SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

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

Device Trade Name: Senza Spinal Cord Stimulation (SCS) System

Device Procode: LGW

Applicant's Name and Address: Nevro Corp.
4040 Campbell Avenue, Suite 210
Menlo Park, CA 94025

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P130022

Date of FDA Notice of Approval:

II. INDICATIONS FOR USE

The Senza SCS System 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.

III. CONTRAINDICATIONS

The Senza SCS System should not be used for those patients who:

- Are poor surgical candidates.
- Fail to receive effective pain relief during trial stimulation.
- Are unable to operate the SCS system.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Senza SCS System labeling.

V. DEVICE DESCRIPTION

The Senza SCS System is a totally implanted device that delivers electrical stimulation to the dorsal column of the spinal cord for the treatment of chronic intractable pain of the trunk and/or limbs. The Senza SCS System is shown in Figure 1 below:

Figure 1: Senza SCS System Implantable Pulse Generator (IPG) and Percutaneous Leads

A. Implanted Components

The implanted components of the Senza SCS System include the following:

- Implanted Pulse Generator (IPG) (Model 1500): The IPG is a rechargeable implantable device with 16 output channels. Each of the 16 outputs can be programmed as a cathode or an anode. The IPG is powered by a 3.6 V nominal Li-Ion rechargeable battery (single cell). It is capable of stimulating the spinal cord nerves through the electrodes of the leads connected to any combination of the output terminals, using a single current source. The battery of the IPG can be transcutaneously recharged using a Nevro Charger. There are two versions of the IPG which vary slightly in the shape of the header. Approximate dimensions of the IPGs are 53.5mm (height without header; with header 69mm), 47.5mm (width) and 12.5mm (thickness). The stimulation output parameters are listed in Table 1 below:

Table 1: Stimulation Output Parameters

Number of Programs	1 to 3
Number of Channels	16
Waveform	Charged Balanced Biphasic
Pulse Shape	Rectangular
Current or Voltage Regulated	Current
Maximum Current Amplitude @ 500 Ω	0 to 15 mA per channel
Maximum Output Voltage @ 500 Ω	7.5 V
Pulse Width	20 to 1000 µs
Frequency	2 to 10,000 Hz
Current Path Options	Bipolar or Multipolar

- Percutaneous Leads:
  The lead specifications are depicted in Table 2 below:

Table 2: Percutaneous Lead Specifications

	Percutaneous Leads
Lead Length (cm)	30-90 in increments of 5
Lead Diameter (mm)	1.4
Number of Electrodes	8
Electrode Material	Platinum/Iridium
Electrode Spacing (edge-to-edge) (mm)	1-9
Electrode Span (cm)	3.1-8.7
Electrode Surface Area (mm^2)	12.7
Impedance (Ω)	< 18
Conductor Material	Ethylene tetrafluoroethylene (ETFE) insulated MP35N cable with Silver core
Lead Body Insulation	Pellethane 55D – Dow Corning 2363

- Lead Extensions: Used when the implant site for the IPG is located too far from the stimulation site to directly connect to the Percutaneous Lead. The design, material and construction methods on the proximal end and lead body of the Lead Extension are identical to the Percutaneous Lead. They come in lengths of 15 to 60 cm in 5 cm increments.

- Lead anchors: Used to anchor the Percutaneous Lead to the fascia or supraspinous ligament (Asymmetrical Eyelets, N100, N200, and N300).

- Lead Adapters: The M8 and S8 Lead Adaptors allow a physician to connect an implanted Medtronic or St. Jude Medical lead, respectively, with the Nevro Lead Extension or IPG.

B. External Components

- Clinician Programmer (Model PG2000): Used by the clinician to program output stimulation parameters. It is an off-the-shelf laptop installed with proprietary Nevro software to allow the programming of the IPG or Trial Stimulator and Patient Remote via the Programmer Wand.

- Patient Remote (Models RC1000 and RC2000): A handheld battery operated unit able to communicate via radio frequency (RF) energy with the IPG or Trial Stimulator. There are two versions of the Patient Remote available. One version includes multiple controls and indicators that allow patients the ability to turn the Patient Remote on or off, turn off stimulation, select from three stimulation

programs, control and observe the stimulation level, and observe the status of the Trial Stimulator battery. The other version has a simpler user interface design and allows patients to select one of two stimulation programs.

- Trial Stimulator: Provides stimulation by emulating the IPG during the intraoperative test and during the stimulation trial. The Trial Stimulator stimulation parameters are the same as the IPG.

- IPG Charger: Used to transcutaneously recharge the IPG battery

- Operating Room Cables: Used during intraoperative testing and stimulation trial. One end of the cable is plugged into a connector which holds the leads proximal ends, and the other end of the cable is attached to the Trial Stimulator.

- Programmer Wand: The Programmer interface that allows the communication with an IPG or Trial Stimulator. The Programmer Wand connects to the Programmer laptop through a USB port and communicates via RF with the IPG or Trial Stimulator.)

- Mx Trial Adaptor: The Mx Trial Adaptor is intended to connect a Medtronic operating room (OR) cable to the Nevro Trial Stimulator.

- Surgical Accessories:

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

    - Insertion Needle: Used during implant surgery to introduce the Percutaneous Lead between the vertebrae into the epidural space.

    - Coiled Lead Blank: Optionally used during surgery to clear a path for the introduction of the Percutaneous Lead into the epidural space.

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

    - IPG Port Plug: Provided to seal the port of the IPG that is not in use when only one Lead is implanted.

    - IPG Template: Acts as an optional aid for physicians in proper sizing of the IPG implant pocket.

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 Senza SCS System has been in commercial distribution in the European Union (EU) (approval in May 2010) and Australia (approval in June 2011). 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 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 Senza 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; complications of pregnancy including miscarriage and fetal birth defects; 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.

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

IX. SUMMARY OF PRECLINICAL STUDIES

A. Laboratory Studies

1. Implanted Pulse Generator (IPG)
   Testing was conducted on the Model 1500 IPG, including: mechanical design verification (including testing on devices subjected to accelerated aging), electrical/firmware design verification testing, electromagnetic compatibility testing, and medical procedure compatibility testing. Key testing on the IPGs is summarized in Table 3 below. Testing demonstrated the IPGs operated according to specifications after exposure to the tested conditions (i.e., passed testing).

Table 3: Summary of key testing performed and passed on the Senza SCS System IPG

Test	Test Purpose	Acceptance Criteria
Measurement of Output Pulses	The characteristics of the output pulses shall be measured as described in ISO 14708-3 clause 6.101. Verify proper output (amplitude, pulse width, frequency, etc.) of the IPG function are within specified tolerances	Amplitude, Pulse width, Frequency, and Inter pulse delay are within output specifications.
Dimensional Requirements	To demonstrate IPGs meet shape and profile requirements.	IPG samples must meet size specifications for IPG width, height, thickness, volume, mass, and radius.
DC Leakage Current	Verify the leakage current is in an acceptable range. Leakage current was measured with a 500 Ω load per the instructions in ISO 14708-3, clause 16.2.	The maximum leakage current < 1 μA
Environmental Conditions	Atmospheric Pressure Exposure: To expose each IPG to pressure extremes the device may encounter during storage and distribution.	Testing per ISO 14708-3, 25
	Operating Temperature: To demonstrate the IPG remains mechanically intact and capable of normal operation during exposure to low and high temperatures.	Testing per ISO 14708-1, 26.2. The IPG shall remain mechanically intact and capable of normal operation during exposure to low (0°C) and high temperatures (45°C) for 3

Test	Test Purpose	Acceptance Criteria
		hours.
	Mechanical Forces: Verify device conforms to functional requirements and is not damaged by mechanical forces that may occur during conditions of use	Testing per ISO 14708-1, 23
Hermetic Leak Test	To demonstrate that the IPG (including feedthroughs) maintains hermeticity after exposure to environmental testing.	Must be hermetically- sealed titanium can, helium leak shall be < 1x10-8 std/cc/s
Header Adhesion Testing	To demonstrate the header meets fatigue requirements the IPG maintains isolation between channels and externally.	After a 10-day saline soak, the IPGs were subjected to a 50 N pull force applied in axial (to the IPG port), lateral and vertical directions. This stress conditions far exceeds worst case clinical scenarios. Visual and electronic do not reveal any damage and demonstrate that the header is securely bonded to the IPG.
Lead Insertion and withdrawal Forces	To demonstrate that the IPG, port plug, and lead meet specified interface requirements for insertion force and withdrawal force (without setscrew engaged) when the IPG and lead are in a dry and wet conditions.	- Port plug and lead retention force shall be more than 15N - Port plug and Lead insertion force shall be < 8.9N (2.0 Lbf).
Particulate matter	Verify there is no unacceptable release of particulate matter when the device is used as intended.	The excess average count of particles from the test specimen compared to a reference sample shall not exceed 100 counts/ml greater than 5.0 µm and shall not exceed 5 counts/ml greater than 25 µm.
Temperature	Verify the protection of patients from damage caused from heat	Based on clinical data from IDE G110156 (88 subjects) and outside U.S. (1738 patients) (42°C for an average of approximately 23 minutes (approximate 90 minutes maximum) during recharge)
Battery	Battery Charge/Discharge Cycle Verification (Longevity).	For 12-hour therapy days the longevity of the batteries on a single charge shall > 4 days and for 24-hour therapy days and longevity of the batteries on a single charge > 10 days.
	Electrical, Visual, Dimensional, Hermeticity, Short Circuit Testing, Environmental, and Forced Discharge Tests	Meets specifications.

2. Percutaneous Lead Testing

The percutaneous and paddle leads underwent numerous testing for dimensional verification, electrical safety, environmental, and mechanical conditions. Key testing on the leads is summarized in Table 4 below. Testing demonstrated the percutaneous and paddle leads operated according to specifications after exposure to the tested conditions (i.e., passed testing).

Table 4: Summary of Key Testing Performed on the Percutaneous Leads

Test	Purpose	Acceptance Criteria
Dimensional	To ensure the leads meet dimensional requirements for Overall Lead Length Lead Body Diameter, Distal Electrode Dimensions, Lead Tip Length, Connector Dimensions.	Meets dimensional specifications
DC Resistance	Demonstrate protection from electricity.	DC resistance between electrodes and contact shall not exceed 10 Ohms.
Stylet Interactions – Insertion/Removal	To demonstrate the force required to fully insert or remove each stylet into the lead	Fully insert a 0.014" straight stylet into a 50cm length percutaneous lead. Apply 1.1 lb (5N) push force to the stylet for 30 seconds. The percutaneous lead shall not exhibit any signs of damage.
Insertion Needle Insertion/Withdrawal	Demonstrate lead compatibility with Touhy Needle.	The insertion and extraction force of the insertion needle shall be less than 1.5 pounds
Hipot	Demonstrate the safety of the electrical insulation.	The leakage current shall not exceed 50 microamps
Pull Test	Demonstrate the integrity of the lead body joints after the Percutaneous lead is stressed by a saline soak and wet pull.	- No lead bond separation, cracks, tears, permanent elongation in excess of 5% or lead resistance change > 10% after the tensile force is applied. - Lead leakage current ≤ 50 microamperes when a 100V is applied between any two conductor pairs or any conductor pair and reference electrode
Tensile Strength	Demonstrate the lead remains electrically and mechanically intact after a tensile load.	Apply a 8.8N (2 lbs) +10% -0% tensile force between the proximal and distal most section of the lead and hold this force a minimum of 1 minute. No conductor failure shall be observed during the testing.
Lead Body Flex Fatigue	Demonstrate that the leads do not fatigue after flexural stressors.	The resistance on any of the conductor shall not change by more than 25% after a minimum of 47,000 cycles (1X CENELEC) when compared to DC resistance prior to the testing
Connector End Flex Fatigue	Demonstrate that the lead connector ends do not fatigue after flexural stressors.	The DC resistance on any of the eight conductors on the samples shall not increase by more than 25% after a minimum of 82,000 cycles (1X CENELEC) when compared to DC resistance prior to the testing
Lead Anchor Testing	To verify the lead anchors slide into position and provide appropriate retention force for clinical usage and verify a tied suture material does not damage the underlying lead anchor or percutaneous lead.	- The maximum sliding force of the untied anchor tested dry is 0.30 lb. (1.3N). - The maximum sliding force of the untied anchor tested wet is 0.25 lb. (1 .IN). - The minimum retention force of the tied anchor tested wet is 0.7 lb. (3.1N). - The lead body and anchor shall not exhibit any tears, rips or delamination.

Test	Purpose	Acceptance Criteria
M8 and S8 Lead Adaptors	Verify the compatibility of specified leads	Programmed outputs should be at safe levels. Meet same criteria as Nevro leads for DC Resistance, Hipot, and Seal Integrity Connector is compatible Accurate Impedance measurements

3. Programmers
   The software associated with the Clinician Programmer, Patient Remote, Trial Stimulator, and Programmer Wand was tested in accordance with the FDA guidance document entitled, "Guidance for the Content of Pre-market Submission for Software Contained in Medical Devices" (May 11, 2005) and all requirements were met. Electrical and mechanical verification and environmental testing (per ISO 14708-3 and IEC 60068-2-14) were also performed and all testing met specifications.

4. Electromagnetic Compatibility (EMC) and Wireless Technology
   EMC and wireless technology (including quality of service (QOS), coexistence, and security of wireless transmissions testing) was performed using appropriate essential performance criteria in accordance with the relevant clauses of the following standards and met specified acceptance criteria:

   - IEC 60601-1-2: 2007, "Medical electrical equipment - Part 1-2: General requirements for basic safety and essential performance - Collateral standard: Electromagnetic compatibility - Requirements and tests"

   - ISO 14708-3:2008(E): Implants for surgery – Active implantable medical devices – Part 3: Implantable neurostimulators", Part 27

   - Wireless radio testing per United States FCC CFR Title 47 Parts 15 and 95 Subpart I

5. System Testing
   Testing to verify that system-level design requirements were met for interactions between Senza SCS System components was performed. All test articles met defined acceptance criteria for the system integration tests conducted. System validation testing demonstrated that the system operated as expected and has been validated for safe and effective use.

6. IPG Medical Compatibility Testing
   The Senza SCS System was tested for compatibility with external defibrillation, High Power Electric Fields, diagnostic ultrasound, and diagnostic x-ray exposure (see Table 5 below). All samples met all functional requirements of the testing after exposure to medical therapy conditions, verifying that the IPG meets requirements for compatibility with these therapies. The Senza SCS System was also tested for compatibility with magnetic resonance imaging (MRI) and was determined to be safe

when the patient is scanned according to the Senza SCS System MR Conditional labeling.

Table 5: IPG Medical Compatibility Testing

Test	Acceptance Criteria
External Defibrillator Test	Verify that the device meets functional electrical test requirements after exposure to external defibrillation per ISO 14708-3, clause 20.2
High Power Electrical Fields Test	Verify protection from high power electrical fields according to standard ISO 14708-3, clause 21
Diagnostic Ultrasound Test	Verify that the IPG withstands exposure to ultrasound specified in EN45502-1:1997 and ISO 14708-3, clause 22
X-Ray Compatibility Test	Device remains functional after exposure to x-ray; radiographic marker is visible in x-ray; and minimal to no distortion of anatomical features adjacent to device
MRI Compatibility	Verify it is safe when scanned according to the Senza SCS System MR Conditional labeling.

B. Animal Studies

Safety of stimulation at 10 kHz was assessed in goats. Twelve goats were implanted (Day 0) with one Advanced Bionics 50cm 8-contact trial linear lead placed at or near midline in the epidural space overlying (dorsal to) the L2 – L3 intervertebral space. In six animals, Nevro Therapy was applied to the Advanced Bionics 50cm 8-contact trial linear lead 24 hours per day for 10 +/- 1 day at a frequency of 10 kHz with a 100% duty cycle using the Nevro Trial Stimulator (NTS). A duty cycle refers to the ratio of stimulation on time versus stimulation off time; a duty cycle of 100% states that the stimulation is on all the time, with no stimulation off time. The stimulation amplitude was set below the animal's discomfort stimulation threshold and above the animal's perception stimulation threshold. The average stimulation amplitude ranged from 0.2 to 1.5 mA. The remaining six animals received the same implant as the therapy group and were fitted with a mock external NTS, but at no time was stimulation applied. There were no morphologic differences between the therapy and Mock (control) groups. All morphologic changes were interpreted to be due to the placement and/or presence of the implanted lead or to the inevitable manipulation of the spinal cord and adjacent tissues during such an implant procedure. The morphologic changes were interpreted to be non-adverse and to represent the consequence of the administration of a therapy via a device implanted into the epidural space.

