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.
1800 Bridge Parkway
Redwood City, CA 94065

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P130022

Date of FDA Notice of Approval: July 16, 2021

The original PMA P130022 was approved on May 08, 2015, and is indicated as an aid in the management of chronic intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with the following: failed back surgery syndrome, intractable low back pain, and leg pain. The SSED to support the indication is available on the CDRH website (https://www.accessdata.fda.gov/cdrh_docs/pdf13/P130022B.pdf) and is incorporated by reference here. The current supplement was submitted to expand the indication for Senza® Spinal Cord Stimulation (SCS) System

II. INDICATIONS FOR USE

The Senza®, Senza II™ and Senza Omnia™ neuromodulation systems are indicated as aids in the management of chronic intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with the following: failed back surgery syndrome, intractable low back pain, and leg pain.

The Senza®, Senza II™ and Senza Omnia™ neuromodulation systems, when programmed to include a frequency of 10 kHz, are indicated as aids in the management of chronic intractable pain of the lower limbs, including unilateral or bilateral pain, associated with diabetic neuropathy.

III. CONTRAINDICATIONS

The Senza, Senza II, and Senza Omnia Systems should not be used for those patients who:

- Are poor surgical candidates, including those with poor glycemic control in whom the safety of the device has not yet been characterized, i.e. hemoglobin A1c (HbA1C) >10%.
- Fail to receive effective pain relief during trial stimulation.
- Are unable to operate the SCS system.

IV. WARNINGS AND PRECAUTIONS

Patients with diabetes – This device was only studied in patients with an A1C up to 10%. In general, patients with diabetes have a higher risk of surgical complications, especially those who are at high risk for ischemic heart disease and those with autonomic neuropathy or renal failure.

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

V. DEVICE DESCRIPTION

The Senza® Spinal Cord Stimulation (SCS) System (includes Senza, Senza II and Senza Omnia) is a neuromodulation device designed to deliver electrical stimulation for the treatment of chronic pain. The Senza System is totally implantable and delivers stimulation using implantable leads and a rechargeable, implantable pulse generator (IPG). The Senza System is implanted using a minimally invasive surgical procedure that is reversible. The IPG is implanted in a subcutaneous pocket and is capable of stimulating the spinal cord nerves when used with one or more leads. The IPG is controlled by a Patient Remote and/or the Clinician Programmer. Other components of the Senza System include an external Trial Stimulator capable of delivering the same stimulation as the IPG, Lead Extensions, Adaptors, Charger and charging system, operating room (OR) cables and surgical accessories. The Senza SCS System is shown in Figure 1 below:

Figure 1: Senza SCS System: Left to right: IPG1500, IPG2000 and IPG2500

Senza System Details – Major Components

- Implantable Pulse Generator Models: The Implantable Pulse Generator (IPG) is a rechargeable implantable device with 16 output channels capable of stimulating the spinal cord nerves through electrode leads. The IPG is designed to produce current-regulated, charge-balanced, biphasic, capacitively-coupled, rectangular output pulses. The IPG header contains the charging coil and two ports to allow the insertion of leads. The rechargeable battery is contained in a hermetically sealed housing, which is inside the hermetic IPG Titanium enclosure.

- Trial Stimulator: The Trial Stimulator is a battery-powered, handheld device capable of providing the same stimulation as the IPG. During the Trial Phase of SCS, the subject wears this external Trial Stimulator for a period of time to evaluate the effectiveness of the stimulation prior to receiving a permanent implant. The Trial Stimulator is connected to the subject's implanted leads by the use of OR cables.

- IPG or Trial Stimulator interface with other Senza components: The Charger transmits energy transcutaneously to recharge the IPG battery. The IPG and Trial Stimulator communicate with the Patient Remote or Clinician Programmer via the Programmer Wand. Patients are also able to send commands to the IPG or Trial Stimulator directly using the Patient Remote. The IPG also includes a magnetic switch for turning the therapy off by using an external magnet.

- Patient Remote Control: The Patient Remote Control is a handheld battery- operated unit able to communicate with the IPG or Trial Stimulator. The Patient Remote includes multiple controls and indicators for the purpose communicating with these components.

- Charger: This Charger is used by the subject to transcutaneously charge the IPG battery. It is a portable device powered by a rechargeable battery and can be held in one hand.

- Programmer: The Clinician Programmer programs the IPG or Trial Stimulator via the Programmer Wand via a graphical user interface (GUI).

- Programmer Wand: The Programmer Wand is the Clinician Programmer interface that allows the communication with the IPG or Trial Stimulator.

- Percutaneous Leads, Lead Extensions and Lead Adaptors: The Nevro Lead is intended to be used with the IPG or Trial Stimulator for use in delivering stimulation. The Percutaneous Lead is for single use and interfaces with the IPG, Lead Extensions, OR Cable, and lead accessories.

  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. The construction of the Lead Adaptors is identical to the Lead Extension.

Senza System Details - Surgical Accessories

- Torque Wrench: The Torque Wrench is used to tighten the set screws that lock the Percutaneous Lead into the IPG, to lock the Percutaneous Lead into a Lead Extension/Adaptors, or to activate the retention mechanism on the Active Anchors.

- Lead anchors: The Lead Anchors are used to anchor the Percutaneous Lead to the fascia or supraspinous ligament.

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

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

- Stylets: The Stylets are used to maneuver the Lead through the epidural space to the desired implant location.

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

- OR Cables: The Operating Room (OR) Cables make electrical and mechanical connections between the Trial Stimulator and the Percutaneous Leads or Lead Extensions.

