimulator System
Spectra WaveWriter™ Spinal Cord Stimulator System

Collectively referred to as the Precision™ and Spectra WaveWriter™ Spinal Cord Stimulation (SCS) Systems

Device Procode: LGW

Applicant's Name and Address: Boston Scientific Neuromodulation Corporation
24242 Rye Canyon Loop
Valencia, CA 91355

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P030017/S275

Date of FDA Notice of Approval: August 11, 2017

The original PMA P030017 was approved on April 27, 2004 and is indicated as an aid in the management of chronic intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with the following: failed back surgery syndrome, intractable low back pain and leg pain. The SSED to support the indication is available on the CDRH website and is incorporated by reference here. The current supplement was submitted to expand the indication for the Boston Scientific Spinal Cord Stimulator Systems.

II. INDICATIONS FOR USE

The Boston Scientific Spinal Cord Stimulator Systems are indicated as an aid in the management of chronic intractable pain of the trunk and/or limbs including unilateral or bilateral pain associated with the following: failed back surgery syndrome, Complex Regional Pain Syndrome (CRPS) Types I and II, intractable low back pain and leg pain.

Associated conditions and etiologies may be

- radicular pain syndrome,

- radiculopathies resulting in pain secondary to failed back syndrome or herniated disc,
- epidural fibrosis,
- degenerative disc disease (herniated disc pain refractory to conservative and surgical interventions),
- arachnoiditis,
- multiple back surgeries.

III. CONTRAINDICATIONS

The following patients are contraindicated from being treated with Boston Scientific Spinal Cord Stimulator Systems:

- Poor surgical candidates;
- Unable to operate the SCS system;
- Failed trial stimulation by failing to receive effective pain relief;
- Pregnant.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Boston Scientific Spinal Cord Stimulator Systems labeling.

V. DEVICE DESCRIPTION

Boston Scientific Spinal Cord Stimulator (SCS) Systems are totally implanted devices that deliver electrical stimulation to the dorsal column of the spinal cord for the treatment of chronic intractable pain of the trunk and/or limbs. Figures 1 and 2 display main system components and the typical location of implanted components.

Figure 1: The Boston Scientific Spinal Cord Stimulation System

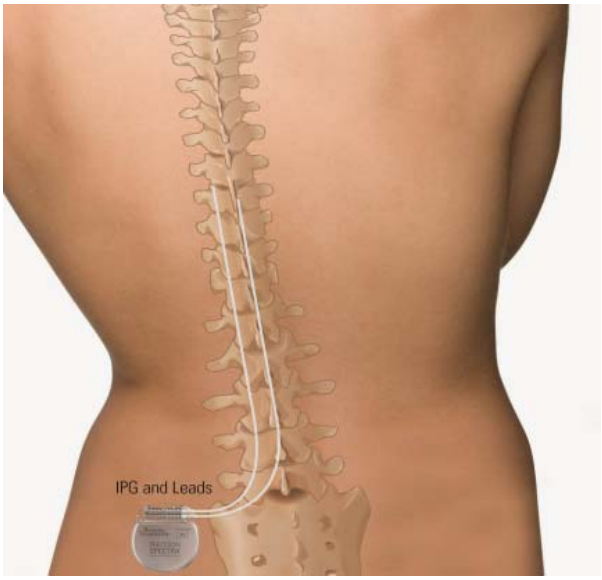

Figure 2: Typical location of implanted pulse generator and percutaneous leads.

A. Implanted Components

The implanted components of the Boston Scientific SCS System include the following:

- Implanted Pulse Generator (IPG): Generates programmable electrical pulses that are conducted to the spinal cord via leads. Includes rechargeable or non-rechargeable batteries.
    - IPG models include Precision, Precision Spectra, Precision Novi, Spectra Wavewriter, Precision Montage and Precision Montage MRI
- Percutaneous and Surgical Leads: Available in various lengths and configurations, the leads are connected to the IPG to deliver stimulation to the spinal cord.
    - Percutaneous lead models include Linear, Linear ST, Linear 3-4, Linear 3-6, Infinion, Infinion CX, Avista MRI that is used specifically with Precision Montage MRI System
    - Surgical lead models include CoverEdge that is used with the Precision Spectra and Spectra Wavewriter Systems, and Artisan
- Lead Extension: Lead Extensions are designed to provide additional length to connect the leads to the stimulator. Lead extensions come in lengths of 25cm, 35cm, and 55cm.