C. Biocompatibility

Biocompatibility testing was performed for all patient-contacting components of the Senza SCS System in accordance with ISO 10993-1 Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process, on the finished sterilized devices. All biocompatibility studies were conducted in compliance with Good Laboratory Practices (GLP), 21 CFR Part 58. The implanted components of the Senza SCS System are considered permanent (> 30 days) implants in contact with tissue/bone. The Senza SCS System also contains external communicating and

skin-contacting components with both prolonged (> 24 hours – 30 days) and limited (≤ 24 hours) tissue/bone contact. All pre-specified test acceptance criteria were met and all tests passed.

D. Sterility and Packaging

The Senza SCS System components that are provided sterile are terminally sterilized using a 100% ethylene oxide (EO) sterilization process to provide a minimum sterility assurance level (SAL) of 10^{-6}. Validation of the sterilization process is in compliance with ANSI/AAMI/ISO 11135-1:2007. Sterilization of health care products – Ethylene oxide – Part 1: Requirements for development, validation, and routine control of a sterilization process for medical devices. Sterilant residuals conform to the maximum allowable limits of EO and ethylene chlorohydrin (ECH) residuals specified in ISO 109937: 2008. Biological Evaluation of Medical Devices – Part 7: Ethylene Oxide Sterilization Residuals. The product bacterial endotoxin limits are based on FDA's Guidance for Industry - Pyrogen and Endotoxins Testing: Questions and Answers (June 2012) and are verified using Limulus Amebocyte Lysate (LAL) testing

Packaging and shelf- life validation tests were completed in compliance with ISO 11607-1:2009 *Packaging for Terminally Sterilized Medical Devices. Part 1: Requirements for materials, sterile barrier systems and packaging systems*. Shelf life for the sterile system components has been established as three (3) years from the date of manufacturing.

X. SUMMARY OF PRIMARY CLINICAL STUDIES

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of 10 kHz stimulation with the Senza SCS System for treatment of chronic, intractable pain of the trunk and/or limbs in the US under IDE #G110156. Data from this clinical study were the basis for the PMA approval decision for 10 kHz stimulation without paresthesia.

The safety and effectiveness of the Senza SCS System for stimulation parameters similar to commercially available SCS systems (i.e., output is between 2 and 1,200 Hz with paresthesia) for the treatment of chronic intractable pain of the trunk and/or limb was based on published literature.

A summary of the clinical study and literature review is presented below.

A. Study Design

Patients were enrolled between June 7, 2012 and December 28, 2012. The database for this PMA reflected data collected through February 6, 2014 and included 241 patients. There were 11 investigational sites.

The study was a prospective, randomized, multi-center non-inferiority trial comparing the Senza SCS System to a legally marketed SCS system (control group). The

control group consisted of subjects treated with a legally marketed device from a single manufacturer which delivers stimulation in the 2 to 1,200 Hz frequency range. The legally marketed device has a similar indication for use.

Subjects were not blinded as to their device assignment. Subjects were randomized in a 1:1 ratio to the treatment arms and a frequentist statistical analysis was performed. The primary objective of the study was to demonstrate that a composite endpoint of safety and effectiveness of the Senza SCS System was non-inferior to the legally-marketed SCS comparator. The sample size required was estimated to be 77 subjects in each group (154 subjects total). In addition at least 60 subjects implanted with the Senza SCS System who were programmed to 10 kHz were required to have 12 month follow-up to assess safety. To account for potential drop-out, a total of up to 125 subjects per group (250 subjects total) were allowed to be randomized. The success rate was estimated to be 58% in the Senza SCS System group and 48% in the control group. The rate of stimulation-related neurological deficit was estimated to be 2% in both the test and control groups.

A Data Safety Monitoring Board (DSMB) monitored the study.

1. Clinical Inclusion and Exclusion Criteria
   Enrollment in the Senza SCS System study was limited to patients who met the following inclusion criteria:

   a. Have been diagnosed with chronic, intractable pain of the trunk and/or limbs which has been refractory to conservative therapy for a minimum of 3 months. Previous conservative therapy includes pain medications and physical therapy, and may include other treatment modalities such as nerve root blocks or facet joint blocks/denervations.

   b. Considering daily activity and rest, have average back pain intensity of ≥ 5 out of 10 cm on the Visual Analog Scale (VAS) at enrollment.

   c. Be severely disabled or crippled as defined by an Oswestry Disability Index score of 41-80 out of 100 at enrollment.

   d. Be an appropriate candidate for the surgical procedures required in this study based on the clinical judgment of the implanting physician.

   e. Be on stable pain medications, as determined by the Investigator, for at least 28 days prior to enrolling in this study.

   f. Be 18 years of age or older at the time of enrollment

   Patients were not permitted to enroll in the Senza SCS System study if they met any of the following exclusion criteria:

a. Have a medical condition or pain in other area(s), not intended to be treated with SCS, that could interfere with study procedures, accurate pain reporting, and/or confound evaluation of study endpoints, as determined by the Investigator.

b. Have evidence of an active disruptive psychological or psychiatric disorder or other known condition significant enough to impact perception of pain, compliance of intervention and/or ability to evaluate treatment outcome, as determined by a psychologist.

c. Have a current diagnosis of a progressive neurological disease such as multiple sclerosis, chronic inflammatory demyelinating polyneuropathy, rapidly progressive arachnoiditis, rapidly progressive diabetic peripheral neuropathy, brain or spinal cord tumor, or severe/critical spinal stenosis.

d. Have a current diagnosis of a coagulation disorder, bleeding diathesis, progressive peripheral vascular disease or uncontrolled diabetes mellitus.

e. Have a diagnosis of scoliosis that precludes lead placement.

f. Have mechanical spine instability detected by > 4 mm translational movement or excessive angular movement manifested by 20 degrees greater angular movement than in an adjacent segment based on flexion/extension films of lumbar spine (imaging is required for this determination and must have been done within the past 6 months).

g. Be benefitting within 30 days prior to enrollment from an interventional procedure and/or surgery to treat back and/or leg pain.

h. Have an existing drug pump and/or SCS system or another active implantable device such as a pacemaker.

i. Have prior experience with SCS.

j. Have a condition currently requiring or likely to require the use of MRI or diathermy.

k. Have metastatic malignant disease or active local malignant disease.

l. Have a life expectancy of less than 1 year.

m. Have an active systemic or local infection.

n. Be pregnant (if female and sexually active, subject must be using a reliable form of birth control, be surgically sterile or be at least 2 years post-menopausal).

o. Have within 6 months of enrollment a significant untreated addiction to dependency producing medications or have been a substance abuser (including alcohol and illicit drugs).

p. Be concomitantly participating in another clinical study.

q. Be involved in an injury claim under current litigation.

r. Have a pending or approved worker's compensation claim.

2. Follow-up Schedule

All patients were scheduled to return for follow-up examinations during the trial phase and at 1, 3, 6, 9, and 12 months post-implantation. Subjects had the option of consenting to an additional year of follow-up with 18 and 24 month study visits to collect longer term data.

Preoperatively, subjects had a pregnancy test, flexion/extension imaging, a psychological exam and pain and disability assessments. Postoperatively, the objective parameters measured during the study included a pain assessment (using the visual analog scale (VAS) and Short-form McGill Pain Questionnaire), the Oswestry Disability Inventory, the Global Assessment of Functioning, Short Form-12, Quality of Life Assessment, Beck Depression Inventory, Pittsburg Sleep Quality Index, Patient Global Impression of Change, Clinician Global Impression of Change, Subject Satisfaction and Neurological Assessment. The key timepoints for each assessment are shown in Table 6 and Table 7 below. Adverse events and complications were recorded at all visits.

Table 6: Assessment Timepoints for Pre-Trial and Trial Study Phases

Assessment	**Pre-Trial**		**Trial Phase**	
Visit	Enrollment	Entry Criteria/ Baseline	Trial Implant	End of Trial
Informed Consent	X			
Pregnancy Test	X[1]			
Flexion/Extension Imaging	X			
Psychological Evaluation	X			
Pain Diary	X		X	
Entry Criteria Evaluation		X		
Medical/Surgical History		X		
Visual Analog Scale (VAS)	X	X		X
Short-form McGill Pain Questionnaire (SF-MPQ2)		X		
Percent Pain Relief (PPR)				X

Assessment	Pre-Trial		Trial Phase	
Visit	Enrollment	Entry Criteria/ Baseline	Trial Implant	End of Trial
Oswestry Disability Inventory (ODI)	X	X		
Medication Usage		X		
Global Assessment of Functioning (GAF)		X		
Short Form 12 Quality of Life Assessment (SF-12)		X		
Beck Depression Inventory (BDI-II)		X		
Pittsburg Sleep Quality Index (PSQI)		X		
AP and Lateral X-Rays			X	X
Paresthesia Questionnaire				
Patient Global Impression of Change (PGIC)				
Clinician Global Impression of Change (CGIC)				
Subject Satisfaction				
Neurological Assessment		X		X
Adverse Event Monitoring			X	X
Device Programming			X	
Device Follow-Up[3]				
Study Completion				X[2]

[1] Completed for females of child bearing potential
[2] Completed for those subjects who do not pass the Trial Phase.
[3] For subjects randomized to the Nevro arm only

Table 7: Assessment Timepoints for Permanent Implant Study Phase

Assessment	Permanent Implant Phase						
Visit	Permanent Implant	Device Activation	1 Month Visit	3 Month Visit	6 Month Visit	9 Month Visit	12 Month Visit
Informed Consent							
Pregnancy Test							
Flexion/Extension Imaging							
Psychological Evaluation							
Pain Diary	X	X	X	X	X	X	
Entry Criteria Evaluation							
Medical/Surgical History							
Visual Analog Scale (VAS)			X	X	X	X	X
Short-form McGill Pain Questionnaire (SF-MPQ2)				X	X		X
Percent Pain Relief (PPR)			X	X	X	X	X
Oswestry Disability Inventory (ODI)				X	X		X

Assessment	Permanent Implant Phase						
Visit	Permanent Implant	Device Activation	1 Month Visit	3 Month Visit	6 Month Visit	9 Month Visit	12 Month Visit
Medication Usage		X	X	X	X	X	X
Global Assessment of Functioning (GAF)				X	X		X
Short Form 12 Quality of Life Assessment (SF-12)				X	X		X
Beck Depression Inventory (BDI-II)				X	X		X
Pittsburg Sleep Quality Index (PSQI)				X	X		X
AP and Lateral X-Rays	X		[X]	[X]	[X]	[X]	[X]
Paresthesia Questionnaire				X			X
Patient Global Impression of Change (PGIC)				X			X
Clinician Global Impression of Change (CGIC)				X			X
Subject Satisfaction				X			X
Neurological Assessment		X	X	X	X	X	X
Adverse Event Monitoring	X	X	X	X	X	X	X
Device Programming		X	[X]	[X]	[X]	[X]	[X]
Device Follow-Up[1]				X	X		X
Study Completion							[X]

[X] Optional.

[1] For subjects randomized to the Nevro arm only

3. Clinical Endpoints

The primary endpoint was a composite of safety and effectiveness, specifically, the percentage of subjects who respond (referred to as "responders") to SCS therapy for back pain and do not have a stimulation-related neurological deficit at the primary endpoint assessment (non-inferiority analysis).

Individual Subject Success

Individual subject success was defined by the following:

a. Effectiveness Components:

- A decrease in back pain VAS by at least 50% at 3 months Post-Permanent Device Activation as compared with Baseline, and
- No increase in any pain medication two weeks prior to scheduled follow-up visits as compared to baseline, and
- No increase from Baseline in pain medication used to treat their back and/or leg pain for duration of greater than 5 days.

b. Safety Component: No stimulation-related clinically meaningful neurological deficit at 3 months post-permanent device activation as compared with baseline neurological status. Neurological status includes motor, sensory and reflex functions.

Study Success

Study success was defined as the percentage of subjects who met each success criteria in the test group and the control group, using a 10% non-inferiority margin.

Secondary Endpoints

The following secondary endpoints were successively evaluated (hierarchical test approach) in the order shown with a 0.05 significance until statistical significance was not achieved. A 10% non-inferiority margin was used to evaluate all secondary endpoints.

a. Comparison of percentage change from baseline in back pain between test and control groups (as assessed by VAS) at the primary efficacy assessment (non-inferiority analysis).

b. Comparison of percentage change from baseline in leg pain between test and control groups (as assessed by VAS) at the primary efficacy assessment (non-inferiority analysis).

c. Comparison of change from baseline between the test and control groups in disability as measured by Oswestry Disability Index (ODI) at the primary efficacy assessment (non-inferiority analysis).

d. Comparison of percentage change from baseline in back pain between test and control groups (as assessed by VAS) at the 6-month secondary efficacy assessment (noninferiority analysis).

e. Comparison of percentage change from baseline in leg pain between test and control groups (as assessed by VAS) at the 6-month secondary efficacy assessment (noninferiority analysis).

f. Comparison of percentage change from baseline in back pain between test and control groups (as assessed by VAS) at the 12-month secondary efficacy assessment (noninferiority analysis).

g. Comparison of percentage change from baseline in leg pain between test and control groups (as assessed by VAS) at the 12-month secondary efficacy assessment (noninferiority analysis).

B. Accountability of PMA Cohort

At the time of database lock, of 241 patients enrolled in the PMA study, 198 (82.2%) were randomized, 101 in the Senza SCS System (Test) group and 97 in the Control

group and this comprised the Intent-to-Treat (ITT) analysis population. The Per Protocol (PP) analysis population included 179 subjects (92 in the Test group and 87 in the Control group). A total of 171 randomized subjects received a permanent implant, defining a Permanent Implant Subset (PS) of 90 Test subjects and 81 Control subjects. One-hundred and fifty-five (155) subjects (86 in the Test group and 69 in the Control group) completed the 12 month follow-up visit. See Figure 2 below.

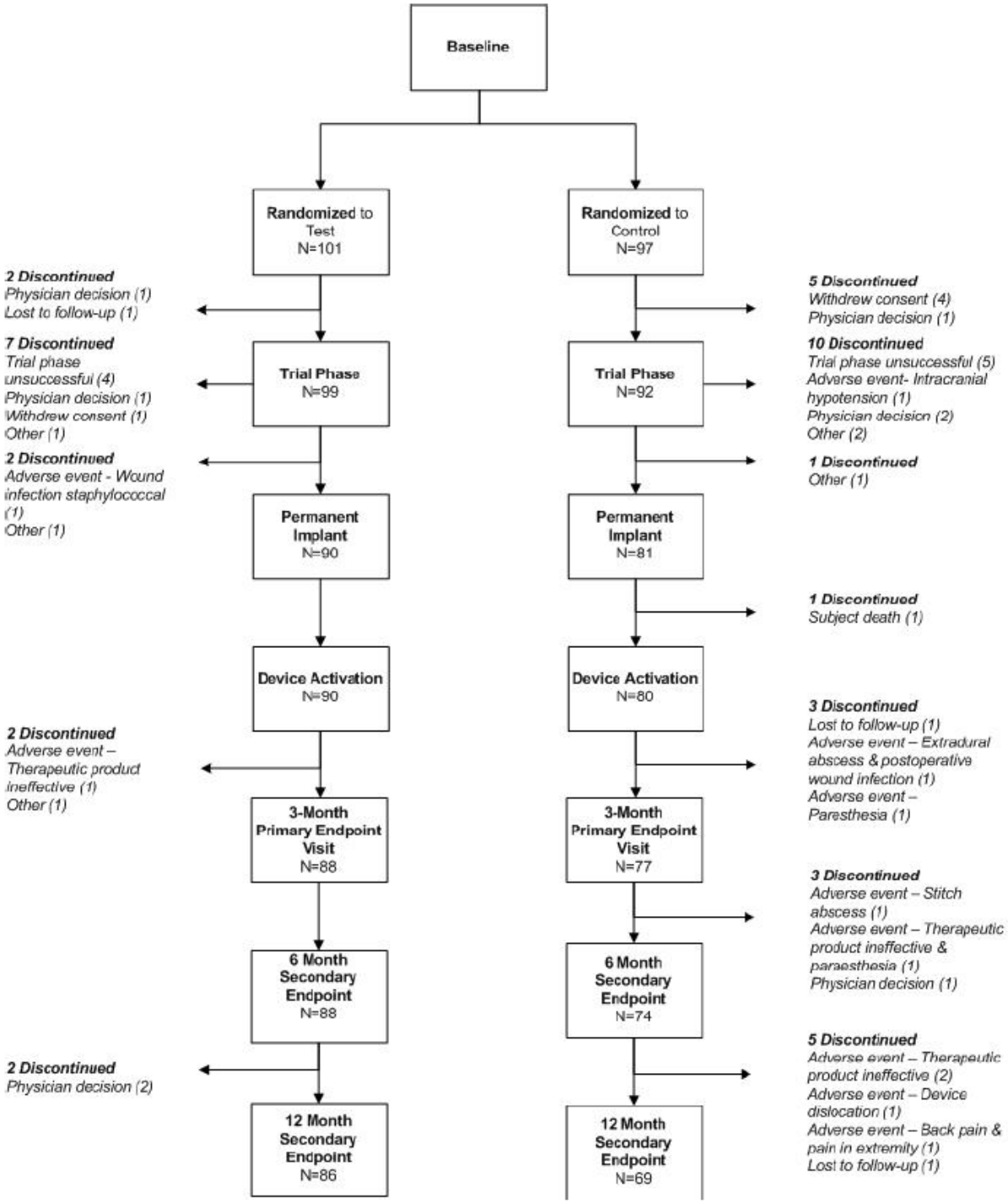


Figure 2: Accountability of PMA Cohort

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a pain study performed in the US. See Table 8 below.