- Tunneling Tool: The Tunneling Tool creates a subcutaneous tunnel for the leads from the IPG site to the midline incision.

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

- Mx Trial Adaptor: The Mx Trial Adaptor is intended to connect a Medtronic OR cable to the Nevro External Trial Stimulator.

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 System has been in commercial distribution in the U.S, European Union (EU) and Australia for several years. Regulatory agency marketing approvals were received for the Senza System in May 2010 for the EU, June 2011 for Australia and May 2015 for the US. 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 Implant Procedures

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

Risks associated with SCS Stimulation

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

- Other undesirable sensation such as tingling or prickling

Risks associated with Implanted Device Components

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

Risk associated with External Device Components

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

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

IX. SUMMARY OF NONCLINICAL STUDIES

Pre-clinical studies (bench and animal) previously submitted to FDA in the Original PMA application (P30022) and supplements continue to support the safety of the commercially available The Senza SCS System for treatment of chronic intractable pain of the trunk and/or limbs. No additional preclinical studies were required to evaluate the safety of The Senza SCS therapy for the treatment of the new patient populations. The previously approved supplements which support the device and its components are listed below in **Table 1.**

Table 1: Summary of Senza SCS system Approvals

System/Device Copoment	Approval Reference
Approval for software and firmware updates to Senza components	P130022/S038
Approval for Oscor, a second source for percutaneous lead manufacturing	P130022/S037

Approval for the Senza Bluetooth Trial system including the next generation Trial stimulator, a compatible Bluetooth Trial Patient remote and a software update to the clinician programmer to configure the Bluetooth Trial Stimulator.	P130022/S036
Transfer of FDA approved Nordson facility from Sunnyvale to San Jose for manufacturing Implantable Pulse generators	P130022/S035
Addition of a second Cirtec site in Costa Rica for percutaneous lead production	P130022/S034
Approval for adding B1+RMS scanner limits to support 1.5T Full Body MRI conditional labeling for IPG1000/1500/2000/2500 with Surpass surgical and Percutaneous leads to enhance the safety of the Senza SCS system.	P130022/S033
Approval for additional lead sizes and configurations designated as Surpass-C Surgical Leads.	P130022/S031
Change in manufacturing site for IPG header component	P130022/S029
Approval for use of alternate proposed Integer battery (M3580) on Senza Implantable Pulse Generator, model IPG2000 (Senza II) of Nevro's Senza Spinal Cord Stimulator (SCS) System and associated firmware updates.	P130022/S028
Approval for mechanical and design changes made to the current charger (CGR1000) for the Senza Spinal Cord Stimulation (SCS) system to improve cosmetics and reduce the size of the charger. The modified patient remote charger will now be offered as model CGR2500.	P130022/S027
Approval to make changes to the software for the Clinical Programmer, model CLPG2000/CLPG2500 upgrading the software from version 1.7 to 2.0.	P130022/S026
Approval for a change in the approved packaging for the IPG (NIPG1500, NIPG2000), Lead Extension kits (MADP2008-25B M8, SADP2008-25B S8), and Lead Adapter kits (LEAD2008-25B, LEAD2008-35B, LEAD2008-60B) of your Senza Spinal Cord Stimulation (SCS) System.	P130022/S025
Approval for a new optional accessory tool - Nevro passing elevator accessory tool (PEAT) for use with Nevro Senza Spinal Cord Stimulation (SCS) System.	P130022/S024
Approval to modify the patient remote cosmetically and to reduce the size; update the patient remote model numbers to PTR2300 and PTR2500; update the firmware for patient remote, model PTR2500 and the clinician programmer, model CLPG2000/CLPG2500 to support 5 stimulation therapy settings; and update the firmware to the IPG (renamed Omnia Senza IPG, Model NIPG2500) to support up to 5 stimulation settings.	P130022/S023
Approval for a manufacturing site located at Integer (dba Greatbatch Medical S. de R.L. de C.V.), Blvd. Hector Teran Teran No. 20120, Ciudad Industrial Tijuana, Baja California, Mexico 22444 for the manufacturing of implantable pulse generators for the Senza Spinal Cord Stimulation (SCS)	P130022/S022

System.	
Approval for changes made to MRI Guidelines Manual for the Senza System by adding a new MRI claim for IPG1000/1500/2000.	P130022/S021
Approval for conditional Magnetic Resonance labeling for the Senza Implantable Pulse Generator (IPG) model IPG2000.	P130022/S019
Approval for changing the length and shape of the handle, and the method of securing the cap and wire to the handle of the Stylets distributed with the Senza Spinal Cord Stimulation System	P130022/S018
Approval for a manufacturing site located at Pro-Tech Design & Mfg, Inc., 13719 Borate St, Sante Fe Springs, CA	P130022/S017
Alternate supplier of the Litz Wire used for manufacturing the Senza SCS System Charger sub-assembly	P130022/S016
Second contract manufacturer (Sparton) to conduct manufacturing activities for one of Senza SCS System's components (i.e., Trial Stimulator)	P130022/S015
Approval for Magnetic Resonance (MR) conditional labeling changes	P130022/S014
Approvals for changes made for the Senza Implantable Pulse Generator, IPG2000	P130022/S013
Implement manufacturing process changes to allow for the use of virtual machine software (VMware) to provide an isolated and safe environment from which to run the FDA approved PG2000 Clinician Programmer software v1.7	P130022/S012
Packaging configuration change (i.e., pre-loaded percutaneous lead with the 0.014" curved stylet) to the Senza SCS System	P130022/S011
Approval for a manufacturing site located at Pro-Tech, 4041 Express Street, Arlington, Texas for kitting of components in cleanrooms, final packaging including labeling and visual inspection of the final product prior to shipment for sterilization.	P130022/S010
Approval for a design change for the Surpass Surgical Lead to remove the marker band and change the color of one lead leg	P130022/S009
Approval for software changes to the Clinician Programmer Model PG2000	P130022/S008