- Lead Splitters: Optional component used to connect multiple leads to the IPG.

- Implantable Adaptors: Adaptors are provided to connect other manufacturer's leads to Boston Scientific IPGs.

- Suture Sleeves and Anchors: Used to anchor the lead to the supraspinous ligament or deep fascia.

B. External Components

The external components of the Boston Scientific SCS System include the following:

- External Trial Stimulator (ETS): The ETS is intended to provide trial stimulation with implanted leads before permanent placement of the IPG. It provides the identical stimulation capabilities as the IPG.

    - ETS models are the Precision ETS used with the Precision System, and the Precision Spectra ETS used with all other Boston Scientific SCS Systems

- Clinician Programmer (CP): The CP is used by the clinician to program the IPG and ETS, and thus prescribe stimulation therapy for the patient.

- Remote Control (RC): The Remote Control is a hand-held, battery operated unit that uses telemetry to communicate with the IPG and ETS. It allows the patient to control the stimulation therapy prescribed by the clinician (e.g., turn SCS system on and off).

    - RC models are the Precision RC used with the Precision System, and the FreeLink RC used with all other Boston Scientific SCS Systems

- Programming Wand: The programming wand is used with some systems to allow the CP to communicate wirelessly with the IPG and ETS.

- Charger: The Charger is used with all rechargeable IPGs to transcutaneously charge the IPG battery.

C. Accessories

Accessories provided with the Boston Scientific SCS Systems include the following:

- Torque Wrench: Used to tighten the set screws that lock the lead into the IPG.

- Stylets: Used to maneuver the lead through the epidural space to the desired implant location.

- IPG Template: guides the physician to create the correct sizing of the subcutaneous pocket.
- Insertion Needle: used during implant procedure to introduce the percutaneous lead into the epidural space.
- Lead Blank: optionally used during implant procedure to clear a path for the introduction of the lead into the epidural space.
- Tunneling Tool: Used to create a subcutaneous tunnel from the IPG site to the lead implant location.
- IPG Connector Plug/Port Plug: Provided to seal the port(s) of the IPG that are not in use.
- OR (Operating Room) Cable and Extension: Used to connect the lead to the ETS during intraoperative testing and trial phase.
- External Adaptors: For connecting other manufacturer's SCS leads to the Boston Scientific external stimulators during in-office evaluation.

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 (including Non-Steroidal Anti-inflammatory Drugs and opioids), 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

Currently, the Boston Scientific Spinal Cord Stimulator System for the treatment of chronic pain of the trunk and limbs is approved for commercial distribution in the United States, European Community (EC) countries, Canada, Australia/New Zealand, Brazil, Kuwait, Israel, Japan, Argentina, Chile, Colombia, Costa Rica, Ecuador, El Salvador, Guatemala, Mexico, Panama, Peru, Russia, South Africa, Turkey, and United Arab Emirates.

The device has not been withdrawn from marketing for any reason related to its safety or effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of SCS Systems. The Boston Scientific SCS systems are similar to other legally-marketed SCS systems in intended use, target patient population, technology, device design and output characteristics. Therefore, the following list of potential adverse effects have been identified from peer-reviewed published literature that describes studies of all legally-marketed 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 Boston Scientific 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 any surgical procedure: abscess; cellulitis; excessive fibrotic tissue; wound dehiscence; wound, local or systemic infection; wound necrosis; edema; inflammation; foreign body reaction; hematoma; seroma; thrombosis; ischemia; embolism; thromboembolism; hemorrhage; thrombophlebitis; adverse reactions to anesthesia; hypertension; pulmonary complications; organ, nerve or muscular damage; gastrointestinal or genitourinary compromise; seizure, convulsion, or changes to mental status; inability to resume activities of daily living; and death.