Table 8: Subject Demographics

Characteristics	Test (N=92)	Control (N=87)	P-value
Gender - n (%)			
Female	57 (62.0%)	51 (58.6%)	0.760[a]
Male	35 (38.0%)	36 (41.4%)	
Age (years) at enrollment			
Mean ± SD	54.6 ± 12.4	55.2 ± 13.4	0.717[b]
Range	32.8 to 82.2	19.2 to 82.3	
Years since diagnosis			
Mean ± SD	13.0 ± 10.4	14.2 ± 12.2	0.659[b]
Range	1.0 to 52.0	1.0 to 62.0	
Ethnicity - n (%)			
Non-Hispanic/Latino	89 (96.7%)	85 (97.7%)	1.000[a]
Hispanic/Latino	3 (3.3%)	2 (2.3%)	
Race - n (%)			
White	85 (92.4%)	77 (88.5%)	
Black/African American	3 (3.3%)	5 (5.7%)	
American Indian/Alaska Native	2 (2.2%)	3 (3.4%)	0.703[a]
Asian	1 (1.1%)	0 (0.0%)	
Other	1 (1.1%)	2 (2.3%)	
Diagnosis[c] - n (%)			
Chronic intractable back pain	92 (100.0%)	87 (100.0%)	1.000[a]
Chronic intractable leg pain	91 (98.9%)	87 (100.0%)	
Leg pain - n (%)			
Bilateral	49 (53.3%)	54 (62.1%)	0.290[a]
Unilateral	43 (46.7%)	33 (37.9%)	
Pain etiology[d] - n (%)			
Failed back surgery syndrome	73 (79.3%)	65 (74.7%)	482[a]
Radiculopathy	61 (66.3%)	53 (60.9%)	534[a]
Degenerative disc disease	57 (62.0%)	49 (56.3%)	452[a]
Spondylosis	38 (41.3%)	32 (36.8%)	544[a]
Mild/moderate spinal stenosis	21 (22.8%)	17 (19.5%)	715[a]
Sacroiliac dysfunction	19 (20.7%)	14 (16.1%)	448[a]
Other neuropathic pain	19 (20.7%)	11 (12.6%)	166[a]
Other chronic pain	18 (19.6%)	18 (20.7%)	855[a]
Lumbar facet-mediated pain	14 (15.2%)	14 (16.1%)	1.000[a]
Internal disc disruption/annular tear	8 (8.7%)	2 (2.3%)	0.101[a]
Spondylolisthesis	8 (8.7%)	2 (2.3%)	0.101[a]
Previous back surgery - n (%)	80 (87.0%)	75 (86.2%)	1.000[a]
Baseline use of opioids - n (%)	83 (90.2%)	75 (86.2%)	0.488[a]
Baseline VAS scores			

Characteristics	Test (N=92)	Control (N=87)	P-value
Back pain:			
Mean ± SD	7.4 ± 1.2	7.8 ± 1.2	0.060[b]
Range	5.0 to 9.7	5.2 to 10.0	
Leg pain			
Mean ± SD	7.1 ± 1.5	7.6 ± 1.4	0.017[b]
Range	2.7 to 9.9	3.0 to 9.8	

Abbreviations: SD = standard deviation; VAS = visual analog scale

[a] P-value by Fisher's exact test or Fisher-Freeman-Halton test

[b] P-value by Wilcoxon rank sum test

[c] Subjects may have both diagnoses.

[d] Subjects may have more than one pain etiology. Pain etiology was reported by a study Investigator; no criteria were prespecified. Pain etiology information is provided for descriptive purposes and should not be interpreted as claims of effectiveness.

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the ITT population which included171 subjects with permanent implants (90 Test and 81 Control subjects) with follow-up through 12 months. On average, Test subjects had a permanent implant for 50.4 weeks, while Control subjects had a permanent implant for 47.6 weeks, resulting in a total of 82.1 implant-years for Test subjects and 71.1 implant-years for Control subjects.

The key safety outcome for this study was the neurological assessment of motor, sensory and reflex functions. At baseline, the majority of subjects had normal motor, sensory, and reflex function but with some expected abnormalities typical of chronic pain patients. One Test subject at Month 3 and one Test subject at Month 12 had a neurological deficit that was determined by the Investigator to be unrelated to stimulation. All other assessments showed either "No Change" or "Improvement" in neurological function and the results in the categories were similar between treatment groups.

Among the 198 randomized subjects, 22 serious adverse events (SAEs) were reported in 15 Test subjects (15/101, 14.9%) and 23 SAEs were reported in 16 Control subjects (16/97, 16.5%). None of the SAEs were categorized as both unanticipated and device-related. A similar percentage of Test and Control subjects experienced a non-serious AE (67.3% and 69.1%, respectively). See Table 9 below.

Table 9: Overall Summary of Adverse Events Intent-to-Treat Population

	Test		Control	
	Number of AEs	**Number (%) of Subjects with AE (N=101)**	**Number of AEs**	**Number (%) of Subjects with AE (N=97)**
All adverse events	312	71 (70.3%)	293	71 (73.2%)
Serious adverse events	22	15 (14.9%)	23	16 (16.5%)
Study-related serious adverse events	5	4 (4.0%)	8	7 (7.2%)
Non-serious adverse events	290	68 (67.3%)	270	67 (69.1%)
Study-related non-serious adverse events	39	28 (27.7%)	48	32 (33.0%)
Unanticipated adverse device effects[1]	0	0 (0.0%)	0	0 (0.0%)

[1] An unanticipated adverse device effect is defined as an event that is unanticipated in nature (e.g., is not pre-defined in the protocol), is device-related, and is serious.

Serious Adverse Events

Table 10 lists study-related serious adverse events (SAEs) by treatment group.

Table 10: Study-Related Serious Adverse Events, Intent-to-Treat Population

	Test		Control		Total	
MedDRA Preferred Term	**No. of SAEs**	**No. (%) of Subjects with SAE[a]** (N=101)	**No. of SAEs**	**No. (%) of Subjects with SAE[a]** (N= 97)	**No. of SAEs**	**No. (%) of Subjects with SAE[a]** (N= 198)
Total SAEs	**5**	**4 (4.0%)**	**8**	**7 (7.2%)**	**13**	**11 (5.6%)**
Wound infection staphylococcal	2	2 (2.0%)	0	0 (0.0%)	2	2 (1.0%)
Arrhythmia	0	0 (0.0%)	1	1 (1.0%)	1	1 (0.5%)
Cardiac arrest	0	0 (0.0%)	1	1 (1.0%)	1	1 (0.5%)
Extradural abscess	0	0 (0.0%)	1	1 (1.0%)	1	1 (0.5%)
Impaired healing	1	1 (1.0%)	0	0 (0.0%)	1	1 (0.5%)
Intracranial hypotension	0	0 (0.0%)	1[b]	1 (1.0%)	1	1 (0.5%)
Paresis	1	1 (1.0%)	0	0 (0.0%)	1	1 (0.5%)
Post lumbar puncture syndrome	0	0 (0.0%)	1[c]	1 (1.0%)	1	1 (0.5%)
Postoperative wound infection	0	0 (0.0%)	1	1 (1.0%)	1	1 (0.5%)
Procedural pain	0	0 (0.0%)	1	1 (1.0%)	1	1 (0.5%)
Stitch abscess	0	0 (0.0%)	1	1 (1.0%)	1	1 (0.5%)
Wound dehiscence	1	1 (1.0%)	0	0 (0.0%)	1	1 (0.5%)

Abbreviations: No., number; SAE, serious adverse event.

[a] Subjects may have experienced more than one event.

[b] Reported by the site as "fluid leak at lead insertion site".

[c] Reported by the site as "post dural puncture headache".

Table 11 provides an overview of the SAEs by treatment group. Neither group had a stimulation-related SAE. The majority of SAEs in both treatment groups occurred in the Permanent Phase (21/22, 95.5% in the Treatment group and 19/23, 82.6% in the Control group). Thirty-six of the 45 (80.0%) total SAEs were categorized as severe with 91.1% of the events (41 of the 45 total events) resolved.

Table 11: Serious Adverse Events by Treatment Group

	Test		Control	
MedDRA Preferred Term	**No. of SAEs**	**No. (%) of Subjects with SAE (N=101)**	**No. of SAEs**	**No. (%) of Subjects with SAE (N=97)**
Total SAEs[1]	22	15 (14.9%)	23	16 (16.5%)
Arthralgia	2	2 (2.0%)	1	1 (1.0%)
Pneumonia	2	2 (2.0%)	1	1 (1.0%)
Intervertebral disc degeneration	1	1 (1.0%)	1	1 (1.0%)
Wound infection staphylococcal	2	2 (2.0%)	0	0 (0.0%)
Ankle fracture	0	0 (0.0%)	1	1 (1.0%)
Aortic valve incompetence	0	0 (0.0%)	1	1 (1.0%)
Aphasia	0	0 (0.0%)	1	1 (1.0%)
Arrhythmia	0	0 (0.0%)	1	1 (1.0%)
Benign prostatic hyperplasia	1	1 (1.0%)	0	0 (0.0%)
Bradycardia	1	1 (1.0%)	0	0 (0.0%)
Bronchitis	1	1 (1.0%)	0	0 (0.0%)
Cardiac arrest	0	0 (0.0%)	1	1 (1.0%)
Cholelithiasis	0	0 (0.0%)	1	1 (1.0%)
Chronic obstructive pulmonary disease	2	1 (1.0%)	0	0 (0.0%)
Clostridial infection	0	0 (0.0%)	1	1 (1.0%)
Concussion	0	0 (0.0%)	1	1 (1.0%)
Convulsion	2	1 (1.0%)	0	0 (0.0%)
Dyspnoea	0	0 (0.0%)	1	1 (1.0%)
Encephalopathy	1	1 (1.0%)	0	0 (0.0%)
Extradural abscess	0	0 (0.0%)	1	1 (1.0%)
Gastroenteritis	1	1 (1.0%)	0	0 (0.0%)
Impaired healing	1	1 (1.0%)	0	0 (0.0%)
Intestinal obstruction	1	1 (1.0%)	0	0 (0.0%)
Intracranial hypotension[2]	0	0 (0.0%)	1	1 (1.0%)
Medical device complication[3]	1	1 (1.0%)	0	0 (0.0%)
Migraine	0	0 (0.0%)	1	1 (1.0%)
Myocardial infarction	0	0 (0.0%)	1	1 (1.0%)
Pain in extremity	0	0 (0.0%)	1	1 (1.0%)
Paresis	1	1 (1.0%)	0	0 (0.0%)

MedDRA Preferred Term	Test		Control	
	No. of SAEs	No. (%) of Subjects with SAE (N=101)	No. of SAEs	No. (%) of Subjects with SAE (N=97)
Post lumbar puncture syndrome[4]	0	0 (0.0%)	1	1 (1.0%)
Postoperative wound infection	0	0 (0.0%)	1	1 (1.0%)
Procedural pain	0	0 (0.0%)	1	1 (1.0%)
Rib fracture	1	1 (1.0%)	0	0 (0.0%)
Spinal compression fracture	0	0 (0.0%)	1	1 (1.0%)
Stitch abscess	0	0 (0.0%)	1	1 (1.0%)
Upper respiratory tract infection	0	0 (0.0%)	1	1 (1.0%)
Wound dehiscence	1	1 (1.0%)	0	0 (0.0%)

Abbreviations: No., number; SAE, serious adverse event.

[1] Subjects may have experienced more than one event.
[2] Reported by the site as "fluid leak at lead insertion site".
[3] Reporeted by the site as "fractured fusion hardware, lumbar spine".
[4] Reported by the site as "post dural puncture headache".

Deaths

There were 2 study subject deaths. One control subject died as a result of a myocardial infarction during the device implant procedure. One test subject was diagnosed with hepatic neoplasm malignant after their Month 12 visit and subsequently died.

All Adverse Events

Table 12 provides a summary of all study-related adverse events (both serious and non-serious) by treatment group through one year. Among the 198 randomized subjects, a total of 44 study-related AEs were reported in 28 Test subjects (28/101, 27.7%) and a total of 56 study-related AEs were reported in 35 Control subjects (35/97, 36.1%). The most frequent study-related AEs were 1) implant site pain with 11 events occurring in 10 Test subjects (10/101, 9.9%) and 10 events occurring in 9 Control subjects (9/97, 9.3%), and 2) uncomfortable paresthesia with no occurrences in Test subjects and 11 events occurring in 11 Control subjects (11/97, 11.3%).

Table 12: Study-Related Adverse Events Ordered by Percent of Total Subjects with Event
Intent-to-Treat Population

MedDRA Preferred Term	Test		Control		Total	
	No. of AEs	No. (%) of Subjects with AE (N=101)	No. of AEs	No. (%) of Subjects with AE (N= 97)	No. of AEs	No. (%) of Subjects with AE (N= 198)
Total AEs[1]	44	28 (27.7%)	56	35 (36.1%)	100	63 (31.8%)
Implant site pain	11	10 (9.9%)	10	9 (9.3%)	21	19 (9.6%)

MedDRA Preferred Term	Test		Control		Total	
	No. of AEs	No. (%) of Subjects with AE (N=101)	No. of AEs	No. (%) of Subjects with AE (N= 97)	No. of AEs	No. (%) of Subjects with AE (N= 198)
Paraesthesia[2]	0	0 (0.0%)	11	11 (11.3%)	11	11 (5.6%)
Device dislocation[3]	3	3 (3.0%)	5	5 (5.2%)	8	8 (4.0%)
Therapeutic product ineffective[4]	1	1 (1.0%)	6	6 (6.2%)	7	7 (3.5%)
Impaired healing	3	3 (3.0%)	0	0 (0.0%)	3	3 (1.5%)
Implant site effusion	2	2 (2.0%)	1	1 (1.0%)	3	3 (1.5%)
Intracranial hypotension[5]	1	1 (1.0%)	2	2 (2.1%)	3	3 (1.5%)
Rash	3	1 (1.0%)	2	2 (2.1%)	5	3 (1.5%)
Dermatitis contact[6]	2	2 (2.0%)	0	0 (0.0%)	2	2 (1.0%)
Implant site haematoma	0	0 (0.0%)	2	2 (2.1%)	2	2 (1.0%)
Implant site swelling	2	2 (2.0%)	0	0 (0.0%)	2	2 (1.0%)
Muscle spasms	0	0 (0.0%)	2	2 (2.1%)	2	2 (1.0%)
Pain in extremity	2	2 (2.0%)	0	0 (0.0%)	2	2 (1.0%)
Wound infection staphylococcal	2	2 (2.0%)	0	0 (0.0%)	2	2 (1.0%)
Anxiety	0	0 (0.0%)	1	1 (1.0%)	1	1 (0.5%)
Arrhythmia	0	0 (0.0%)	1	1 (1.0%)	1	1 (0.5%)
Cardiac arrest	0	0 (0.0%)	1	1 (1.0%)	1	1 (0.5%)
Cellulitis	1	1 (1.0%)	0	0 (0.0%)	1	1 (0.5%)
Device battery issue	0	0 (0.0%)	1	1 (1.0%)	1	1 (0.5%)
Device stimulation issue[7]	0	0 (0.0%)	1	1 (1.0%)	1	1 (0.5%)
Extradural abscess	0	0 (0.0%)	1	1 (1.0%)	1	1 (0.5%)
Implant site erythema	1	1 (1.0%)	0	0 (0.0%)	1	1 (0.5%)
Implant site irritation	0	0 (0.0%)	1	1 (1.0%)	1	1 (0.5%)
Implant site pruritus	1	1 (1.0%)	0	0 (0.0%)	1	1 (0.5%)
Implant site rash	1	1 (1.0%)	0	0 (0.0%)	1	1 (0.5%)
Incision site pain	1	1 (1.0%)	0	0 (0.0%)	1	1 (0.5%)
Limb discomfort	0	0 (0.0%)	1	1 (1.0%)	1	1 (0.5%)
Micturition urgency	0	0 (0.0%)	1	1 (1.0%)	1	1 (0.5%)
Motor dysfunction	1	1 (1.0%)	0	0 (0.0%)	1	1 (0.5%)
Paresis	1	1 (1.0%)	0	0 (0.0%)	1	1 (0.5%)
Post lumbar puncture syndrome[8]	0	0 (0.0%)	1	1 (1.0%)	1	1 (0.5%)