Approval to use a larger volume of sterilization load (from 4 pallets to 10 pallets) for the ethylene oxide (EO) sterilization of Senza SCS System products	P130022/S007
Process changes to the battery charger, including the addition of an adhesive to a component on the printed circuit board (PCB), minor alterations to the PCB layout to improve manufacturability, and the addition of torque wrenches	P130022/S006
Approval to update the design of the charging coil to eliminate the termination wraps at the end of the charging coil	P130022/S005
Approval for Surgical Lead Models LEAD3005-xx, LEAD3015-xx, and LEAD3025-xx	P130022/S004
Approval for minor changes in the Senza SCS System Implantable Pulse Generator (IPG) and trial simulation (TSM) firmware	P130022/S002
Modification in the manufacturing process of the Connector stack sub- assembly	P130022/S001
Approval for the Nevro Senza SCS System	P130022

X. SUMMARY OF PRIMARY CLINICAL STUDY(IES)

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

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of the use of the Senza SCS System when programmed to include a frequency of 10 kHz aids in the management of chronic intractable pain of the limbs due to Painful Diabetic Neuropathy (PDN) in the US. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

Patients were enrolled between August 2017 and August 2019. The database for this PMA Supplement P130022/S039 reflected data collected through November 2020 and included 216 patients. There were 18 study sites.

Senza-PDN is a post-market, multi-center, prospective, randomized controlled study to compare the addition of 10 kHz Spinal Cord Stimulation (HF10™ therapy) to Conventional

Medical Management (CMM) with CMM alone in PDN subjects. Data from follow-up visits were compared between the treatment groups as well as to baseline data within each treatment group.

The control group continued to receive their conventional medical management (CMM) only and did not receive the Nevro Senza® HF10 therapy as the test group. All subjects in the control group who attended the 3-month follow-up and those in the test group who passed the trial phase, received a permanently implanted Senza System and attended 3-month follow-up were part of the Per Protocol (PP) population

1. Clinical Inclusion and Exclusion Criteria

   Enrollment in the Senza SCS System study was limited to patients who met the specified inclusion criteria. Key inclusion criteria were:

   a. Symptoms of painful diabetic neuropathy (PDN) in the lower limbs that are refractory to conservative care, including pregabalin or gabapentin and at least one other class of analgesic.
   b. Pain intensity of at least 5 out of 10 cm on the visual analog scale (VAS) in the lower limbs.
   c. At least 22 years of age at the time of enrollment.
   d. An appropriate candidate for the surgical procedures required in this study based on the clinical judgment of the implanting physician.
   e. Willing and capable of giving informed consent.
   f. Willing and able to comply with study-related requirements, procedures, and scheduled visits.

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

   a. Lower limb mononeuropathy (e.g., causalgia and tibial or peroneal neuropathies), lower limb amputation due to diabetes (other than toes), or large and/or gangrenous ulcers of the lower limbs.
   b. Average pain intensity of at least 3 out of 10 cm on the VAS in the upper limbs due to diabetic neuropathy.
   c. Hemoglobin A1c (HbA1c) > 10%.
   d. Body Mass Index (BMI) > 45.
   e. Prior experience with SCS, dorsal root ganglion (DRG) stimulation, peripheral nerve field stimulation (PNfS), or peripheral nerve stimulation (PNS) for chronic intractable pain.
   f. An existing drug pump and/or another active implantable device such as a pacemaker.
   g. A local infection at the anticipated surgical entry site or an active systemic infection.
   h. Pregnancy or a plan to become pregnant during the study.

i. Evidence of an active disruptive psychological or psychiatric disorder significant enough to impact perception of pain, compliance with intervention and/or ability to evaluate treatment outcome, as determined by a psychologist.

2. Follow-up Schedule

Following completion of the baseline procedures, implantation and use of the Senza System (delivering HF10 therapy) followed the Nevro Physician's Manual and supporting manuals. Subjects randomized to the HF10 therapy group underwent a trial stimulation phase lasting up to 14 days with an external stimulator to determine his/her response to this therapy. At the end of the trial phase, subjects had a neurological assessment as well as an assessment for pain. Those who had a successful trial phase, defined as a 50% or greater reduction in lower limb pain from baseline, were eligible to proceed to permanent implantation of a Senza System. HF10 therapy subjects will undergo 24 months of stimulation delivery with assessments at 1, 3, 6, 9, 12, 18, and 24 months post-permanent device activation. At the 6- month assessment, dissatisfied subjects with insufficient pain relief and agreement of the Investigator could opt to crossover to the CMM only treatment arm. Subjects who crossed over will complete the remainder of the scheduled 24 months of follow-up. Adverse events and complications were recorded at all visits. The key time points for each assessment are shown in figure 2.