- Risks associated with SCS system placement procedures: temporary pain at the implant site, infection, cerebrospinal fluid (CSF) leakage, CSF fistula, epidural hemorrhage, bacterial meningitis, seroma, hematoma, and paralysis. Patient use of anticoagulation therapies may increase the risk of procedure-related complications such as hematomas, which could produce paralysis.

- Risks associated with the use of a SCS system: lead migration; IPG migration; allergic response or tissue reaction to the implanted system material; hematoma or seroma at the implant site; skin erosion at the implant site; persistent pain at the IPG, extension, or lead site; radicular chest wall stimulation; disturbed urination; dysesthesia; decubitus; premature battery depletion; loss of pain relief over time; and uncomfortable stimulation or ineffective pain control caused by random failure of the system components or battery, changes in electrode position, loose electrical connections, lead or extension insulation breaches or fractures.

IX. SUMMARY OF NONCLINICAL STUDIES

Pre-clinical studies (bench and animal) previously submitted to FDA in the Original PMA application (P030017) and supplements continue to support the safety of the commercially available Boston Scientific SCS System for treatment of chronic intractable pain of the trunk and/or limbs. No additional preclinical studies were required to evaluate the safety of Boston Scientific SCS therapy for the treatment of the new patient populations. The previously approved supplements which support the device and its components are listed below in Table 1.

Table 1. Summary of System/Device Components and Their Respective Approval References

System/Device Component	Approval Reference
Precision™ Spinal Cord Stimulator System Includes IPG, Linear Leads, Lead Extensions, External Trial Stimulator, Remote Control, Charger, Base Station, Clinician Programmer	P030017
Artisan Leads	P030017/S008
Linear ST Leads	P030017/S020
Connector M1	P030017/S025
Linear 3-4 and Linear 3-6 Leads	P030017/S100
Infinion Leads	P030017/S119
Precision Spectra™ Spinal Cord Stimulator System Includes IPG, FreeLink Remote Control, External Trial Stimulator, Programming Wand, Clinician Programmer	P030017/S134
CoverEdge Leads	P030017/S152
Infinion CX Leads	P030017/S191
M8 Adapter	P030017/S202
S8 Adapter	P030017/S210
Precision Novi™ Spinal Cord Stimulator System	P030017/S217
Precision™ Montage™ MRI Spinal Cord Stimulator System Includes Avista MRI leads	P030017/S235
Precision™ Montage™ Spinal Cord Stimulator System	P030017/S235
Spectra WaveWriter™ Spinal Cord Stimulator System	P030017/S271

X. SUMMARY OF PRIMARY CLINICAL STUDIES

The Boston Scientific SCS Systems are approved as an aid in the management of chronic intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with the following: failed back surgery syndrome, intractable low back pain and leg pain.

A. Study Design

The safety and effectiveness of the Boston Scientific SCS System was based on a systematic review of published clinical studies of the safety and effectiveness of commercially available, fully implantable SCS systems in treating chronic intractable pain of the trunk and/or limb, including unilateral or bilateral pain associated with Complex Regional Pain Syndrome Types I and II, radicular pain syndrome,

radiculopathies resulting in pain secondary to failed back syndrome or herniated disc, epidural fibrosis, degenerative disc disease (herniated disc pain refractory to conservative and surgical interventions), arachnoiditis, and multiple back surgeries. The Boston Scientific SCS System is similar in design, technology, performance, and intended use to the SCS systems used to treat the patient populations in the submitted published clinical studies. Therefore, data obtained from these published studies were used to establish a reasonable assurance of safety and effectiveness of the Boston Scientific SCS Systems for use in these specific patient populations, and were the basis for the PMA approval decision.

A total of 44 publications that reported data on 40 study populations (some publications reported data on the same patient population at different time points), representing a total of 3413 patients were identified for inclusion in the safety analysis. A total of 22 papers (19 studies) representing a total of 633 implanted patients were included in the effectiveness analysis.

The Boston Scientific 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 effectiveness of SCS Systems when they are used to treat chronic intractable pain of the trunk and/or limb, including unilateral or bilateral pain associated with Complex Regional Pain Syndrome Types I and II, radicular pain syndrome, radiculopathies resulting in pain secondary to failed back syndrome or herniated disc, epidural fibrosis, degenerative disc disease (herniated disc pain refractory to conservative and surgical interventions), arachnoiditis, and multiple back surgeries.