MedDRA Preferred Term	Test		Control		Total	
	No. of AEs	No. (%) of Subjects with AE (N=101)	No. of AEs	No. (%) of Subjects with AE (N= 97)	No. of AEs	No. (%) of Subjects with AE (N= 198)
Postoperative wound infection	0	0 (0.0%)	1	1 (1.0%)	1	1 (0.5%)
Procedural pain	0	0 (0.0%)	1	1 (1.0%)	1	1 (0.5%)
Stitch abscess	0	0 (0.0%)	1	1 (1.0%)	1	1 (0.5%)
Suture removal	1	1 (1.0%)	0	0 (0.0%)	1	1 (0.5%)
Tinnitus	0	0 (0.0%)	1	1 (1.0%)	1	1 (0.5%)
Urinary retention	0	0 (0.0%)	1	1 (1.0%)	1	1 (0.5%)
Wound complication	1	1 (1.0%)	0	0 (0.0%)	1	1 (0.5%)
Wound dehiscence	1	1 (1.0%)	0	0 (0.0%)	1	1 (0.5%)
Wound secretion	2	1 (1.0%)	0	0 (0.0%)	2	1 (0.5%)

Abbreviations: No., number; AE, adverse event.[1] Subjects may have experienced more than one event.
[2] Reported as uncomfortable paresthesia.
[3] Reported as lead migration.
[4] Reported as lack of pain relief.
[5] Reported as CSF leak or possible CSF leak.
[6] Reported as bandage allergy.
[7] Reported as "stimulation that continues after IPG is turned off".
[8] Reported as post dural puncture headache

Table 13 provides a summary of all adverse events (both serious and non-serious), through one year, by treatment group. Among the 198 randomized subjects, a total of 312 AEs were reported in 71 Test subjects (71/101, 70.3%) and a total of 293 AEs were reported in 71 Control subjects (71/97, 73.2%). Stimulation related AEs were reported in 3 (3/101, 3.0%) of Test subjects and 17 (17/97, 17.5%) 17.5% of Control subjects. The majority of AEs in both treatment groups occurred in the Permanent Phase (287/312, 92.0% of events in Test subjects and 256/293, 87.4% of events in the Control subjects). Most events were categorized as mild or moderate (284/312, 91.0% of events in the Test subjects and 269/293, 91.8% of Control subjects) and the majority of the events had resolved as of the data cutoff for this report (62/101, 61.4% and 61/97, 62.9% of the events in Test and Control subjects, respectively). Most AEs were classified as mild or moderate.

Table 13: All Adverse Events - Intent-to-Treat Population

MedDRA Preferred Term	Test		Control	
	No. of AEs	No. (%) of Subjects with AE (N=101)	No. of AEs	No. (%) of Subjects with AE (N= 97)
Total AEs[1]	**312**	**71 (70.3%)**	**293**	**71 (73.2%)**

MedDRA Preferred Term	Test		Control	
	No. of AEs	No. (%) of Subjects with AE (N=101)	No. of AEs	No. (%) of Subjects with AE (N= 97)
Related to Stimulation	**5**	**3 (3%)**	**20**	**17 (17.5%)**
AEs by phase at onset				
Before randomization	3	3 (3.0%)	4	3 (3.1%)
Between randomization and Trial Phase	2	2 (2.0%)	2	2 (2.1%)
Trial Phase	12	10 (9.9%)	15	11 (11.3%)
Between Trial and Permanent Implant	8	5 (5.0%)	16	10 (10.3%)
Permanent Implant Phase	287	67 (66.3%)	256	65 (67.0%)
Permanent implant to Month 3	94	41 (40.6%)	104	49 (50.5%)
Month 3-6	86	39 (38.6%)	61	29 (29.9%)
Month 6-12	107	46 (45.5%)	91	38 (39.2%)
AEs by severity				
Mild	138	52 (51.5%)	143	56 (57.7%)
Moderate	146	48 (47.5%)	126	45 (46.4%)
Severe	28	19 (18.8%)	24	15 (15.5%)
AEs by outcome				
Resolved	176	62 (61.4%)	164	61 (62.9%)
Ongoing[2]	136[3]	36 (35.6%)	128[4]	33 (34.0%)
Death[5]	0	0 (0%)	1	1 (1.0%)
Arthralgia	22	16 (15.8%)	23	15 (15.5%)
Back pain	23	18 (17.8%)	7	6 (6.2%)
Implant site pain	13	12 (11.9%)	11	10 (10.3%)
Pain in extremity	13	10 (9.9%)	8	7 (7.2%)
Paraesthesia	1	1 (1.0%)	14	13 (13.4%)
Bronchitis	7	6 (5.9%)	5	5 (5.2%)
Therapeutic product ineffective	2	2 (2.0%)	7	7 (7.2%)
Device dislocation	3	3 (3.0%)	5	5 (5.2%)
Insomnia	5	5 (5.0%)	3	3 (3.1%)
Muscle spasms	3	3 (3.0%)	5	5 (5.2%)
Depression	4	4 (4.0%)	3	3 (3.1%)
Headache	3	3 (3.0%)	5	4 (4.1%)
Hypoaesthesia	5	5 (5.0%)	2	2 (2.1%)
Spinal osteoarthritis	4	4 (4.0%)	3	3 (3.1%)
Upper respiratory tract infection	2	2 (2.0%)	5	5 (5.2%)
Hypertension	2	2 (2.0%)	4	4 (4.1%)
Migraine	3	2 (2.0%)	4	4 (4.1%)
Nasopharyngitis	4	4 (4.0%)	2	2 (2.1%)

MedDRA Preferred Term	Test		Control	
	No. of AEs	No. (%) of Subjects with AE (N=101)	No. of AEs	No. (%) of Subjects with AE (N= 97)
Nausea	4	4 (4.0%)	2	2 (2.1%)
Pain	2	2 (2.0%)	4	4 (4.1%)
Anxiety	3	2 (2.0%)	3	3 (3.1%)
Constipation	3	3 (3.0%)	2	2 (2.1%)
Fall	2	2 (2.0%)	4	3 (3.1%)
Fatigue	2	2 (2.0%)	3	3 (3.1%)
Oedema peripheral	3	3 (3.0%)	3	2 (2.1%)
Pneumonia	4	3 (3.0%)	2	2 (2.1%)
Chest pain	1	1 (1.0%)	3	3 (3.1%)
Hypothyroidism	2	2 (2.0%)	2	2 (2.1%)
Implant site effusion	3	3 (3.0%)	1	1 (1.0%)
Influenza	2	2 (2.0%)	2	2 (2.1%)
Neck pain	1	1 (1.0%)	3	3 (3.1%)
Oropharyngeal pain	1	1 (1.0%)	3	3 (3.1%)
Tinnitus	2	2 (2.0%)	2	2 (2.1%)
Bursitis	1	1 (1.0%)	2	2 (2.1%)
Cervicobrachial syndrome	2	2 (2.0%)	1	1 (1.0%)
Contusion	1	1 (1.0%)	2	2 (2.1%)
Diverticulitis	2	2 (2.0%)	1	1 (1.0%)
Fungal infection	0	0 (0.0%)	3	3 (3.1%)
Impaired healing	3	3 (3.0%)	0	0 (0.0%)
Influenza like illness	3	3 (3.0%)	0	0 (0.0%)
Intracranial hypotension	1	1 (1.0%)	2	2 (2.1%)
Ligament sprain	1	1 (1.0%)	2	2 (2.1%)
Muscular weakness	1	1 (1.0%)	2	2 (2.1%)
Musculoskeletal pain	3	2 (2.0%)	1	1 (1.0%)
Nephrolithiasis	1	1 (1.0%)	2	2 (2.1%)
Rash	3	1 (1.0%)	2	2 (2.1%)
Sinusitis	0	0 (0.0%)	3	3 (3.1%)
Vomiting	1	1 (1.0%)	2	2 (2.1%)
Amenorrhoea	1	1 (1.0%)	1	1 (1.0%)
Ankle fracture	1	1 (1.0%)	1	1 (1.0%)
Arthropathy	1	1 (1.0%)	1	1 (1.0%)
Blood pressure increased	1	1 (1.0%)	1	1 (1.0%)
Bradycardia	1	1 (1.0%)	1	1 (1.0%)
Cellulitis	2	2 (2.0%)	0	0 (0.0%)
Cholelithiasis	1	1 (1.0%)	2	1 (1.0%)
Dermatitis contact	2	2 (2.0%)	0	0 (0.0%)

MedDRA Preferred Term	Test		Control	
	No. of AEs	No. (%) of Subjects with AE (N=101)	No. of AEs	No. (%) of Subjects with AE (N= 97)
Device stimulation issue	0	0 (0.0%)	2	2 (2.1%)
Diarrhoea	0	0 (0.0%)	2	2 (2.1%)
Dizziness	1	1 (1.0%)	2	1 (1.0%)
Drug withdrawal syndrome	2	2 (2.0%)	0	0 (0.0%)
Dysphagia	2	2 (2.0%)	0	0 (0.0%)
Dyspnoea	0	0 (0.0%)	2	2 (2.1%)
Erythema	0	0 (0.0%)	2	2 (2.1%)
Eyelid cyst	2	2 (2.0%)	0	0 (0.0%)
Gastritis	1	1 (1.0%)	1	1 (1.0%)
Gastroenteritis	2	2 (2.0%)	0	0 (0.0%)
Gastrooesophageal reflux disease	0	0 (0.0%)	2	2 (2.1%)
Groin pain	1	1 (1.0%)	1	1 (1.0%)
Herpes zoster	2	2 (2.0%)	0	0 (0.0%)
Implant site haematoma	0	0 (0.0%)	2	2 (2.1%)
Implant site irritation	1	1 (1.0%)	1	1 (1.0%)
Implant site rash	2	2 (2.0%)	0	0 (0.0%)
Implant site swelling	2	2 (2.0%)	0	0 (0.0%)
Intervertebral disc degeneration	1	1 (1.0%)	1	1 (1.0%)
Joint injury	2	2 (2.0%)	0	0 (0.0%)
Malaise	0	0 (0.0%)	2	2 (2.1%)
Memory impairment	1	1 (1.0%)	1	1 (1.0%)
Motor dysfunction	2	2 (2.0%)	0	0 (0.0%)
Muscle tightness	2	2 (2.0%)	0	0 (0.0%)
Myalgia	1	1 (1.0%)	1	1 (1.0%)
Neuroma	3	2 (2.0%)	0	0 (0.0%)
Piriformis syndrome	2	2 (2.0%)	0	0 (0.0%)
Procedural pain	1	1 (1.0%)	1	1 (1.0%)
Rib fracture	2	2 (2.0%)	0	0 (0.0%)
Sciatica	2	2 (2.0%)	0	0 (0.0%)
Seasonal allergy	0	0 (0.0%)	2	2 (2.1%)
Sensory loss	1	1 (1.0%)	1	1 (1.0%)
Sleep apnoea syndrome	0	0 (0.0%)	2	2 (2.1%)
Temperature intolerance	1	1 (1.0%)	2	1 (1.0%)
Toothache	1	1 (1.0%)	1	1 (1.0%)
Weight decreased	2	2 (2.0%)	0	0 (0.0%)
Wound infection staphylococcal	2	2 (2.0%)	0	0 (0.0%)
Abdominal distension	0	0 (0.0%)	1	1 (1.0%)
Abdominal pain	0	0 (0.0%)	1	1 (1.0%)

MedDRA Preferred Term	Test		Control	
	No. of AEs	No. (%) of Subjects with AE (N=101)	No. of AEs	No. (%) of Subjects with AE (N= 97)
Abdominal pain upper	0	0 (0.0%)	1	1 (1.0%)
Affect lability	0	0 (0.0%)	1	1 (1.0%)
Amnesia	0	0 (0.0%)	1	1 (1.0%)
Androgen deficiency	1	1 (1.0%)	0	0 (0.0%)
Antinuclear antibody positive	1	1 (1.0%)	0	0 (0.0%)
Aortic valve incompetence	0	0 (0.0%)	1	1 (1.0%)
Aphasia	0	0 (0.0%)	1	1 (1.0%)
Appetite disorder	1	1 (1.0%)	0	0 (0.0%)
Arrhythmia	0	0 (0.0%)	1	1 (1.0%)
Arthritis	3	1 (1.0%)	0	0 (0.0%)
Asthenia	0	0 (0.0%)	1	1 (1.0%)
Asthma	0	0 (0.0%)	1	1 (1.0%)
Back injury	1	1 (1.0%)	0	0 (0.0%)
Bacterial infection	0	0 (0.0%)	1	1 (1.0%)
Basal cell carcinoma	1	1 (1.0%)	0	0 (0.0%)
Benign prostatic hyperplasia	1	1 (1.0%)	0	0 (0.0%)
Blood glucose increased	0	0 (0.0%)	1	1 (1.0%)
Blood testosterone decreased	0	0 (0.0%)	1	1 (1.0%)
Breast mass	1	1 (1.0%)	0	0 (0.0%)
Breath sounds abnormal	1	1 (1.0%)	0	0 (0.0%)
Burning sensation	1	1 (1.0%)	0	0 (0.0%)
Cardiac arrest	0	0 (0.0%)	1	1 (1.0%)
Carotid artery stenosis	0	0 (0.0%)	1	1 (1.0%)
Cataract	2	1 (1.0%)	0	0 (0.0%)
Chest injury	1	1 (1.0%)	0	0 (0.0%)
Chills	0	0 (0.0%)	1	1 (1.0%)
Chronic obstructive pulmonary disease	2	1 (1.0%)	0	0 (0.0%)
Clostridial infection	0	0 (0.0%)	1	1 (1.0%)
Coccydynia	1	1 (1.0%)	0	0 (0.0%)
Colitis ischaemic	1	1 (1.0%)	0	0 (0.0%)
Concussion	0	0 (0.0%)	1	1 (1.0%)
Convulsion	2	1 (1.0%)	0	0 (0.0%)
Coronary artery disease	0	0 (0.0%)	1	1 (1.0%)
Cough	0	0 (0.0%)	1	1 (1.0%)
Cyst	1	1 (1.0%)	0	0 (0.0%)
Cystitis	0	0 (0.0%)	1	1 (1.0%)
Dehydration	0	0 (0.0%)	1	1 (1.0%)
Dental discomfort	0	0 (0.0%)	1	1 (1.0%)