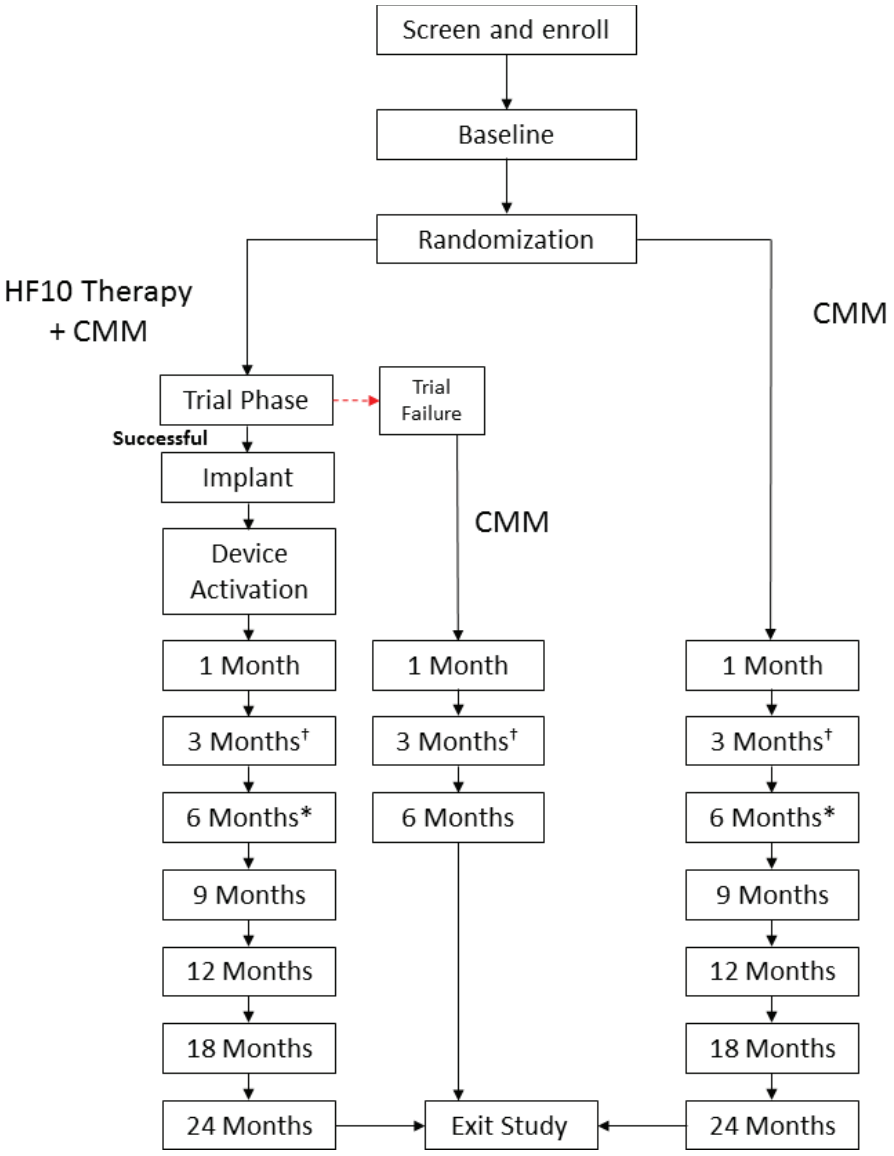

Figure 2: Study Flowchart

(†Primary endpoint analysis; *Option to cross-over to other therapy arm)

3. Clinical Endpoints

The primary endpoint of this study is a composite of safety and effectiveness, specifically the difference between treatment groups in responder rates at 3- month follow-up in subjects without a clinically meaningful neurological deficit compared with baseline. A responder is defined as a subject with ≥ 50% lower limb pain reduction from baseline.

The effectiveness of the Senza SCS system was demonstrated by a decrease in back pain VAS by at least 50% at 3 months Post-Permanent Device Activation as compared with Baseline

The safety of the Senza SCS system was assessed by characterizing clinically meaningful deficits in neurological status (primary) and adverse events (secondary) at all study visits.

Neurologic status includes motor, sensory and reflex functions, which will be characterized as improved, maintained, or a deficit as compared with baseline status as follows:

- A clinically meaningful neurological improvement is defined as a significant persistent improvement in neurological function that impacts subject's well-being and is attributable to a neurological finding; and is new or improved as compared with the baseline assessment.
- A clinically meaningful neurological deficit is defined as a treatment-related significant persistent abnormality in neurological function that impacts subject's well-being and is attributable to a neurological finding; and is new or worsened as compared with the baseline assessment.
- If neither a clinically meaningful neurological improvement nor a clinically meaningful neurological deficit is observed, then neurologic status is maintained.

For a clinically meaningful neurological deficit from Baseline, persistent is defined as lasting beyond what would be expected for a transient event in this population and unable to be resolved through device reprogramming.

Secondary endpoints:

If the primary endpoint was found to be statistically significant at an alpha level of 0.05, then the following secondary endpoints were successively tested in a hierarchical manner in the order shown with the same two-sided alpha level of 0.05 until statistical significance cannot be demonstrated.

1. Difference between the treatment groups in proportion of subjects with a lower limb pain VAS score $\leq$ 3.0 cm at 3 months.
2. Difference between the treatment groups in crossover rates.
3. Difference between the treatment groups in responder rates at 6 months.
4. Difference between the treatment groups in the proportion of remitters (remission is defined as having a lower limb pain VAS score of $\leq$ 3.0 cm for at least 6 months) at 6 months.

5. Difference between the treatment groups in the proportion of subjects with overall improvement from baseline in neurological assessment (motor, sensory, reflex) at 3 months.
6. Difference between the treatment groups in the proportion of subjects with overall improvement from baseline in neurological assessment (motor, sensory, reflex) at 6 months.
7. Difference between the treatment groups in changes in health-related quality of life as assessed by the EuroQol Five Dimensions questionnaire (EQ-5D-5L) at 6 months.
8. Difference between the treatment groups in the average percentage change from baseline in HbA1c levels at 6 months.