Effectiveness was demonstrated by patient-reported outcome measures of pain, and using one or more of the following:

1. A reduction of pain as demonstrated by a clinically significant reduction in the Visual Analog Scale (VAS) score;

2. A 50% reduction in pain using a validated patient-reported assessment of pain relief (e.g., a 3 or 4 point scale), in at least 30% of patients included in the study;

3. A clinically significant difference in pain reduction as measured by a clinically validated patient-reported outcome (e.g., VAS) when compared to a control group.

Safety of the Boston Scientific SCS System was established using literature articles by examining the incidence of complications of the SCS systems used in each study. The articles describe studies of SCS Systems when used to treat chronic intractable pain of the trunk and/or limb, including unilateral or bilateral pain associated with Failed Back Surgery Syndrome (FBSS), intractable low back and leg pain, Complex Regional Pain Syndrome Types I and II, radicular pain syndrome, radiculopathies resulting in pain secondary to failed back syndrome or herniated disc, epidural

fibrosis, degenerative disc disease (herniated disc pain refractory to conservative and surgical interventions), arachnoiditis, and multiple back surgeries. Literature articles that identified patients as having FBSS, with no further delineation of their pain condition or etiology, were included in the safety analysis because we believe it is reasonable to assume that the majority of these patients received surgery for one of the conditions of interest (e.g., herniated disc) or developed one or more of the conditions or etiologies following the surgery (e.g., arachnoiditis, radicular pain syndrome).

B. Literature Search Strategy

The strategy for the SCS literature search was chosen to ensure inclusion of specific populations of SCS subjects into the safety and effectiveness analysis. These populations were patients who had pain from: multiple back operations, post-laminectomy, post-discectomy or other disc surgery, epidural fibrosis, arachnoiditis, herniated disc, degenerative disc disease, radiculopathy or other radicular syndromes, and complex regional pain syndrome (CRPS), previously known as reflex sympathetic dystrophy (RSD) and causalgia.

The literature search strategy consisted of the following steps:

1. Search of PubMed database for indexed articles using search terms for SCS systems, treatment of trunk and/or limb pain, and treatment of the specific pain conditions and etiologies of interest (e.g., CRPS Type I and II, arachoiditis) (Pubmed database available through National Center for Biotechnology Information [NCBI] at the National Library of Medicine [NLB] located at the National Institute of Health [NIH]).

2. The following exclusion criteria were applied to the search results:

    - Angina, peripheral nerve stimulation, peripheral vascular disease, peripheral artery disease, spinal cord injury, SCS to induce movement, cervical SCS.
    - All data in the study were for single contact leads.
    - Case reports with 3 or fewer subjects.
    - Trial SCS data only.
    - SCS used only with other treatments under study; e.g. intrathecal drug pump.
    - Article in language other than English.

3. Determination of studies appropriate for the safety summary (total of 44 publications and 40 subject populations), which required that the article be published within the last 20 years, and that it include a report of adverse event or device complication data.

4. Determination of studies appropriate for the effectiveness summary (total of 22 publications and 19 subject populations), which required the following:

    - A defined population that included one or more of the conditions or etiologies of interest (i.e., adequate inclusion/exclusion criteria).

- Effectiveness outcomes assessed at least 6 months after implantation.
- Specific pain endpoints (e.g., VAS)
- Analysis of effectiveness outcomes for specific patient population having one or more of the conditions or etiologies of interest.

C. Safety and Effectiveness Results

1. Safety Results

   Table 2 provides a summary of Adverse Events (AEs) reported in 44 publications that reported data on 40 study populations (4 publications reported on the same subjects at later time points), and that included a total of 3413 implanted patients, were analyzed and summarized. Some studies reported the number of AEs whereas others reported the number of patients in which the AEs occurred. To combine data from these studies, each event was included as an AE count. For example, if one patient was reported as having three additional interventions for two infections, this was counted as five total AE counts, three toward Additional Intervention Required and two toward Infection. The incidence of each event is reported as a percentage of occurrences in total implanted patients, i.e. Incidence = (Number of AEs / Number of implanted patients) x 100.