MedDRA Preferred Term	Test		Control	
	No. of AEs	No. (%) of Subjects with AE (N=101)	No. of AEs	No. (%) of Subjects with AE (N= 97)
Depressed level of consciousness	0	0 (0.0%)	1	1 (1.0%)
Device battery issue	0	0 (0.0%)	1	1 (1.0%)
Diabetes mellitus	1	1 (1.0%)	0	0 (0.0%)
Diarrhoea haemorrhagic	0	0 (0.0%)	1	1 (1.0%)
Discomfort	0	0 (0.0%)	1	1 (1.0%)
Disorientation	1	1 (1.0%)	0	0 (0.0%)
Dry eye	0	0 (0.0%)	1	1 (1.0%)
Dysuria	0	0 (0.0%)	1	1 (1.0%)
Ear infection	0	0 (0.0%)	1	1 (1.0%)
Ear pain	1	1 (1.0%)	0	0 (0.0%)
Electrocardiogram abnormal	1	1 (1.0%)	0	0 (0.0%)
Encephalopathy	1	1 (1.0%)	0	0 (0.0%)
Epicondylitis	1	1 (1.0%)	0	0 (0.0%)
Extradural abscess	0	0 (0.0%)	1	1 (1.0%)
Eyelid ptosis	0	0 (0.0%)	1	1 (1.0%)
Fibromyalgia	1	1 (1.0%)	0	0 (0.0%)
Flank pain	0	0 (0.0%)	1	1 (1.0%)
Food poisoning	0	0 (0.0%)	1	1 (1.0%)
Foot fracture	1	1 (1.0%)	0	0 (0.0%)
Gastrointestinal viral infection	1	1 (1.0%)	0	0 (0.0%)
Glaucoma	1	1 (1.0%)	0	0 (0.0%)
Hallucination	0	0 (0.0%)	1	1 (1.0%)
Hemiparesis	1	1 (1.0%)	0	0 (0.0%)
Hypercholesterolaemia	0	0 (0.0%)	1	1 (1.0%)
Hyperglycaemia	1	1 (1.0%)	0	0 (0.0%)
Hyponatraemia	1	1 (1.0%)	0	0 (0.0%)
Hypoxia	1	1 (1.0%)	0	0 (0.0%)
Implant site cellulitis	1	1 (1.0%)	0	0 (0.0%)
Implant site erythema	1	1 (1.0%)	0	0 (0.0%)
Implant site pruritus	1	1 (1.0%)	0	0 (0.0%)
Incision site cellulitis	0	0 (0.0%)	1	1 (1.0%)
Incision site pain	1	1 (1.0%)	0	0 (0.0%)
Increased appetite	0	0 (0.0%)	1	1 (1.0%)
Infected dermal cyst	0	0 (0.0%)	1	1 (1.0%)
Infection	0	0 (0.0%)	1	1 (1.0%)
Intervertebral disc protrusion	1	1 (1.0%)	0	0 (0.0%)
Intestinal obstruction	1	1 (1.0%)	0	0 (0.0%)
Intraocular pressure increased	1	1 (1.0%)	0	0 (0.0%)

MedDRA Preferred Term	Test		Control	
	No. of AEs	No. (%) of Subjects with AE (N=101)	No. of AEs	No. (%) of Subjects with AE (N= 97)
Joint range of motion decreased	0	0 (0.0%)	1	1 (1.0%)
Keratitis	0	0 (0.0%)	1	1 (1.0%)
Kidney infection	1	1 (1.0%)	0	0 (0.0%)
Laceration	1	1 (1.0%)	0	0 (0.0%)
Ligament pain	1	1 (1.0%)	0	0 (0.0%)
Limb discomfort	0	0 (0.0%)	1	1 (1.0%)
Lip swelling	0	0 (0.0%)	1	1 (1.0%)
Lumbar spinal stenosis	1	1 (1.0%)	0	0 (0.0%)
Lymphadenopathy	1	1 (1.0%)	0	0 (0.0%)
Medical device complication	1	1 (1.0%)	0	0 (0.0%)
Menorrhagia	0	0 (0.0%)	1	1 (1.0%)
Micturition urgency	0	0 (0.0%)	1	1 (1.0%)
Muscle strain	1	1 (1.0%)	0	0 (0.0%)
Muscle twitching	1	1 (1.0%)	0	0 (0.0%)
Musculoskeletal chest pain	1	1 (1.0%)	0	0 (0.0%)
Musculoskeletal stiffness	0	0 (0.0%)	1	1 (1.0%)
Myocardial infarction	0	0 (0.0%)	1	1 (1.0%)
Myositis	1	1 (1.0%)	0	0 (0.0%)
Nasal congestion	0	0 (0.0%)	1	1 (1.0%)
Neuropathy peripheral	0	0 (0.0%)	1	1 (1.0%)
Night sweats	0	0 (0.0%)	1	1 (1.0%)
Nightmare	1	1 (1.0%)	0	0 (0.0%)
Osteoarthritis	0	0 (0.0%)	1	1 (1.0%)
Osteoporosis	1	1 (1.0%)	0	0 (0.0%)
Palpitations	0	0 (0.0%)	1	1 (1.0%)
Panic attack	1	1 (1.0%)	0	0 (0.0%)
Paresis	1	1 (1.0%)	0	0 (0.0%)
Paronychia	0	0 (0.0%)	1	1 (1.0%)
Pharyngitis	1	1 (1.0%)	0	0 (0.0%)
Pharyngitis streptococcal	1	1 (1.0%)	0	0 (0.0%)
Pleurisy	1	1 (1.0%)	0	0 (0.0%)
Pollakiuria	0	0 (0.0%)	1	1 (1.0%)
Post herpetic neuralgia	1	1 (1.0%)	0	0 (0.0%)
Post lumbar puncture syndrome	0	0 (0.0%)	1	1 (1.0%)
Postoperative wound infection	0	0 (0.0%)	1	1 (1.0%)
Proteinuria	1	1 (1.0%)	0	0 (0.0%)
Pruritus	1	1 (1.0%)	0	0 (0.0%)
Radicular pain	0	0 (0.0%)	1	1 (1.0%)

MedDRA Preferred Term	Test		Control	
	No. of AEs	No. (%) of Subjects with AE (N=101)	No. of AEs	No. (%) of Subjects with AE (N= 97)
Radiculitis cervical	1	1 (1.0%)	0	0 (0.0%)
Renal cyst	0	0 (0.0%)	1	1 (1.0%)
Restlessness	0	0 (0.0%)	1	1 (1.0%)
Road traffic accident	0	0 (0.0%)	1	1 (1.0%)
Rotator cuff syndrome	1	1 (1.0%)	0	0 (0.0%)
Sacroiliitis	0	0 (0.0%)	1	1 (1.0%)
Seborrhoeic keratosis	0	0 (0.0%)	1	1 (1.0%)
Sinus headache	0	0 (0.0%)	1	1 (1.0%)
Small intestinal bacterial overgrowth	1	1 (1.0%)	0	0 (0.0%)
Spinal compression fracture	0	0 (0.0%)	1	1 (1.0%)
Spinal pain	1	1 (1.0%)	0	0 (0.0%)
Spondylolisthesis	1	1 (1.0%)	0	0 (0.0%)
Stitch abscess	0	0 (0.0%)	1	1 (1.0%)
Suture removal	1	1 (1.0%)	0	0 (0.0%)
Syncope	2	1 (1.0%)	0	0 (0.0%)
Synovial cyst	1	1 (1.0%)	0	0 (0.0%)
Tendonitis	1	1 (1.0%)	0	0 (0.0%)
Thermal burn	1	1 (1.0%)	0	0 (0.0%)
Thirst	0	0 (0.0%)	1	1 (1.0%)
Tongue oedema	0	0 (0.0%)	1	1 (1.0%)
Tooth infection	0	0 (0.0%)	1	1 (1.0%)
Torticollis	1	1 (1.0%)	0	0 (0.0%)
Urinary incontinence	0	0 (0.0%)	1	1 (1.0%)
Urinary retention	0	0 (0.0%)	1	1 (1.0%)
Urinary tract infection	0	0 (0.0%)	1	1 (1.0%)
Vaginal infection	0	0 (0.0%)	1	1 (1.0%)
Vertigo	0	0 (0.0%)	1	1 (1.0%)
Vitamin D deficiency	0	0 (0.0%)	1	1 (1.0%)
Weight increased	1	1 (1.0%)	0	0 (0.0%)
Wound complication	1	1 (1.0%)	0	0 (0.0%)
Wound dehiscence	1	1 (1.0%)	0	0 (0.0%)
Wound secretion	2	1 (1.0%)	0	0 (0.0%)
Wrist fracture	1	1 (1.0%)	0	0 (0.0%)

Abbreviations: AE = adverse event; SAE = serious adverse event; IPG = implantable pulse generator.

Columns (no. (%) of subjects with AE) may not add to total as subjects may have experienced more than one event.

[1] Device-related events include those related to the Trial Stimulator, Lead, Extension, IPG, or Charger.

[2] Includes events that were ongoing at the time of the March 19, 2014 database snapshot and also those events that were ongoing at study completion (in discontinued subjects).
[3] 131 of the 136 ongoing adverse events in the Test group are unrelated to the study.
[4] 119 of the 128 ongoing adverse events in the Control group are unrelated to the study.Abbreviations: No., number; AE, adverse event.
[5] Death occurred following completion of 12 month visit.

In subjects who underwent a permanent implant (PS Subset), there were 11 additional surgical procedures in 9 (10.0%) Test subjects and 18 additional procedures in 15 (18.5%) Control subjects. A summary of these additional procedures is presented in Table 14 below.

Five (5.6%) Test subjects and 9 (11.1%) Control subjects underwent system explant. Four of the 5 Test subjects and all 9 of the Control subjects with system explant were discontinued from the study after the explant. One Test subject was explanted and then re-implanted a month later.

Table 14: Additional Surgical Procedures by Type and Treatment Group for the Permanent Implant Subset

	Test		Control	
Procedure Type	**Number of Procedures**	**Number (%) of Subjects** (N=90)	**Number of Procedures**	**Number (%) of Subjects** (N=81)
Total	11	9 (10.0%)	18	15 (18.5%)
System (IPG and leads)				
Repositioning	0	0 (0.0%)	1	1 (1.2%)
Replacement	1	1 (1.1%)	0	0 (0.0%)
Explant	5[1]	5 (5.6%)	9[2]	9 (11.1%)
IPG only				
Repositioning	3	3 (3.3%)	2	2 (2.5%)
Replacement	0	0 (0.0%)	1	1 (1.2%)
Leads only				
Repositioning	1	1 (1.1%)	4	4 (4.9%)
Replacement	1	1 (1.1%)	1	1 (1.2%)

Abbreviations: IPG, implantable pulse generator.
[1] Therapeutic product ineffective (2), wound infection staphylococcal (1) impaired healing (1) and due to incarceration (1).
[2] Therapeutic product ineffective (3), paresthesia (1), stitch abscess (1), postoperative wound infection and extradural abscess (1), muscle weakness and paresthesia (1), back pain and pain in extremity (1), and device dislocation and bradycardia (1).

The safety of the device at 10 kHz was only studied at output levels that do not produce paresthesia and the safety of the device at paresthesia inducing amplitudes has not been studied. It should also be noted that the safety of the

device for device settings between 2 and 1200 Hz with paresthesia was based on adverse events that occurred in the literature (see Section 3 below.)

2. Effectiveness Results

The Per Protocol (PP) analysis of effectiveness was based on the 179 evaluable subjects at the 3-month time point and the Intent-to-Treat (ITT) analysis of effectiveness was based on the 198 evaluable at the 3-month time point.

The following effective analyses were performed:

- *PP*: All randomized subjects who completed the Primary Endpoint Assessment.

- *ITT*: All subjects who met the enrollment criteria and received a randomization assignment.

One hundred and seventy-nine (179) subjects of the 198 randomized subjects are included in the PP population (92 in the Test group and 87 in the Control group.) All of the 198 randomized subjects are included in the ITT population (101 in the Test group and 97 in the Control group.)

For the Test group, only subjects receiving 10 kHz stimulation were included toward the primary endpoint analysis. Neurologic status (including motor, sensory and reflex functions) was characterized as improved, maintained, or a deficit as compared with baseline.

Subjects who did not have a successful Trial Phase were considered failures (non-responders) toward the primary endpoint. Additionally, a subject was classified as a non-responder for the 3-month primary effectiveness endpoint and subsequent assessments if there was an increase in morphine equivalent dose of a baseline opioid. Exceptions were temporary increases in dosage to treat the following:

- Post-operative pain (the clinical site's standard practice for prophylactic pre-surgery antibiotics and post-surgery pain medications was followed)
- An acute co-morbidity unrelated to the initial indication that is not expected to respond to spinal cord stimulation.

A subject was also classified as a non-responder toward the primary endpoint if there was an increase from baseline in non-opiate pain medication used to treat their back and/or leg pain as indicated for this study for duration of greater than 5 days.

A subject was included in the PP population if the subject received a randomization assignment, met all eligibility criteria, reached an endpoint and there were no missing assessments required to determine the subject's primary endpoint success. A subject was also included in the PP population if the subject received a randomization assignment, met all eligibility criteria, did not reach an endpoint but met either of the following criteria:

- Subject had a successful trial but did not reach the month 3 endpoint due to a device-related adverse event or device/procedure issue (subject was considered a non-responder)
- Subject had a successful trial (had <50% reduction in back pain VAS during the trial phase), and elected not to have a permanent implant (subject was considered a non-responder)

The composite primary endpoint was met for the PP and ITT analysis populations. For the PP population, 75.0% of the Test subjects met the primary endpoint compared to 37.9% of the Control subjects. For the ITT population, 75.0% of the Test subjects met the primary endpoint compared to 37.9% of the Control subjects. Both the PP and ITT analyses demonstrated the non-inferiority of the Test group to the Control group with a pre- specified 10% non-inferiority margin ($p<0.001$). Table 15 below summarizes the primary efficacy results for the PP and ITT populations.

Table 15: Primary Endpoint Analysis Per-Protocol and Intent-to-Treat Populations

	Test Number (%) of Subjects	**Control Number (%) of Subjects**	**10% Non-Inferiority P-value**
Per Protocol Population	**N=92**	**N=87**	
Met overall primary endpoint	**69 (75.0%)**	**33 (37.9%)**	**< 0.001[1]**
Met effectiveness component of primary endpoint	69 (75.0%)	33 (37.9%)	
≥ 50% improvement of back pain VAS score	72 (78.3%)	34 (39.1%)	
No increase in baseline pain medications[2]	85 (92.4%)	81 (93.1%)	
Met safety component of primary endpoint[3]	92 (100.0%)	87 (100.0%)	
Intent-to-Treat Population	**N=101**	**N=97**	
Met overall primary endpoint	**75.7 (75.0%)**	**36.6 (37.7%)**	**< 0.001[4]**
Met effectiveness component of primary endpoint	75.7 (75.0%)	36.6 (37.7%)	
≥ 50% improvement of back pain VAS score	78.7 (77.9%)	37.6 (38.8%)	
No increase in baseline pain medications[2]	94 (93.1%)	91 (93.8%)	
Met safety component of primary endpoint[3]	101 (100.0%)	97 (100.0%)	

Abbreviations: VAS, visual analog scale.

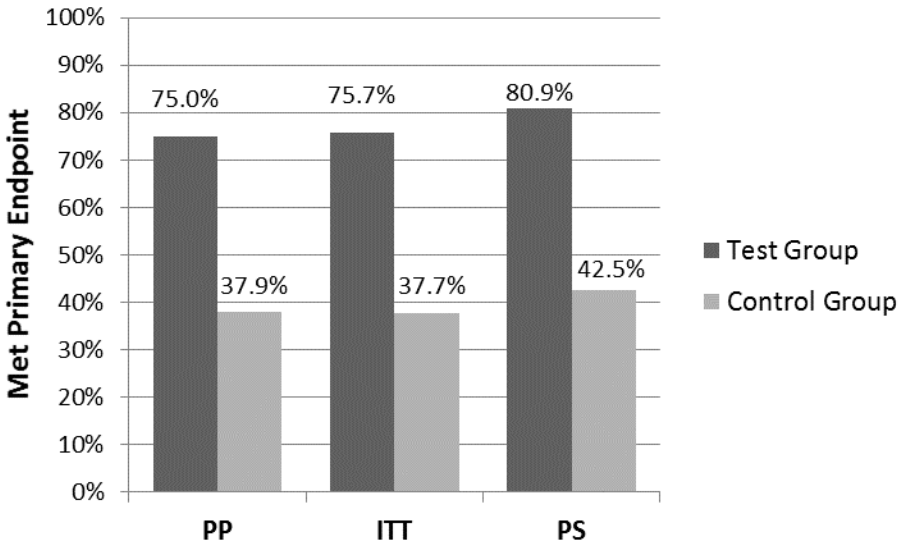
[1] By exact binomial test.

[2] No increase in morphine equivalent dose of a baseline opioid and no increase in pain medication used to treat back and/or leg pain (as indicated for this study) for duration greater than 5 days.

[3] No stimulation-related neurological deficit.