B. Accountability of PMA Cohort

At the time of database lock, of a total of 430 subjects were enrolled in this study at 18 US clinical sites. A total of 216 subjects were randomized, 113 in the HF10+CMM group and 103 in the CMM alone group. These 216 subjects comprise the intent to treat (ITT) analysis population, with 184 of these subjects (88 in the HF10+CMM group and 96 in the CMM alone group) included in the PP analysis population. Figure 1 summarizes the number of subjects in each study phase.

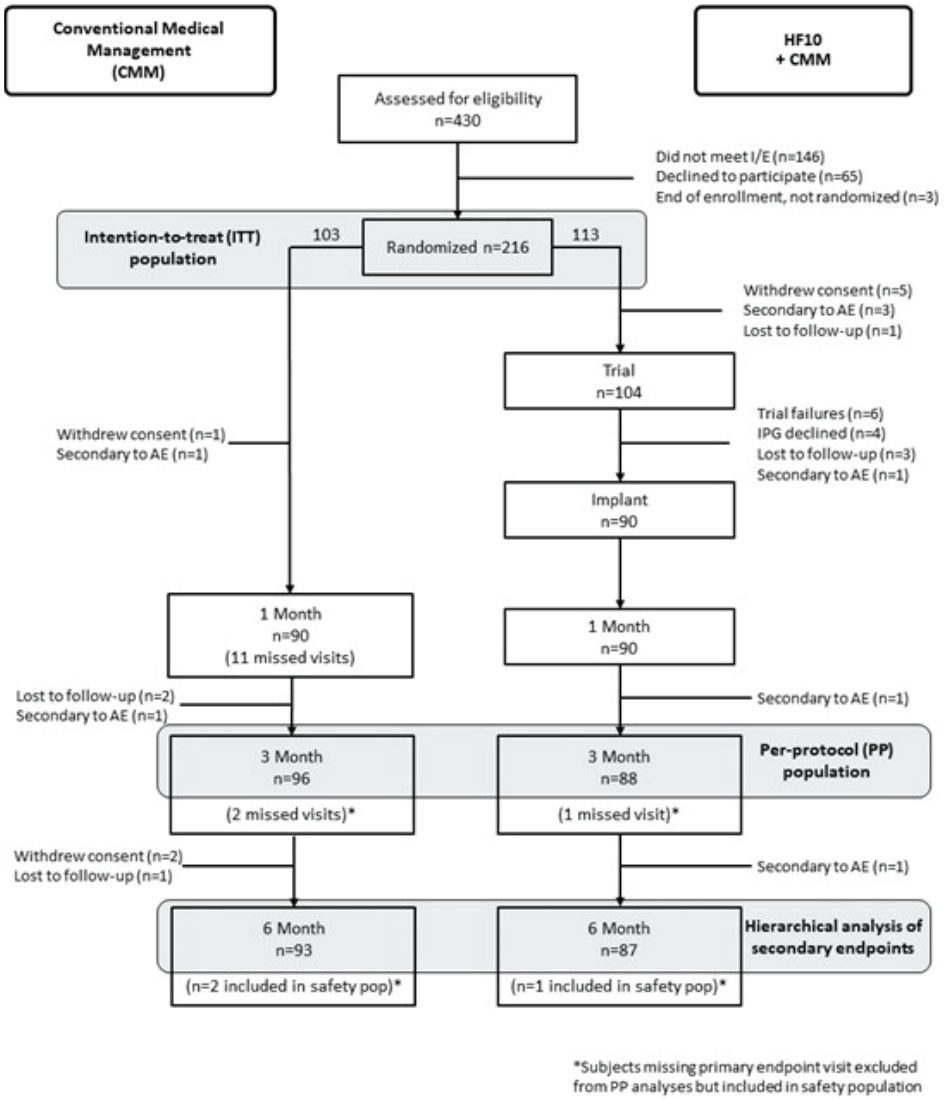

Figure 3: Number of Subjects in the Study by Phase

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 2** below.

Table 2: Demographic and Baseline Characteristics

	CMM n = 103	HF10 + CMM n = 113	Standardized Difference*
Age in years, mean (SD)	60.8 (9.9)	60.7 (11.4)	0.01
Sex			
Male, n (%)	66 (64%)	70 (62%)	0.04
Female, n (%)	37 (36%)	43 (38%)	
Race			
White, n (%)	85 (82.5%)	87 (77.0%)	0.14
Black of African American, n (%)	13 (12.6%)	18 (15.9%)	
Native Hawaiian or other Pacific Islander, n (%)	1 (1.0%)	3 (2.7%)	
American Indian or Alaska Native, n (%)	0 (0.0%)	2 (1.8%)	
Asian, n (%)	1 (1.0%)	1 (0.9%)	
Other, n (%)	3 (2.9%)	2 (1.8%)	
Ethnicity			
Non-Hispanic or Latino, n (%)	97 (94%)	104 (92%)	0.08
Hispanic or Latino, n (%)	6 (6%)	9 (8%)	
Diabetes			
Type 1, n (%)	3 (3%)	8 (7%)	0.19
Type 2, n (%)	100 (97%)	105 (93%)	
Duration in years			
Diabetes, mean (SD)	12.2 (8.5)	12.9 (8.5)	0.09
Peripheral neuropathy, mean (SD)	7.1 (5.1)	7.4 (5.7)	0.06
Lower limb pain VAS in cm, mean (SD)	7.1 (1.6)	7.5 (1.6)	0.22
< 7.5 cm, n (%)	57 (55%)	54 (48%)	0.15
≥ 7.5 cm, n (%)	46 (45%)	59 (52%)	
HbA1c, mean (SD)	7.4% (1.2%)	7.3% (1.1%)	0.11
< 7.0%, n (%)	40 (39%)	46 (41%)	0.04
≥ 7.0%, n (%)	63 (61%)	67 (59%)	
BMI in kg/m^2, mean (SD)	33.9 (5.2)	33.6 (5.4)	0.06
Severity of neuropathic pain			
DN4, mean (SD)	6.5 (1.9)	6.6 (1.7)	0.12
	3 (3%)	1 (1%)	