Table 2. Summary of SCS Risks Identified in Clinical Studies

Clinical Harm	Counts	Incidence = (Count/3413 implanted patients)*100
Accidental Injuries, Secondary to Stimulation	4	0.12%
Abnormal Healing	4	0.12%
Adhesions	4	0.12%
Additional Intervention Required	816	23.91%
Allergic Reaction	3	0.09%
Cerebrospinal Fluid (CSF) Leak	8	0.23%
Death (none described as related to SCS)	4	0.12%
Dehiscence	6	0.18%
Discomfort	51	1.49%
Erosion	6	0.18%
Hematoma	21	0.62%
Inadequate Stimulation	103	3.02%
Infection	119	3.49%
Inflammation	5	0.15%
Muscle Spasm, Stimulation Related	4	0.12%

Clinical Harm	Counts	Incidence = (Count/3413 implanted patients)*100
Musculoskeletal Stiffness or Spasm, Not Stimulation Related	2	0.06%
Nerve Injury	23	0.67%
Neurostimulation Effects on Other Systems, e.g. dizziness, urinary effects	8	0.23%
Overstimulation of Tissue	2	0.06%
Pain	276	8.09%
Paralysis	13	038%
Seroma	14	0.41%
Tissue Damage	1	0.03%
Undesired Sensations, Target or Non-Target Stimulation Area	127	3.72%

Additional interventions were the most commonly occurring AEs at a rate of 23.91%. This category combines surgical revisions to correct lead migration, IPG discomfort, and battery depletion, as well as device explants to treat infection and replace fractured leads or malfunctioning equipment.

Among the other reported AEs, pain (8%), undesired sensations (4%), infection (3.5%), inadequate stimulation (3%), and discomfort (1.5%) were the five most common clinical harms. All other harms were seen at less than 1%. In the population of chronic pain patients, incidence of pain is commonly reported, and these counts include device-related pain, postoperative pain, and pain in other areas. Most of these events were temporary and related to the procedure itself and were resolved. Subjects with inadequate stimulation either had incomplete paresthesia coverage or experienced other problems with the device.

Table 3 provides a summary of device-related or hardware complications. A total of 759 device-related complications were reported in the safety data population of 3413 patients, for a rate of 22.24%. The incidence of each event is reported as a percentage of occurrences in total implanted patients, i.e. Incidence = (Number of device complications/Number of implanted patients) x 100.

Table 3. Summary of Device-Related Complications

Complications	Counts	Incidence = (Count/3413 implanted patients)*100
Lead Migration	413	12.1%
Lead Breakage or Malfunction	121	3.55%

Complications	Counts	Incidence = (Count/3413 implanted patients)*100
IPG Malfunction	83	2.43%
Disconnection of Lead or Extension	51	1.49%
IPG Migration or Discomfort	45	1.32%
Loss of Paresthesia	33	0.97%
Battery depletion within 1st year of implant	12	0.35%
Charger Dysfunction	1	0.03%
Total	***759***	***22.24%***

Among the reported device-related complications, lead migration had the most common incidence of 12% followed by lead breakage or malfunction at about 4%. Lead migrations and malfunctions typically required lead repositioning or replacement.

2. Effectiveness Results

Table 4 provides a summary of effectiveness data reported in 15 publications and obtained from 13 studies of patients diagnosed with CRPS Type I, CRPS Type II, or CRPS Not-Otherwise-Specified (NOS). The study design (SD) varied among the 13 studies with five prospective (P) studies, one randomized controlled trial (RCT), and seven retrospective (R) studies.

We indicate both the number of patients enrolled in each study and the number of patients permanently implanted with an SCS System. For the RCT and the prospective studies, the principal reason the number of patients implanted is different than the number of patients enrolled is because some patients did not experience at least 50% pain relief during trial stimulation with an external trial stimulator (and therefore, they are not implanted with a permanent system). For the retrospective studies, the principal reason the number of enrolled vs. implanted patients are different is due to the heterogenous nature of the patient populations included in the study.