[4] By Z test for difference between two proportions.

The primary endpoint analysis by population and treatment group is presented graphically in Figure 3 and Figure 4.



Between group and non-inferiority p-values are <0.001 for all three analyses.
Abbreviations: PP, Per Protocol; ITT, Intent to Treat; PS, Permanent Implant Subset.

Figure 3: Primary Endpoint Results by Analysis Population and Treatment Group

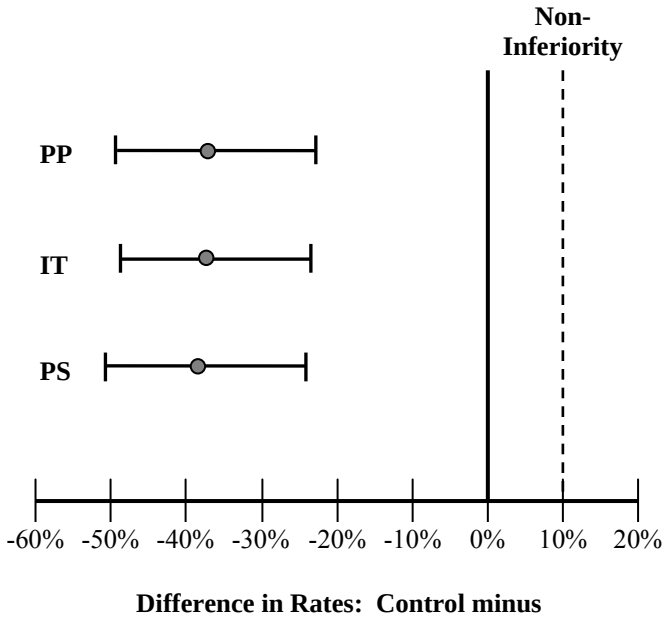


Figure 4: Differences in Treatment Group Responder Rates and Associated 95% Confidence Intervals for the Primary Endpoint by Analysis Populations

Secondary Endpoints

All predefined, hierarchically evaluated secondary endpoints demonstrated non-inferiority of the Test group to the Control group in the ITT and PP populations ($p<0.001$). Table 16 shows the results for percent change from baseline in back and leg pain (the first two analyses in the hierarchical testing order), Table 17 shows results for the Oswestry Disability Index (the third analyses in the

hierarchical testing order), and Table 18 shows results for back and leg Pain (as assessed by VAS) percent change from baseline at the Month 6 and Month 12 Assessments (the fourth through seventh analyses in the hierarchical testing order).

Table 16: Back and Leg Pain (as Assessed by VAS) Percent Change from Baseline at the Primary Endpoint Analysis in the Intent-to-Treat and Per Protocol Population

	Test (N=92[1])	**Control (N=87[1])**	**10% Non-Inferiority P-value[1]**
ITT Back Pain (VAS)			
Baseline Mean ± SD Median, Range	7.4 ± 1.3 7.4, 4.9 to 9.8	7.8 ± 1.2 7.8, 5.2 to 10.0	
PEA Mean ± SD Median, Range	2.7 ± 2.3 1.9, 0.0 to 9.6	4.8 ± 2.8 4.7, 0.2 to 9.7	
Change from Baseline Mean ± SD Median, Range	-4.7 ± 2.4 -4.8, -9.5 to 0.0	-3.0 ± 2.9 -3.0, -9.0 to 1.7	<0.001
% change from baseline Mean ± SD Median, Range	-63.3 ± 30.4 -72.4, -100.0 to 0.0	-38.6 ± 35.2 -37.8, -97.8 to 25.9	<0.001
PP Back Pain (VAS)			
Baseline Mean ± SD Median, Range	7.4 ± 1.2 7.4, 4.9 to 9.7	7.8 ± 1.2 7.9, 5.2 to 10.0	
PEA Mean ± SD Median, Range	2.7 ± 2.3 1.9, 0.0 to 9.6	4.8 ± 2.8 4.6, 0.2 to 9.7	
Change from Baseline Mean ± SD Median, Range	-4.7 ± 2.5 -4.8, -9.5 to 0.0	-3.0 ± 2.9 -3.0, -9.0 to 1.7	<0.001
% change from baseline Mean ± SD Median, Range	-62.8 ± 30.6 -72.3, -100.0 to 0.0	-38.4 ± 35.1 -38.1, -97.8 to 25.9	<0.001
ITT Leg Pain (VAS)			
Baseline Mean ± SD Median, Range	7.1 ± 1.5 7.2, 2.6 to 9.9	7.6 ± 1.4 7.7, 2.9 to 9.8	
PEA Mean ± SD Median, Range	2.5 ± 2.4 1.7, 0.0 to 8.6	4.1 ± 2.7 3.7, 0.1 to 9.7	
Change from Baseline			

	Test (N=92[1])	Control (N=87[1])	10% Non-Inferiority P-value[1]
Mean ± SD Median, Range	-4.6 ± 2.6 -4.9, -9.7 to 0.5	-3.5 ± 3.0 -3.6, -9.4 to 2.5	0.001
% change from baseline Mean ± SD Median, Range	-65.4 ± 32.9 -75.1, -100.0 to 7.2	-44.6 ± 37.6 -48.4, -98.9 to 54.4	<0.001
PP Leg Pain (VAS)			
Baseline Mean ± SD Median, Range	7.1 ± 1.5 7.3, 2.6 to 9.9	7.6 ± 1.4 7.7, 2.9 to 9.8	
PEA Mean ± SD Median, Range	2.5 ± 2.4 1.7, 0.0 to 8.6	4.1 ± 2.7 3.7, 0.1 to 9.7	
Change from Baseline Mean ± SD Median, Range	-4.6 ± 2.6 -4.9, -9.7 to 0.5	-3.5 ± 3.0 -3.5, -9.4 to 2.5	0.001
% change from baseline Mean ± SD Median, Range	-64.9 ± 33.3 -74.9, -100.0 to 7.2	-44.1 ± 37.6 -48.3, -98.9 to 54.4	<0.001

Abbreviations: PEA, Primary Endpoint Assessment; VAS, visual analog scale; SD, standard deviation.

[1] Baseline values are used at the PEA for subjects with increased opioid usage or missing data due to termination reasons other than "Lost to Follow-up". The last non-missing value was carried forward for subjects with missing data due to a termination reason of "Lost to Follow-up".

Table 17: Oswestry Disability Index – Percent Change from Baseline at the Primary Analysis Endpoint Timepoint in the Intent-to-Treat and Per Protocol Population

	Test (N=92[1])	Control (N=87[1])	10% Non-Inferiority P-value[1]
ITT ODI			
Baseline ODI Mean ± SD Median, Range	52.8 ± 9.9 53.0, 22.0 to 74.0	55.3 ± 9.1 54.0, 36.0 to 80.0	
PEA ODI Mean ± SD Median, Range	35.8 ± 15.1 34.0, 0.0 to 72.0	41.5 ± 13.3 43.0, 6.0 to 78.0	0.021
% change from baseline Mean ± SD Median, Range	-32.2 ± 25.6 -31.8, -100.0 to 17.2	-24.5 ± 22.0 -22.2, -87.0 to 13.0	<0.001

PP ODI			
Baseline ODI			
Mean ± SD	53.1 ± 9.5	55.4 ± 9.0	
Median, Range	53.7, 28.0 to 74.0	54.0, 36.0 to 80.0	
PEA ODI			
Mean ± SD	36.5 ± 15.4	42.0 ± 13.5	0.025
Median, Range	34.0, 0.0 to 72.0	44.0, 6.0 to 77.8	
% change from baseline			
Mean ± SD	-31.5 ± 26.2	-24.0 ± 22.1	<0.001
Median, Range	-31.1, -100.0 to 17.2	-21.7, -87.0 to 13.0	

Abbreviations: ODI, Oswestry Disability Index; PEA, Primary Endpoint Assessment; VAS, visual analog scale; SD, standard deviation.

[1] Baseline values are used at the PEA for subjects with increased opioid usage or missing data due to termination reasons other than "Lost to Follow-up". The last non-missing value was carried forward for subjects with missing data due to a termination reason of "Lost to Follow-up".

Table 18: Back and Leg Pain (as Assessed by VAS) Percent Change from Baseline at the Month 6 and Month 12 Assessments in the Intent-to-Treat and Per Protocol Population

	Test (N=92[1])	**Control (N=87[1])**	**10% Non- Inferiority P-value[2]**
ITT Back pain (VAS) – 6 Months			
Baseline			
Mean ± SD	7.4 ± 1.3	7.8 ± 1.2	
Median, Range	7.4, 4.9 to 9.8	7.8, 5.2 to 10.0	
Month 6 SEA			
Mean ± SD	3.2 ± 2.6	4.8 ± 3.0	
Median, Range	2.4, 0.1 to 10.0	5.2, 0.2 to 9.7	
Change from Baseline			
Mean ± SD	-4.2 ± 2.8	-3.0 ± 3.0	<0.001
Median, Range	-4.6, -9.4 to 4.6	-2.4, -9.3 to 1.8	
% change from baseline			
Mean ± SD	-56.4 ± 35.9	-38.1 ± 37.1	<0.001
Median, Range	-65.6, -98.9 to 86.6	-34.0, -97.8 to 29.4	
PP Back pain (VAS) – 6 Months			
Baseline			
Mean ± SD	7.4 ± 1.2	7.8 ± 1.2	
Median, Range	7.4, 4.9 to 9.7	7.9, 5.2 to 10.0	
Month 6 SEA			
Mean ± SD	3.2 ± 2.6	4.9 ± 3.0	
Median, Range	2.4, 0.1 to 10.0	5.3, 0.2 to 9.7	

	Test (N=92[1])	Control (N=87[1])	10% Non- Inferiority P-value[2]
Change from Baseline			
Mean ± SD	-4.2 ± 2.8	-3.0 ± 3.0	<0.001
Median, Range	-4.6, -9.4 to 4.6	-2.3, -9.3 to 1.8	
% change from baseline			
Mean ± SD	-56.0 ± 36.2	-37.1 ± 37.2	<0.001
Median, Range	-66.1, -98.9 to 86.6	-26.4, -97.8 to 29.4	
ITT Leg pain (VAS) – 6 Months			
Baseline			
Mean ± SD	7.1 ± 1.5	7.6 ± 1.4	
Median, Range	7.2, 2.6 to 9.9	7.7, 2.9 to 9.8	
Month 6 SEA			
Mean ± SD	2.9 ± 2.7	4.2 ± 2.9	
Median, Range	2.1, 0.0 to 10.0	4.1, 0.0 to 9.7	
Change from Baseline			
Mean ± SD	-4.2 ± 2.8	-3.4 ± 3.1	0.009
Median, Range	-4.9, -9.4 to 4.8	-3.1, -9.5 to 2.0	
% change from baseline			
Mean ± SD	-58.7 ± 38.3	-42.6 ± 39.7	<0.001
Median, Range	-71.2, -100.0 to 93.8	-43.1, -100.0 to 64.6	
PP Leg pain (VAS) – 6 Months			
Baseline			
Mean ± SD	7.1 ± 1.5	7.6 ± 1.4	
Median, Range	7.3, 2.6 to 9.9	7.7, 2.9 to 9.8	
Month 6 SEA			
Mean ± SD	2.9 ± 2.7	4.3 ± 2.9	
Median, Range	2.1, 0.0 to 10.0	4.5, 0.0 to 9.7	
Change from Baseline			
Mean ± SD	-4.2 ± 2.9	-3.4 ± 3.2	0.011
Median, Range	-5.0, -9.4 to 4.8	-3.0, -9.5 to 2.0	
% change from baseline			
Mean ± SD	-57.9 ± 38.6	-40.9 ± 39.8	<0.001
Median, Range	-70.2, -100.0 to 93.8	-38.9, -100.0 to 64.6	
ITT Back pain (VAS) – 12 Months			
Baseline			
Mean ± SD	7.4 ± 1.3	7.8 ± 1.2	
Median, Range	7.4, 4.9 to 9.8	7.8, 5.2 to 10.0	
Month 12 SEA			
Mean ± SD	3.3 ± 2.9	5.0 ± 3.1	

	Test (N=92[1])	Control (N=87[1])	10% Non- Inferiority P-value[2]
Median, Range	2.1, 0.0 to 9.7	5.5, 0.1 to 9.7	
Change from Baseline Mean ± SD Median, Range	-4.1 ± 2.9 -5.0, -9.6 to 1.2	-2.8 ± 3.0 -1.8, -9.0 to 1.3	<0.001
% change from baseline Mean ± SD Median, Range	-55.8 ± 37.5 -69.2, -100.0 to 16.6	-36.5 ± 37.3 -22.0, -98.8 to 15.3	<0.001
PP Back pain (VAS) – 12 Months			
Baseline Mean ± SD Median, Range	7.4 ± 1.2 7.4, 4.9 to 9.7	7.8 ± 1.2 7.9, 5.2 to 10.0	
Month 12SEA Mean ± SD Median, Range	3.3 ± 2.9 2.1, 0.0 to 9.7	5.0 ± 3.1 5.4, 0.1 to 9.7	
Change from Baseline Mean ± SD Median, Range	-4.1 ± 2.9 -5.0, -9.6 to 1.2	-2.8 ± 3.0 -1.9, -9.0 to 1.3	0.001
% change from baseline Mean ± SD Median, Range	-55.4 ± 37.7 -69.2, -100.0 to 16.6	-36.4 ± 37.3 -20.5, -98.8 to 15.3	<0.001
ITT Leg pain (VAS) – 12 Months			
Baseline Mean ± SD Median, Range	7.1 ± 1.5 7.2, 2.6 to 9.9	7.6 ± 1.4 7.7, 2.9 to 9.8	
Month 12 SEA Mean ± SD Median, Range	3.0 ± 2.9 1.7, 0.0 to 9.8	4.8 ± 3.1 4.9, 0.0 to 9.7	
Change from Baseline Mean ± SD Median, Range	-4.1 ± 3.0 -4.9, -9.8 to 3.7	-2.8 ± 3.0 -2.0, -9.5 to 2.3	<0.001
% change from baseline Mean ± SD Median, Range	-57.2 ± 40.0 -73.5, -100.0 to 71.5	-36.0 ± 38.3 -28.3, -100.0 to 31.1	<0.001
PP Leg pain (VAS) – 12 Months			
Baseline Mean ± SD Median, Range	7.1 ± 1.5 7.3, 2.6 to 9.9	7.6 ± 1.4 7.7, 2.9 to 9.8	

	Test (N=92[1])	Control (N=87[1])	10% Non- Inferiority P-value[2]
Month 12 SEA			
Mean ± SD	3.1 ± 2.9	4.9 ± 3.1	
Median, Range	1.7, 0.0 to 9.8	5.2, 0.0 to 9.7	
Change from Baseline			
Mean ± SD	-4.1 ± 3.1	-2.7 ± 3.0	<0.001
Median, Range	-5.0, -9.8 to 3.7	-1.8, -9.5 to 2.3	
% change from baseline			
Mean ± SD	-56.4 ± 40.3	-35.0 ± 38.3	<0.001
Median, Range	-73.3, -100.0 to 71.5	-27.2, -100.0 to 31.1	

Abbreviations: SEA, Secondary Endpoint Assessment; VAS, visual analog scale; SD, standard deviation.

[1] Baseline values are used at the Month 12 SEA for subjects with increased opioid usage or missing data due to termination reasons other than "Lost to Follow-up". The last non-missing value was carried forward for subjects with missing data due to a termination reason of "Lost to Follow-up".

[2] By exact binomial test.

Additional endpoints

A Permanent Implant Subset (PS) analysis was performed which included all trialed subjects who responded during the Trial Phase and received a permanent implant. One hundred and seventy-one (171) of the 198 randomized subjects received a permanent implant and are included in the PS (90 in the Test group and 81 in the Control group.) For the PS population, 80.9% of the Test subjects met the primary endpoint compared to 42.5% of the Control subjects. The PS analyses demonstrated the non-inferiority of the Test group to the Control group with a pre- specified 10% non-inferiority margin ($p<0.001$). Results are shown in Table 19 below.