< 3, n (%)	99 (97%)	112 (99%)	
≥ 3, n (%)	6.9 (1.1)	6.8 (1.3)	0.05
mNSS, mean (SD)	2 (2.0%)	2 (1.8%)	
mild (3-4), n (%)	33 (32.4%)	46 (40.7%)	
moderate (5-6), n (%)	67 (65.7%)	65 (57.5%)	
severe (7-9), n (%)			
Pain medications			
Anticonvulsants			
gabapentin, n (%)	50 (49%)	63 (56%)	0.14
pregabalin, n (%)	29 (28%)	25 (22%)	0.14
Antidepressants			
SNRIs, n (%)	29 (28%)	25 (22%)	0.14
duloxetine, n (%)	27 (26%)	18 (16%)	0.25
TCAs, n (%)	14 (14%)	10 (9%)	0.15
SSRIs, n (%)	27 (26%)	23 (20%)	0.14
Opioids, n (%)	44 (43%)	50 (44%)	0.03
NSAIDs, n (%)	40 (39%)	32 (28%)	0.22
Acetaminophen, n (%)	19 (18%)	17 (15%)	0.09
Topicals, n (%)	9 (9%)	11 (10%)	0.03
None, n (%)	1 (1%)	5 (4%)	0.21
Diabetes medications			
Insulin, n (%)	47 (46%)	51 (45%)	0.01
Oral & non-insulin injectable medications, n (%)	84 (82%)	88 (78%)	0.09
metformin, n (%)	69 (67%)	66 (58%)	0.18
other, n (%)	53 (51%)	57 (50%)	0.02
None, n (%)	6 (6%)	9 (8%)	0.08

*Standardized difference - Effect size (Cohen's d): ≥0.20 = small, ≥0.50 = medium, ≥0.80 = large. SD: standard deviation, VAS: visual analog scale, HbA1c: hemoglobin A1c, BMI: body mass index, DN4: Douleur Neuropathique, mNSS: modified Neuropathy Symptom Score, SNRI: serotonin-norepinephrine reuptake inhibitor, TCA: tricyclic antidepressant

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety data was performed in the ITT population comprising of 113 in the HF10+CMM group and 103 in the CMM alone group. This includes 90 subjects with a permanent Senza System device implant, all 90 completed a Month 1 visit, 88 subjects completed a Month 3 visit, and 88 subjects completed a Month 6 visit. On average, study subjects had a permanent implant for 24.5 weeks, resulting in a total of 42.3 implant-years. Of 103 subjects assigned to CMM alone, 90 subjects completed a Month 1 visit, 96 subjects completed a Month 3 visit, and 95 completed a Month 6 visit.

The safety component of the primary endpoint included deterioration of baseline neurological deficits at Month 3. Neurological examinations were conducted at Baseline and at scheduled study visits.
Investigators assessed any changes from the Baseline neurological status and determined if any of the changes were attributed to stimulation.

Table 3 presents the neurological assessment data by visit as compared with Baseline. If a neurological deficit was noted when compared with Baseline, **Table 4** presents the relatedness of neurological deficits. There were more deficits noted in the CMM alone group compared with the HF10+CMM group, likely due to the progression of disease. Overall, there were no stimulation- related neurological deficits reported in the study.

Table 3: Changes from Baseline in Neurological Assessment by Visit Per Protocol Population

End of Trial	CMM alone	HF10 + CMM
N	**NA**	**101**
Motor		
Improvement	-	12 (11.8%)
Maintenance	-	89 (88.1%)
Deficit	-	0 (0.0%)
Sensory		
Improvement	-	60 (59.4%)

Maintenance	-	40 (39.6%)
Deficit	-	1 (0.9%)
Reflexes		
Improvement	-	14 (13.9%)
Maintenance	-	85 (84.2%)
Deficit	-	2 (2.0%)
Month 3, N	**94**	**87**
Motor		
Improvement	2 (2.1%)	7 (8.0%)
Maintenance	83 (88.3%)	80 (92.0%)
Deficit	9 (9.6%)	0 (0%)
Sensory		
Improvement	7 (7.4%)	63 (72.4%)
Maintenance	78 (83.0%)	23 (26.4%)
Deficit	9 (9.6%)	1 (1.1%)
Reflexes		
Improvement	6 (6.4%)	10 (11.5%)
Maintenance	83 (88.3%)	76 (87.4%)
Deficit	5 (5.3%)	1 (1.1%)
Month 6, N	92	84
Motor		
Improvement	1 (1.1%)	5 (6.0%)
Maintenance	84 (91.3%)	78 (92.9%)
Deficit	7 (7.6%)	1 (1.2%)
Sensory		
Improvement	8 (8.7%)	49 (58.3%)
Maintenance	77 (83.7%)	33 (39.3%)
Deficit	7 (7.6%)	2 (2.4%)