We refer to the time between when patients were implanted, and the time when device effectiveness was assessed, as follow-up (FU) time. For most studies, FU time varied among patients and therefore, the mean number of FU months when averaged for all evaluated patients is indicated in Table 4. For the few studies that evaluated patients at specific timepoints following implantation, the FU range is indicated and the success data at each reported timepoint is provided. Success percentages are computed by dividing the number of patients meeting one or more of our definitions of device effectiveness by the total number of patients that were evaluated at least 6 months after implantation.

Table 4. Summary of Effectiveness Results in Clinical Studies: CRPS Types I and II

Author	Year	# Implanted (# Enrolled)	SD	FU	Success % (# of patients)
Geurts	2013	84 CRPS I (84)	P	132	40.5% (34/84)
Kemler	1999	18 CRPS I (23)	R	32	72.2% (13/18)
Kemler	2000 2004 2008	24 CRPS I (54)	RCT	6 - 60	6 mo: 58.3% (14/24) 2 yrs: 62.5% (15/24) 5 yrs: 29.2% (7/24) Significantly reduced VAS vs control (p<0.001), except @ 5 years (p=0.06)
Kumar	1996	9 CRPS II (30)	R	87	66% (6/9)
Kumar	1997	12 CRPS I (12)	R	41	100% (12/12)
Kumar	2006	32 CRPS I and II (452)	R	97.6 (median)	71.9% (23/32)
Lame	2009	32 CRPS I (32)	P	9	38% (12/32)
Moriyama	2012	14 CRPS NOS (55)	P	6	83.3% (10/12)
Oakley	1999	19 CRPS NOS (19)	P	7.9	80% (8/10)
Robaina	1989	6 CRPS I (11)	P	27	90.9% (5/6)
Sanchez-Ledesma	1989	11 CRPS II 8 CRPS I (49)	R	60	100% (19/19)

Sears	2011	18 CRPS NOS (35)	R	52.8	55.6% (10/18)
Verdolin	2007	4 CRPS I 6 CRPS II (10)	R	6	100% (10/10)

Collectively, the data in Table 4 were obtained from a total of 297 implanted patients diagnosed with CRPS Type I, CRPS Type II, or CRPS-NOS. The range of success rates observed across all 13 studies and FU times is 29.2% to 100%, with twelve studies observing success rates greater than 30% and ten studies observing success rates greater than 50%.

Patients specifically diagnosed with CRPS Type I represent 188 of the implanted patients. The range of success rates observed across all FU times and all studies of CRPS Type I patients is 29.2% to 100%. When the success data for CRPS Type I patients is pooled across all studies, the collective success rate is 51% (95 / 188).

Patients specifically diagnosed with CRPS Type II represent 26 of the implanted patients. The range of success rates observed across all FU times and all studies of CRPS Type II patients is 66% to 100%. When the success data for CRPS Type II patients is pooled across all studies, the collective success rate is 88% (23 / 26).

Table 5 provides a summary of effectiveness data reported in 7 publications and obtained from 6 studies of patients diagnosed with radicular pain syndrome, radiculopathies resulting in pain secondary to failed back syndrome or herniated disc, epidural fibrosis, degenerative disc disease (herniated disc pain refractory to conservative and surgical interventions), arachnoiditis, and multiple back surgeries. The study design (SD) varied among the studies with two randomized controlled trials (RCT) and four retrospective studies (R).

The definitions for most columns are the same as those for Table 4. The number of surgeries refers to the mean number of prior back surgeries that occurred prior to treatment with an SCS device, when averaged over all patients. When the article did not specify the mean number of back surgeries for the patient population, we included the author's description of the population's surgical history when it was provided.