Table 19: Primary Endpoint Analysis for the Permanent Implant Subset

	Test Number (%) of Subjects (N=89[1])	Control Number (%) of Subjects (N=80[1])	10% Non-Inferiority P-value
PS Analysis: Met overall primary endpoint	**72 (80.9%)**	**34 (42.5%)**	**<0.001[2]**
Met effectiveness component of primary endpoint	72 (80.9%)	34 (42.5%)	
≥ 50% improvement of back pain VAS score	75 (84.3%)	35 (43.8%)	
No increase in baseline pain medications[3]	82 (92.1%)	74 (92.5%)	
Met safety component of primary endpoint[4]	89 (100.0%)	80 (100.0%)	

Abbreviations: VAS, visual analog scale.

[1] Two subjects in the Permanent Implant Subset were not included in this primary endpoint analysis as they did not have a Primary Endpoint Assessment: 09-421 (Test group) was incarcerated after the Device Activation visit and 09-043 (Control group) was lost to follow-up after the Device Activation visit.

[2] By exact binomial test.

[3] No increase in morphine equivalent dose of a baseline opioid and no increase in pain medication used to treat back and/or leg pain (as indicated for this study) for duration greater than 5 days.
[4] No stimulation-related neurological deficit.

A summary of additional exploratory analyses is presented in Table 20 below. These endpoints were not evaluated with formally tested hypotheses.

Table 20: Summary of Tertiary Endpoints

	PEA		Month 6 SEA		Month 12 SEA	
	Test	**Control**	**Test**	**Control**	**Test**	**Control**
Responder rates (% of subjects)						
Back pain - VAS	78.3%	39.1%	71.7%	47.1%	73.9%	46.0%
Back pain with rest - diary	66.7%	38.4%	62.2%	46.4%	66.7%	40.0%
Back pain with activity - diary	71.3%	33.7%	62.2%	38.1%	70.1%	42.5%
Back pain - PPR	79.3%	48.3%	76.1%	44.8%	79.3%	45.3%
Leg pain - VAS	77.2%	48.3%	75.0%	48.3%	75.0%	43.7%
Leg pain with rest - diary	72.4%	50.0%	67.8%	51.2%	66.7%	45.0%
Leg pain with activity - diary	74.7%	40.7%	71.1%	44.0%	71.3%	46.3%
Leg pain - PPR	77.2%	56.3%	73.9%	57.5%	79.3%	50.0%
% Change from Baseline (mean ± SD, negative change is better)						
Back pain – VAS	-62.8 ± 30.6	-38.4 ± 35.1	-58.8 ± 35.0	-39.7 ± 36.5	-62.7 ± 33.5	-40.3 ± 37.4
Back pain with rest - diary	-56.2 ± 39.9	-39.6 ± 36.4	-47.9 ± 54.1	-41.9 ± 38.8	-56.1 ± 39.4	-33.0 ± 43.3
Back pain with activity - diary	-61.9 ± 28.4	-36.4 ± 32.3	-55.2 ± 32.1	-39.1 ± 32.9	-59.8 ± 31.7	-37.3 ± 33.3
Leg pain - VAS	-64.9 ± 33.3	-44.1 ± 37.6	-62.8 ± 36.3	-44.4 ± 39.2	-65.4 ± 35.6	-42.4 ± 37.9
Leg pain with rest - diary	-63.2 ± 33.9	-45.2 ± 37.6	-56.8 ± 38.9	-42.8 ± 51.2	-56.0 ± 52.2	-35.7 ± 53.2
Leg pain with activity - diary	-65.4 ± 31.2	-42.3 ± 32.6	-59.7 ± 36.2	-45.3 ± 33.5	-61.9 ± 35.0	-42.1 ± 35.0
Oswestry Disability Index	-32.2 ± 25.7	-24.9 ± 22.0	-30.2 ± 28.0	-24.5 ± 25.6	-29.2 ± 27.5	-21.6 ± 27.0
Change from Baseline (mean ± SD)						
Back pain - VAS (negative change is better)	-4.9 ± 2.3	-3.1 ± 2.8	-4.4 ± 2.8	-3.1 ± 3.0	-4.7 ± 2.7	-3.1 ± 3.0
Leg pain - VAS (negative change is better)	-4.9 ± 2.5	-3.7 ± 3.0	-4.5 ± 2.7	-3.5 ± 3.1	-4.7 ± 2.8	-3.3 ± 3.0
MPQ (negative change is better)	-2.5 ± 1.8	-1.7 ± 1.9	-2.3 ± 1.9	-1.5 ± 1.9	-2.4 ± 1.9	-1.4 ± 1.8
SF-12: PCS (positive change is better)	9.4 ± 9.9	6.1 ± 7.9	7.6 ± 9.8	5.2 ± 7.7	8.1 ± 9.3	6.0 ± 8.6
SF-12: MCS (positive change is better)	1.6 ± 10.8	2.0 ± 9.1	1.7 ± 11.2	1.4 ± 8.5	2.6 ± 11.4	1.2 ± 9.1
BDI (negative change is better)	-4.5 ± 8.6	-4.1 ± 6.2	-3.8 ± 8.5	-3.4 ± 7.0	-4.2 ± 8.3	-3.1 ± 6.8
PSQI (negative change is better)	-3.1 ± 4.5	-2.1 ± 3.8	-2.7 ± 4.3	-2.1 ± 3.9	-2.6 ± 4.3	-1.8 ± 3.7
GAF (positive change is better)	9.8 ± 12.2	5.5 ± 11.7	11.9 ± 11.7	7.6 ± 10.5	13.2 ± 12.2	7.7 ± 12.2
Other						
Opioid change (% decreased or eliminated)	20.5	14.6	31.2	21.7	35.5	26.4

	PEA		Month 6 SEA		Month 12 SEA	
	Test	Control	Test	Control	Test	Control
Opioid change (% increased)	6.0	6.3	7.8	11.7	14.5	21.1
Opioid change (% maintained)	73.5	80.0	61.0	66.7	50.0	52.6
Non-Opioid Pain Medication (% increase for > 5 days)	2.2	2.3	-	-	-	-
ODI (% minimal to moderate disability)	64.1	47.1	58.7	41.3	58.7	40.2
GAF (% no symptoms to transient symptoms)	56.5	47.1	61.9	56.3	67.4	55.2
Subject GIC (% better or a great deal better)	52.2	36.7			52.8	33.8
Clinician GIC (% better or a great deal better)	68.5	44.8			69.6	43.6
Subject Satisfaction (% very satisfied)	54.1	33.8			55.4	32.3

Abbreviations: PEA, Primary Endpoint Assessment; SEA, Secondary Endpoint Assessment; VAS, visual analog scale; PPR, percent pain relief; SD, standard deviation; ODI, Oswestry Disability Index; MPQ, McGill Pain Questionnaire; SF-12, Short Form – 12; PCS, physical component summary; MCS, mental component summary; BDI, Beck Depression Inventory; PSQI, Pittsburgh Sleep Quality Index; GAF, Global Assessment of Functioning; GIC, global impression of change.

In addition, the primary and secondary endpoints were tested for superiority. Superiority of the Test group over the Control group was demonstrated for the primary endpoint in the ITT, PP, and PS analyses. Superiority of the Test group over the Control group was also demonstrated for all secondary analyses. Table 21 below shows the results of the superiority analysis for the primary endpoint.

Table 21: Superiority Analysis on Primary Endpoint in Intent-to-Treat, Per-Protocol, Permanent Implant, and Subset Populations

	Test Number (%) of Subjects	Control Number (%) of Subjects	Between-Group P-value
Intent-to-Treat Population	**N=101**	**N=97**	
Met overall primary endpoint	**75.7 (75.0%)**	**36.6 (37.7%)**	< 0.001[1]
Met effectiveness component of primary endpoint	75.7 (75.0%)	36.6 (37.7%)	
≥ 50% improvement of back pain VAS score	78.7 (77.9%)	37.6 (38.8%)	
No increase in baseline pain medications[3]	94 (93.1%)	91 (93.8%)	
Met safety component of primary endpoint[4]	101 (100.0%)	97 (100.0%)	
Per Protocol Population	**N=92**	**N=87**	
Met overall primary endpoint	**69 (75.0%)**	**33 (37.9%)**	< 0.001[2]
Met effectiveness component of primary endpoint	69 (75.0%)	33 (37.9%)	
≥ 50% improvement of back pain VAS score	72 (78.3%)	34 (39.1%)	
No increase in baseline pain medications[3]	85 (92.4%)	81 (93.1%)	

	Test Number (%) of Subjects	Control Number (%) of Subjects	Between-Group P-value
Met safety component of primary endpoint[4]	92 (100.0%)	87 (100.0%)	
Permanent Implant Subset	**N=89**	**N=80**	
Met overall primary endpoint	**72 (80.9%)**	**34 (42.5%)**	< 0.001[1]
Met effectiveness component of primary endpoint	72 (80.9%)	34 (42.5%)	
≥ 50% improvement of back pain VAS score	75 (84.3%)	35 (43.8%)	
No increase in baseline pain medications[3]	82 (92.1%)	74 (92.5%)	
Met safety component of primary endpoint[4]	89 (100.0%)	80 (100.0%)	

Abbreviations: VAS, visual analog scale.

[1] By Fischer's Exact test.

[2] By Z test for difference between two proportions.

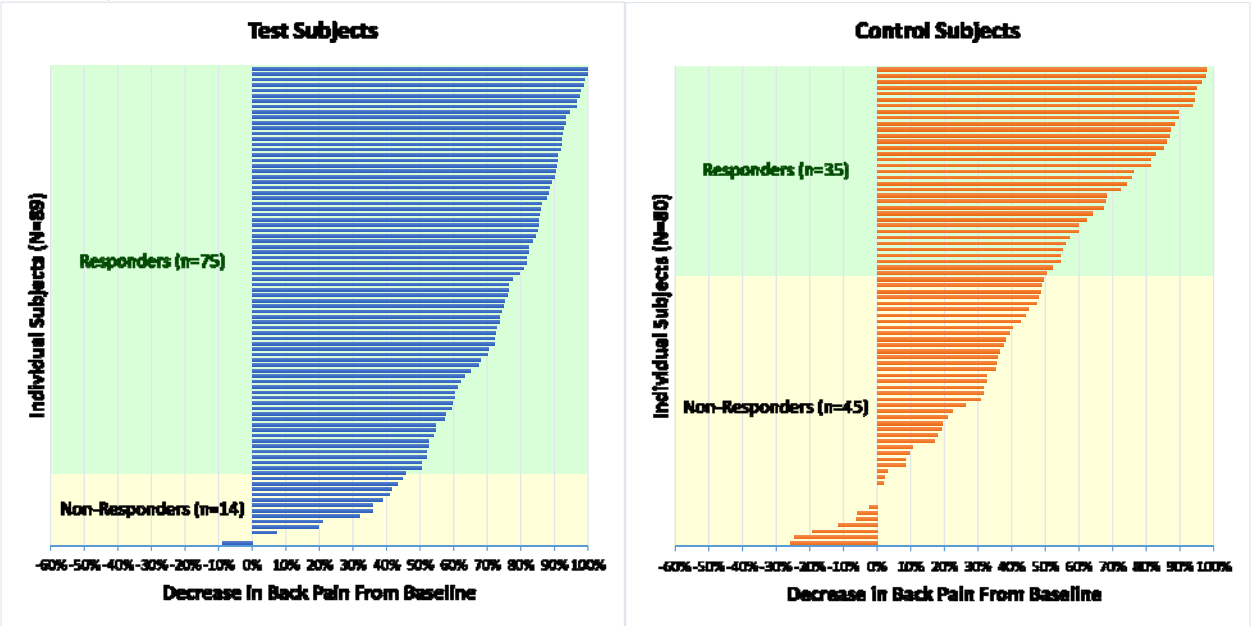
[3] No increase in morphine equivalent dose of a baseline opioid and no increase in pain medication used to treat back and/or leg pain (as indicated for this study) for duration greater than 5 days.

[4] No stimulation-related neurological deficit.

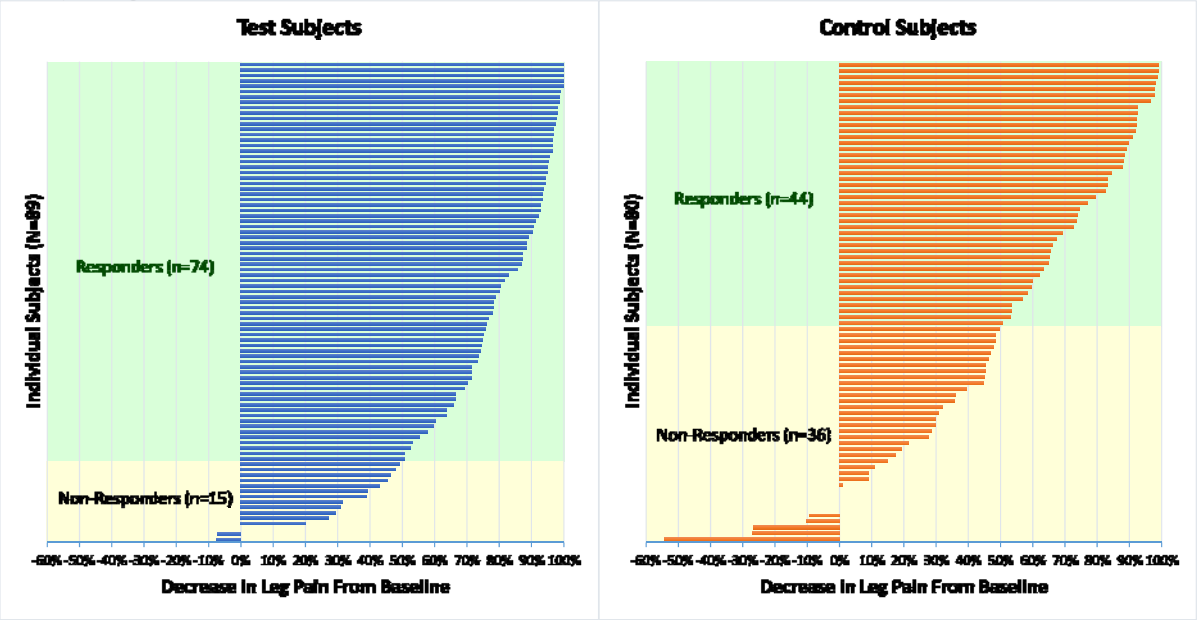
Figure 5 below depicts the individual subject data for percent pain improvement in the VAS for the primary endpoint analysis.

Figure 5: Individual Percent Change from Baseline in the a) back and b) leg pain VAS at the 3 month Primary Endpoint for Subjects in the Permanent Implant Subset.

a) Back Pain Relief



b) Leg Pain Relief



A summary of device programming at the Device Activation and the Month 3, 6 and 12 visits is presented by treatment group in Table 22 and Table 23 for the Test group and for the Control group for the Permanent Implant Subset. As all Test subjects received 10,000 Hz frequency and 30 µs pulse width, mean values are not calculated. Subjects in the Test group were stimulated with a higher frequency, but an overall lower amplitude and pulse width. None of the Test subjects reported paresthesia, compared to 95.9% of the Control subjects at the Month 3 visit.

Table 22: Summary of Programmed Device Parameters Subjects in the Permanent Implant Subset for the Test group[1]

	Test			
	Device Activation (N=90)	**Month 3[2] (N=88)**	**Month 6[2] (N=87)**	**Month 12[2] (N=86)**
Frequency - Hz				
Minimum - mean ± SD	10,000	10,000	10,000	10,000[3]
Maximum - mean ± SD	10,000	10,000	10,000	10,000
Amplitude - mA				
Minimum - mean ± SD	1.7 ± 1.1	1.6 ± 1.1	1.9 ± 0.8	2.0 ± 0.7
Maximum - mean ± SD	3.8 ± 3.4	3.4 ± 0.7	3.4 ± 0.8	3.4 ± 1.0

	Test			
	Device Activation (N=90)	**Month 3[2] (N=88)**	**Month 6[2] (N=87)**	**Month 12[2] (N=86)**
Pulse width - μs				
Minimum - mean ± SD	30.0	30.0	30.0	30.0
Maximum - mean ± SD	30.0	30.0	30.0	30.0[3]

Abbreviations: Hz, Hertz; SD, standard deviation; mA, milliamp; us, microsecond; NA, not applicable.
[1] Subjects in Permanent Implant Subset with a visit at the assessment time point.
[2] Programmed parameters at the time that the subjects arrived for the scheduled visit.
[3] Two subjects (06-254 and 08-358) received intermittent low frequency 60 Hz stimulation concurrent with 10,000 Hz stimulation during the specific reporting period.