Reflexes		
Improvement	1 (1.1%)	15 (17.9%)
Maintenance	84 (91.3%)	67 (79.8%)
Deficit	7 (7.6%)	2 (2.4%)

Table 4: Relatedness of Neurological Deficits in HF10+CMM subjects

Visit	Number of Subjects
End of Trial	
Stimulation-related	0
Not stimulation-related	3
Month 3	
Stimulation-related	0
Not stimulation-related	2
Month 6	
Stimulation-related	0
Not stimulation-related	5

Adverse Events

Among the 216 randomized subjects, 52 Serious Adverse Events (SAEs) were reported in 31 subjects (31/216, 14.4%). There were 30 SAEs reported in 15 subjects (15/109, 13.8%) in the CMM alone group and 22 SAEs reported in 16 subjects (16/107, 15.0%) in the HF10+CMM group. Serious adverse events are presented in **Table 5.** One subject who had been randomized to HF10+CMM did pass away for reasons unrelated to the study and prior to any trial or implant procedure

Table 5: Serious Adverse Events Intention-to-Treat-Baseline Population

	HF10 + CMM		CMM alone	
Preferred Term	**Number of AEs**	**Number (%) of Subjects with AE (N=107)**	**Number of AEs**	**Number (%) of Subjects with AE (N=109)**
Total # of Serious AEs	**22**	**16 (15.0%)**	**30**	**15 (13.8%)**
Abdominal abscess	0	0	1	1 (0.9%)
Acute kidney injury	0	0	1	1 (0.9%)
Acute myocardial infarction	1	1 (0.9%)	1	1 (0.9%)
Acute respiratory failure	1	1 (0.9%)	0	0
Cardiac arrest	1	1 (0.9%)	0	0
Cardiac failure congestive	1	1 (0.9%)	0	0
Cellulitis	1	1 (0.9%)	1	1 (0.9%)
Cerebrovascular accident	0	0	1	1 (0.9%)
Cervical vertebral fracture	0	0	1	1 (0.9%)
Chest pain	1	1 (0.9%)	0	0
Cholangitis acute	1	1 (0.9%)	0	0
Cholecystitis	0	0	1	1 (0.9%)
Coronary artery disease	1	1 (0.9%)	0	0
Device extrusion	1	1 (0.9%)	0	0
Diarrhoea	0	0	1	1 (0.9%)
Dyskinesia	0	0	1	1 (0.9%)
Embolic stroke	0	0	1	1 (0.9%)
Encephalopathy	0	0	1	1 (0.9%)
Endocarditis	0	0	1	1 (0.9%)
Extradural haematoma	1	1 (0.9%)	0	0

Gastric ulcer	0	0	1	1 (0.9%)
Headache	0	0	1	1 (0.9%)
Hypertensive emergency	0	0	1	1 (0.9%)
Hypotension	1	1 (0.9%)	0	0
Impaired gastric emptying	0	0	1	1 (0.9%)
Localised infection	1	1 (0.9%)	0	0
Malnutrition	0	0	1	1 (0.9%)
Myocardial infarction	0	0	2	2 (1.8%)
Nausea	0	0	1	1 (0.9%)
Orthostatic hypotension	1	1 (0.9%)	0	0
Osteoarthritis	1	1 (0.9%)	1	1 (0.9%)
Pancreatic disorder	0	0	1	1 (0.9%)
Pancreatic mass	1	1 (0.9%)	0	0
Pancreatitis chronic	1	1 (0.9%)	0	0
Paraplegia	1	1(0.9%)	0	0
Pneumonia	1	1 (0.9%)	2	2 (1.8%)
Pyrexia	1	1 (0.9%)	0	0
Sepsis	1	1 (0.9%)	2	2 (1.8%)
Septic shock	0	0	2	2 (1.8%)
Staphylococcal infection	0	0	1	1 (0.9%)
Viral infection	1	1 (0.9%)	0	0
Wound infection	1	1 (0.9%)	0	0
Wound infection staphylococcal	0	0	1	1 (0.9%)

Two study-related (SAEs) reported in 2 (1.9%) HF10+CMM subjects. Of note, neither of the study-related SAEs were classified as stimulation-related. Also, neither of the SAEs were categorized as both unanticipated and device-related; thus, they were not considered as an UADE. Study-related SAEs by cause are presented in **Table 6.**

Table 6: Study-Related Serious Adverse Events HF10+CMM Group, Intention-to-Treat Population

Cause Preferred Term	**No. of SAEs**	**No. (%) of Subjects with SAE** (N=107)
Total SAEs	2	2 (1.9%)
Device extrusion	1	1 (0.9%)
Wound infection	1	1 (0.9%)

There were 127 AEs reported in 55 subjects (55/109, 50.4%) in the CMM alone group and 190 AEs reported in 76 subjects (76/107, 71.0%) in the HF10+CMM group. Most events (86.8%) were categorized as mild or moderate and the majority of events (83.3%) had resolved as of the data cutoff.