Table 5. Summary of Effectiveness Results in Clinical Studies: Associated Conditions and Etiologies

Author	Year	Condition / Etiology	# Implant (# Enroll)	Number of Surgeries	SD	FU	Success % (# of Patients)
De La Porte	1983	Arachnoiditis	38 (94)	3.5	R	35.8	12 months: 68% (21/31)
Fiume	1995	Epidural Fibrosis	36 (55)	1.8	R	55	56% (20/36)
Kumar	2007 2008	Radicular pain after surgery for a herniated disc	50 (100)	More than one surgery for 28 subjects implanted	RCT	24	6 months: 48% (24/50) 24 months: 40% (17/42)
North	2005	Radicular pain after spine surgery	31 (60)	2.5	RCT	34.8	52% (15/29)
Probst	1990	Radicular Pain due to Epidural and Intradural Fibrosis after surgery for lumbar disc herniation	92 (112)	85% of patients had history of multiple operations	R	54	6-12 months: 77% (71/92) 13-24 months: 69% (63/92)
Siegfried	1982	Arachnoid and Epidural Fibrosis	89 (191)	Not Reported	R	48	37%

Collectively, the data in Table 5 were obtained from a total of 336 implanted patients diagnosed with radicular pain syndrome, radiculopathies resulting in pain secondary to failed back syndrome or herniated disc, epidural fibrosis, degenerative disc disease (herniated disc pain refractory to conservative and surgical interventions), arachnoiditis, and multiple back surgeries. The range of success rates observed across all 6 studies and FU times is 37% to 77%, with all studies observing success rates greater than 30% and 4 of the 6 studies observing success rates greater than 50%.

3. Pediatric Extrapolation

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

D. Financial Disclosure

A clinical study was not performed and thus, the Financial Disclosure by Clinical Investigators regulation (21 CFR 54) is not applicable to this PMA.

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 was conducted using published clinical studies relevant to Boston Scientific Spinal Cord Stimulation (SCS) System features and indications. A total of 22 publications and 19 subject populations (some articles reported on the same subjects at a later time point) diagnosed with the conditions and etiologies of interest were reviewed. Collectively, these studies report data for 633 implanted patients: 188 diagnosed with CRPS Type I, 26 diagnosed with CRPS Type II, 83 diagnosed with CRPS-NOS, and 336 diagnosed with one or more of the associated conditions or etiologies. SCS treatment was demonstrated to be effective in all 19 subject populations described in these articles.

Patients specifically diagnosed with CRPS Type I represent 188 of the implanted patients. The range of success rates observed across all FU times and all studies of CRPS Type I patients is 29.2% to 100%. When the success data for CRPS Type I patients is pooled across all studies, the collective success rate is 51% (95 / 188).

Patients specifically diagnosed with CRPS Type II represent 26 of the implanted patients. The range of success rates observed across all FU times and all studies of CRPS Type II patients is 66% to 100%. When the success data for CRPS Type II patients is pooled across all studies, the collective success rate is 88% (23 / 26).

Patients specifically diagnosed with radicular pain syndrome, radiculopathies resulting in pain secondary to failed back syndrome or herniated disc, epidural fibrosis, degenerative disc disease (herniated disc pain refractory to conservative and surgical interventions), arachnoiditis, and multiple back surgeries represent 336 of the implanted patients. The range of success rates observed across all 6 studies and FU

times is 37% to 77%, with all 6 studies observing success rates greater than 30%, and 4 of the 6 studies observing success rates greater than 50%.

The results of the review support the effectiveness of SCS therapy in treating patients who suffer from chronic, intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with failed back surgery syndrome, Complex Regional Pain Syndrome Types I and II, intractable leg and back pain, radicular pain syndrome, radiculopathies resulting in pain secondary to failed back syndrome or herniated disc, epidural fibrosis, degenerative disc disease (herniated disc pain refractory to conservative and surgical interventions), arachnoiditis, and multiple back surgeries.

B. Safety Conclusions

The clinical evidence provided to support safety of the Boston Scientific Neuromodulation Spinal Cord Stimulator Systems includes a systematic literature review of clinical research conducted on this and other comparable devices. Adverse Events (AEs) reported in 44 publications that reported data on 40 study populations (4 publications reported on the same subjects at later time points), and that included a total of 3413 implanted patients, were analyzed and summarized.

Additional interventions were the most commonly occurring AEs at a rate of 23.91%. This category combines surgical revisions to correct lead migration, IPG discomfort, and battery depletion, as well as device explants to treat infection and replace fractured leads or malfunctioning equipment. Among the other reported AEs, pain (8%), undesired sensations (4%), infection (3.5%), inadequate stimulation (3%), and discomfort (1.5%) were the five most common clinical harms. All other harms were seen at less than 1%. In the population of chronic pain patients, incidence of pain is commonly reported, and these counts include device-related pain, postoperative pain, and pain in other areas.