Table 23: Summary of Programmed Device Parameters Subjects in Permanent Implant Subset for the Control group[1]

	Test			
	Device Activation (N=80)	**Month 3[2] (N=77)**	**Month 6[2] (N=71[3])**	**Month 12[2] (N=69)**
Frequency - Hz				
Minimum - mean ± SD	39.6 ± 13.4	39.3 ± 14.2	41.6 ± 14.5	39.2 ± 15.0
Maximum - mean ± SD	55.8 ± 14.7	77.3 ± 133.5	77.2 ± 139.1	66.4 ± 43.6
Amplitude - mA				
Minimum - mean ± SD	3.6 ± 2.8	3.7 ± 2.7	3.7 ± 2.9	3.9 ± 3.0
Maximum - mean ± SD	7.3 ± 3.8	7.7 ± 3.7	8.2 ± 4.0	8.5 ± 4.0
Pulse width - μs				
Minimum - mean ± SD	362.9 ± 124.8	363.4 ± 146.1	362.0 ± 158.4	346.5 ± 148.4
Maximum - mean ± SD	543.8 ± 197.6	575.3 ± 216.2	554.9 ± 216.3	591.3 ± 214.0

Abbreviations: Hz, Hertz; SD, standard deviation; mA, milliamp; μs, microsecond
[1] Subjects in Permanent Implant Subset with a visit at the assessment time point.
[2] Programmed parameters at the time that the subjects arrived for the scheduled visit.
[3] One subject with a Month 6 visit (13-601) did not have the device settings recorded.

3. Published Literature Results

With the exception of having the capability of delivering stimulation frequencies up to 10 kHz, the Senza SCS System is similar to the SCS systems cited in the published literature in intended use, target patient population, technology, device design, and output characteristics. Therefore, peer-reviewed published literature on legally marketed SCS systems was used to establish a reasonable assurance of the safety and effectiveness of the Senza SCS System device in the 2-1200 Hz

range with paresthesia for the relief of failed back surgery syndrome, intractable low back, and limb pain.

Effectiveness was demonstrated by 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 either a 3 or 4 point scale in at least 30% of patients included in that study; and

3. A clinically significant difference in pain reduction as measured by a VAS score when compared to a control group.

Five (5) articles from the systematic review of SCS systems reporting on four (4) subject populations (1 article reported on the same subjects at a later time point) were used to summarize the effectiveness of the Senza SCS System (de Vos et al. 2012, Kumar et al. 2007, Kumar et al. 2008, Oakley et al. 2007, and Ohnmeiss et al. 1996). These studies included a total of 202 enrolled patients permanently implanted with a SCS system. These study populations were followed prospectively for a median of 1.5 years (range, 0.9 to 2 years), 119 (58.9%) were female, and the median average age was 51 years. The primary treated disease was failed back surgery syndrome or intractable lower extremity pain for all subjects. These characteristics are consistent with the patient population for which the Senza SCS System is indicated.

- The prospective study by de Vos et al. (2012) evaluated the St. Jude Medical Lamitrode S8 electrode connected to either an EonC or Genesis XP IPG. Patients with failed back surgery syndrome (FBSS) were included with both back and leg pain VAS score >5.0. A total of 45 subjects were trialed with 42 (93%) having a successful trial defined as at least 50% reduction in pain in legs and low back. One subject who had a successful trial got an infection requiring device explant, leaving 41 subjects continuing to permanent implant.

  Leg pain VAS score decreased from an average of 8.0 at baseline to 3.2 (a 60% reduction) at 6 and 12 months. Back pain VAS score decreased from an average of 7.5 at baseline to 3.5 (a 53% reduction) at 6 months and 4.2 (a 44% reduction) at 12 months. 73% of subjects at 6 months and 71% of subjects at 12 months had at least 50% reduction in leg pain. 56% of subjects at 6 months and 51% of subjects at 12 months had at least 50% reduction in back pain.

  In addition to the subject with an infection requiring device explant, one subject had lead migration resulting in an additional implantation of a percutaneous lead. Two other subjects required additional implantation of a percutaneous lead to obtain adequate paresthesia coverage.

- The prospective study by Kumar et al. (2007) compared SCS to conventional medical management (CMM) in FBSS patients with neuropathic pain of radicular origin, predominantly in the legs (VAS > 5). The trial enrolled 100 subjects. Fifty-two (52) subjects were randomized to the SCS group and forty-eight (48) to the conventional medical management (CMM) group. Of the 52 subjects randomized to the SCS group, 43 (82.7%) had a successful trial defined as at least 50% pain relief and 80% paresthesia coverage. Five additional subjects requested to be implanted which brought the total to 48 who received an implanted Medtronic Synergy system.

  At 6 months, 48% of subjects had at least 50% reduction in leg pain, compared to 9% in the CMM group; 22% of SCS subjects had an 80% or greater reduction in leg pain compared to 7% of subjects who received CMM. By 12 months, 5 subjects randomized to SCS crossed over to CMM, compared with 28 subjects randomized to CMM crossing over to SCS.

  Of 84 subjects who received an electrode (either during the screening trial or as a result of system implantation) during the 12 months of the study, 27 (32%) experienced a total of 40 device-related complications. For 20 of these subjects (24%), surgery was required to resolve the event. Principal complications were electrode migration (10%), infection or wound breakdown (8%), and loss of paresthesia (7%).

- Kumar et al. (2008) presented 24 month follow-up on subjects previously reported in Kumar et al. 2007. Forty-two (42) of the fifty-two (52) randomized subjects had two-year follow-up data. At two years, 69% had at least 30% leg pain relief, 40% had at least 50% leg pain relief, and 14% had at least 80% leg pain relief.

  Of the 42 subjects, 19 (45%) experienced a total of 34 SCS related complications. The most frequent were electrode migration (14%), loss of paresthesia (12%), pain at the implanted pulse generator incision site (12%), and infection or wound breakdown (10%). For 13 subjects (31%), surgical revision was required to resolve the event.

- The prospective study by Oakley et al. (2007) evaluated Boston Scientific's Precision system in patients with chronic, intractable pain of the trunk and/or limbs. Subjects were required to have a pain VAS of at least 5 to be eligible for the study. 65 subjects were eligible and underwent and SCS trial, 49 (75%) of whom had at least 50% pain reduction and proceeded to a permanent implant.

  Baseline pain score was 8.0±0.2 for these 49 subjects. Data was available for 38 subjects at 3 months, and pain was reduced from an average of 8.1±0.3 with SCS off to 3.2±0.3 with SCS on. At 6 months (N=34), pain reduced from 8.3±0.3 to 3.9±0.4. At 12 months (N=12), pain reduced from 8.3±0.8 to

2.2±0.5. The percentage of subjects reporting a 50% or greater improvement in pain was 85%, 63%, 55%, and 75% at 3, 6 and 12 months, respectively. The mean pain score as measured by the VAS (0-10 scale) was 8.0 baseline and was reduced to 2.5, 3.2, 3.9, and 2.2, respectively.

Thirty-four (34) device-related AEs were reported among 114 implants. The most common AEs were lead migration (7%), brief uncomfortable stimulation (5%), and component failure (4%; 2 damaged leads noted at surgery before implantation, 1 IPG failure to stimulate, and 1 charger device malfunction).

- The prospective study by Ohnmeiss et al. (1996) evaluated SCS in patients with leg pain greater than back pain. A total of 40 subjects were implanted with a Medtronic Resume lead and Itrel II IPG. Data was available from 38 of these subjects with leg pain decreasing from 7.4 at baseline to 5.5 (a 26% decrease) at 12 months and 6.3 (a 15% decrease) at 24 months. Back pain was 5.4 at baseline and 12 months, and 5.7 at 24 months. 26% of subjects had at least 50% reduction in leg pain at 24 months.

  Three subjects had pain at the IPG implant site and required revision surgery. Three subjects had lead migration requiring revision surgery, with one of these subjects required two revision surgeries. There were 7 IPG explants, 3 of which were re-implanted. One subject had the device removed due to infection and later had a new device implanted. A diabetic subject had skin problems which required device removal; a new device was later implanted. Two patients had the device removed due to unsatisfactory pain relief.

The following table provides a summary of the responder rates for back and leg pain at one year in those studies in which responder rate was reported and used to demonstrate the safety and effectiveness of stimulation in the 2-1200 Hz range.

Table 24: Responder Rates for Back and Leg Pain as Reported in the Literature

Article	Responder Rate (back)	Responder Rate (leg)	Responder Rate (back and leg)
deVos	51%	71%	NR
Kumar	NR	48%	NR
Oakley	NR	NR	75%*
Ohnmeiss	NR	26%	NR

NR: Not reported. *Data reported on 12 of 49 implanted patients.

Overall, these studies provide a range of outcomes for back and leg pain relief due to differences in study populations, methods of reporting pain reduction, and statistical analysis methods. The Kumar and Ohnmeiss studies included predominant leg pain patients, while the de Vos study included patients with both back and leg pain. The Oakley study did not differentiate between back and leg pain. Oakley recorded pain scores with SCS on and off at each designated time point rather than reporting on sustained use of SCS compared with baseline. All

of these studies reported on enriched patient populations, i.e., patients who failed SCS trials were not included in the analysis. Other analysis methods may also have varied, such as the methods used when patients withdrew or were lost to follow-up. For example in the Oakley study, 49 patients were assessed at baseline, 38 at 3 months, 34 at 6 months, and 12 at 12 months. These factors should be noted when drawing effectiveness conclusions.

E. 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. The pivotal clinical study included 24 investigators of which none were full-time or part-time employees of the sponsor and two investigators had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: none
- Significant payment of other sorts: none
- Proprietary interest in the product tested held by the investigator: none
- Significant equity interest held by investigator in sponsor of covered study: two investigators

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Statistical analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. The information provided does not raise any questions about the reliability of the data.

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

The study was a prospective, randomized, multi-center non-inferiority trial comparing the Senza SCS System to a legally marketed SCS system (control group). The non-inferiority design did not blind subjects as to which device they had implanted. This may have resulted in investigator and patient bias, which may have resulted in the response rate in the control group being different than that reported in the literature. Although the data supports the superiority of the Nevro device to the comparator, the comparator response rate was different than that reported in the literature (as summarized in Table 24 above.) The assessment of the comparator response to the published literature, however, is challenged by differences in study populations, methods of reporting pain reduction, and statistical analysis methods The Nevro device is the first SCS system that is approved to allow paresthesia free stimulation. Since the previously approved SCS systems require paresthesia to obtain pain relief, randomized double blind controlled trials were not possible

for those devices since the demonstration of safety and effectiveness because of the inability to blind subjects.

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

In accordance with the provisions of section 515(c)(2) 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.

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

Effectiveness for the Senza SCS System device, using 10 kHz stimulation without paresthesia was based on a non-inferiority pivotal study. Two-hundred and forty-one (241) subjects were enrolled and 198 subjects were randomized (101 in the Test group and 97 in the Control group). The composite primary endpoint was met for the PP and ITT analyses. For the PP population, 75.0% of Test subjects receiving Senza SCS System SCS therapy met the primary endpoint compared to 37.9% of Control subjects receiving SCS from a commercial system, which demonstrated the non-inferiority of the Test group to the Control group with a prespecified 10% non-inferiority margin ($p<0.001$). Similar results were observed in the ITT population (75.0% versus 37.7%) which also demonstrated noninferiority of the Test group compared with the Control group (p-value <0.001).

All predefined secondary endpoints demonstrated non-inferiority of the Test group to the Control group. The average decrease in baseline back pain VAS was sustained for both treatment groups at 12 months, with Test subjects decreasing approximately 55% compared with 36% for Control subjects. Similar results were observed for leg pain VAS, with Test subjects decreasing approximately 56% compared with 35% for Control subjects at 12 months. For the PS, Test subjects had a higher back pain responder rate than Control subjects at both the 3 month (81.1% versus 43.2%, respectively) and 12-month endpoints (71.1% versus 45.7%, respectively).

Effectiveness for the Senza SCS System, in the 2 to 1200 Hz range with paresthesia was based on a literature review. The evaluation of efficacy was conducted using prospective studies relevant to Senza SCS System features and indications. A total of five (5) studies based on 4 subject populations (1 article reported on the same subjects at a later time point) and 202 patients were qualitatively reviewed. The majority of patients had either intractable limb pain or FBSS and SCS treatment was demonstrated to be effective in each of the five studies.

The results of the clinical study demonstrate a clinically meaningful reduction in pain with the Senza SCS System at 10 kHz without paresthesia for patients who suffer from chronic, intractable pain of the trunk and/or limbs. The results from the

published literature demonstrate a clinically meaningful reduction in pain and the Senza SCS System is similar in design, technology, performance, intended use, and patient population for the 2 to 1200 Hz range with paresthesia as the SCS systems evaluated in these studies.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory and animal studies, published literature as well as data collected in a clinical study conducted to support PMA approval as described above. There were no stimulation-related neurological deficits observed for either treatment group. SAEs occurred in 14.9% of Test subjects compared to 16.5% of Control subjects. None of the SAEs were classified as stimulation-related in either treatment group. One death occurred in a Control subject, as a result of a myocardial infarction during the permanent implant procedure. One Test subject was diagnosed with a malignant hepatic neoplasm after their Month 12 visit and subsequently died. There were no unanticipated adverse device effects (UADE).

Regarding total adverse events, there were similar rates in both treatment groups (70.3% of Test subjects versus 73.2% of Control subjects). Implant site pain occurred in 9.9% of Test subjects and 9.3% of Control subjects, uncomfortable paresthesia in 0.0% of Test subjects and 11.3% of Control subjects, and lead migration in 3.0% of Test subjects and 5.2% of Control subjects.

Three percent (3.0%) of Test subjects had an AE that was stimulation-related, whereas 17.5% of Control subjects had a stimulation-related AE (mostly related to uncomfortable stimulation). Most AEs were classified as mild or moderate.

The published literature also supports the safety of SCS therapy with paresthesia in the 2 to 1200 Hz frequency range.

C. Benefit-Risk Conclusions

The probable benefits of the device are based on the clinical study performed for the 10 kHz frequency without paresthesia and data collected in a systematic literature review for stimulation between 2 and 1200 Hz with paresthesia. Effectiveness was demonstrated by an improvement in pain using a VAS score. The majority of Test subjects obtained at least a 50% reduction in pain that lasted through one year as compared to Control subjects. It would be expected that subjects with chronic pain would experience a similar benefit.

As described above, stimulation at 10 kHz was determined to be safe. The adverse events that were reported were consistent with the well-known safety profile of legally marketed SCS systems as described in the literature.

Limitations

Additional factors to be considered in determining probable risks and benefits for the Senza SCS system included the non-inferiority design of the clinical study. The non-

inferiority design did not blind subjects as to which device they had implanted. This may have resulted in investigator and patient bias which may have resulted in the response rate in the control group being different than that reported in the literature (see Table 24 above).

In addition, the non-inferiority design did not allow an assessment of the placebo response. Placebo response is well known in pain studies due to the subjective nature of the pain assessment and the duration of the response may be long lasting. Finally, during the first three months of stimulation, patients were required to maintain stable doses of their adjunctive pain medications. After three months, changes to adjunctive pain medications were allowed therefore results after the 3-month endpoint may be affected by changes in medications.

Effectiveness for the lower frequency of the 2 to 1,200 Hz of the Senza SCS System was based on a review of published literature, rather than a prospective clinical trial. The published literature reports on a variety of patient populations using different methods of reporting pain reduction and differing statistical analysis methods. The literature used to support the approval of the Nevro device in the 2 to 1200 Hz range were open label studies. Open label studies may cause an overestimation of the treatment effect due to 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.

In conclusion, given the available information above, the data support that for the use of the Senza SCS System as an aid in the management of chronic intractable pain of the trunk and/or limbs, the 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 study and published literature support a reasonable assurance of the safety and efficacy of the Nevro 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 Nevro SCS System is on a non-inferiority pivotal study and over 30 years of clinical research and experience as documented in the literature with fully implantable SCS systems and the similarities of the Nevro system to market-released implantable SCS systems. The results from comprehensive pre-clinical testing show that the Nevro SCS System performs as intended. The analyses also support a clinical benefit to risk determination that is favorable

XIV. CDRH DECISION

CDRH issued an approval order on [date]. The final conditions of approval cited in the approval order are described below.

Continued approval of this PMA is contingent upon the submission of periodic reports, required under 21 CFR 814.84, at intervals of one year (unless otherwise specified) from the date of approval of the original PMA.

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

XV. 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.

XVI. REFERENCES

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