A total of 759 device-related complications were reported in the safety data population of 3413 patients, for a rate of 22.24%. Among the reported device-related complications, lead migration had the most common incidence of 12% followed by lead breakage or malfunction at about 4%. Lead migrations and malfunctions typically required lead repositioning or replacement.

The results of the systematic review support the safety of SCS therapy in treating patients who suffer from chronic, intractable pain of the trunk and/or limbs. The Boston Scientific Neuromodulation system is similar to SCS systems approved by the FDA.

C. Benefit-Risk Determination

Chronic pain is very debilitating. Patients have difficulty performing activities of daily living.

Depending upon the condition or etiology, the chronic pain may last for years. Chronic pain by definition has been present for at least 3 months. Treatment options for this population of patients are of great importance. Patients are willing to accept the probable risk given the probable benefit as evidenced by 30 years of SCS use.

The probable benefits of the device are based on data collected in a systematic literature review. A total of 22 publications and 19 subject populations (some articles reported on the same subjects at a later time point) diagnosed with the conditions and etiologies of interest were reviewed. Collectively, these studies report data for 633 implanted patients. SCS treatment was demonstrated to be effective in all 19 subject populations described in these articles.

The improvement in pain ranged from 29.2%-100% for CRPS patients, and 37-77% for those with back and leg pain due to surgery associated conditions and etiologies across the studies.

Follow-up ranged from 6 months to 11 years. At 11 years, Guerts et al (2013) reported a decrease in pain due to CRPS of at least 50% in 40.5% of patients studied (34/84 patients). At a mean of 4.5 years, Fiume et al (1995) found a reduction of at least 50% in pain due to epidural fibrosis in 56% of patients (20/36 patients).

The most common adverse event (AE), at 23.9% was the need for an additional intervention (surgical revisions to correct lead migration, IPG discomfort, battery depletion, infection, fractured leads). Other reported adverse events included pain (8%), unpleasant sensation (4%), infection (3.5%), inadequate stimulation (3%), and discomfort (1.5%). Infection is a common cause for explantation of the device.

As described above, the risks were evaluated in a systematic literature review. This analysis evaluated AEs reported in 44 publications that reported data on 40 study populations (4 publications reported on the same subjects at later time points), and that included a total of 3413 implanted patients. The safety information provided was consistent with the well-known safety profile of SCS systems.

Additional factors to be considered in determining probable risks and benefits for the Boston Scientific SCS System included the open label design of the clinical studies during FDA review. In some of the studies reviewed, open label studies may cause an overestimation of the treatment effect in investigator and subject ratings. Also, open label studies do not assess the magnitude of the placebo response, regression to the mean, the effect of changes in medications or other treatments to alleviate pain or changes in the underlying severity of the pain disorder. SCS is an option for patients who do not have adequate pain relief from medications and/or other treatments for pain.

This submission did not include specific information on patient perspectives for this device.

In conclusion, given the available information above, the data support that the probable benefits outweigh the probable risks for the Boston Scientific SCS System when used as an aid in the management of chronic intractable pain of the trunk and/or limbs in patients, including unilateral or bilateral pain associated with the following: failed back surgery syndrome, Complex Regional Pain Syndrome (CRPS) Types I and II, intractable low back pain and leg pain. Associated conditions and etiologies may be radicular pain syndrome, radiculopathies resulting in pain secondary to failed back syndrome or herniated disc, epidural fibrosis, degenerative disc disease (herniated disc pain refractory to conservative and surgical interventions), arachnoiditis, and multiple back surgeries.

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 efficacy of the Boston Scientific 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 Boston Scientific SCS System is based on a foundation of 30 years of clinical research and experience as documented in the literature with fully implantable SCS systems and the similarities of the Boston Scientific system to market released implantable SCS systems. The analyses also support a clinical benefit to risk determination that is favorable.

XIII. CDRH DECISION

CDRH issued an approval order on August 11, 2017.

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

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NOTE: Publications marked with a '*' were used in both the Safety and Effectiveness analysis

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