There were no study-related adverse events (AEs) reported in the CMM alone group as the protocol did not require any specific study-related treatments for this group. There were 18 reported study-related AEs in 14 (13.1%) HF10+CMM subjects. Stimulation- related AEs were reported in 3 (2.8%) HF10+CMM subjects. The most frequent study- related AEs included infection (n 3) and wound dehiscence (n=2), which are known complications of SCS system implants. Study-related adverse events are presented in **Table 7.**

Table 7: Study-Related Adverse Events Intent-to-treat Population

Preferred Term	**CMM alone (N=109)**		**HF10 + CMM (N=107)**	
	Number of AEs	**Number (%) of Subjects with AE**	**Number of AEs**	**Number (%) of Subjects with AE**
Total # of Study Related AEs	**0**	**0**	**18**	**14 (13.1%)**
Device Related AEs	0	0	2	2 (1.9%)

Impaired healing	0	0	1	1 (0.9%)
Medical device site discomfort	0	0	1	1 (0.9%)
Procedure Related AEs	0	0	13	11 (10.3%)
Wound dehiscence	0	0	2	2 (1.9%)
Dermatitis contact	0	0	1	1 (0.9%)
Device extrusion	0	0	1	1 (0.9%)
Gastrooesophageal reflux disease	0	0	1	1 (0.9%)
Hyporeflexia	0	0	1	1 (0.9%)
Inadequate pain relief	0	0	1	1 (0.9%)
Incision site pain	0	0	1	1 (0.9%)
Medical device site infection	0	0	1	1 (0.9%)
Radiculopathy	0	0	1	1 (0.9%)
Urticaria	0	0	1	1 (0.9%)
Wound infection	0	0	2	2 (1.9%)
Stimulation Related AEs	0	0	3	3 (2.8%)
Arthralgia	0	0	1	1 (0.9%)
Pain	0	0	1	1 (0.9%)
Paraesthesia	0	0	1	1 (0.9%)

Safety Conclusions: Overall, the results support the safety of the Senza System for treatment of the PDN patient population. As such, the results of this study provide a reasonable assurance that Senza System is safe, as defined by 21 CFR 860.7(d) (1). The study demonstrates that the probable benefits to health from use of the Senza System for its intended uses and conditions of use, when accompanied by adequate directions and warnings against unsafe use, outweigh any probable risks.

2. Effectiveness Results

Primary endpoint met:

The primary endpoint in this study is a composite of safety and effectiveness, specifically the difference between treatment groups in responder rates at 3-month follow-up in subjects without a clinically meaningful neurological deficit compared with baseline. A responder is defined as a subject with ≥ 50% lower limb pain reduction from baseline.

In ITT population, the primary endpoint, a composite of safety and effectiveness, was met by 11.7% (12/103) of the CMM alone subjects compared to 66.4% (75/113) of HF10+CMM subjects. This difference is statistically significant with a p-value < 0.0001.

In the PP population, 75 out of 87 HF10+CMM subjects (86.2%) met the overall primary endpoint. Seventy-seven (88.5%) HF10+CMM group subjects reached an improvement of 50% or more in the lower limb pain VAS score and 85 (97.7%) of the subjects met the safety component of the primary endpoint. Although 78 out of 94 (83%) subjects from the CMM alone group met the safety endpoint, only 7 subjects (7.4%) subjects were pain responders, resulting in 5 subjects (5.3%) who met the overall primary endpoint.

Secondary endpoints:
As prespecified in the statistical analysis plan, if the primary endpoint of the study was found to be statistically significant at an alpha level of 0.05, then secondary endpoints were tested successively in the order shown below with the same two-sided alpha level of 0.05 until statistical significance could not be demonstrated. A summary of the secondary endpoints is presented in **Table 8.** Statistical significance was achieved in 7 of 8 secondary endpoints, including measures of profound pain relief sustained over 6 months as well as sensory improvements with HF10 therapy. The final endpoint that did not achieve statistical significance assessed whether HF10+CMM would differentially affect subjects' HbA1c levels which are an indication of glycemic control over time. There was no change for either treatment over 6 months, suggesting the HF10 therapy had neither a positive nor negative effect on glycemic control.

Table 8: Summary of Secondary Endpoints

	CMM	HF10+CMM	Between-Group p-value
Per Protocol Population	**N=96[5]**	**N=88[5]**	
Lower limb pain VAS ≤3 cm at 3 months, n/n (%)	5/96 (5.3%)	69/88 (78.4%)	< 0.001[1]
Subjects crossing over at 6 months, n/n (%)	76/93 (81.7%)	0/87 (0.0%)	< 0.001[1]
Lower limb pain relief ≥50% at 6 months, n/n (%)	5/93 (5.4%)	74/87 (85.1%)	< 0.001[1]
Remitters[2] at 6 months, n/n (%)	1/95 (1.1%)	53/88 (60.2%)	< 0.001[1]
Overall improvement in neurological assessment[3] at 3 months, n/n (%)	6/94 (6.4%)	63/87 (72.4%)	< 0.001[1]
Overall improvement in neurological assessment[3] at 6 months, n/n (%)	2/92 (3.3%)	52/84 (61.9%)	< 0.001[1]
Changes in health-related quality of life at 6 months EQ-5D-5L index, mean±SD EQ-5D-5L health VAS, mean±SD	-0.031±0.127 -1.7±23.0	0.130±0.159 15.9±21.6	< 0.001[4] < 0.001[4]
Percentage change in HbA1c at 6 months, mean±SD	2.6%±15.4%	1.5%±14.9%	0.649[4]

[1]By Fisher's Exact test, 2-sided
[2]Remission is defined as pain VAS score ≤3 cm for 6 consecutive months
[3] Overall improvement on neurological assessment defined as no deficit compared to baseline in any motor, sensory, or reflex outcomes and improvement in at least one outcome
[4]Student's t-test, 2-sided Abbreviations: VAS, visual analog scale, cm, centimeter
[5]The N for each assessment may vary due to missing data

Effectiveness Conclusions:
The HF10 subjects in the study have demonstrated favorable primary and secondary endpoint results. The results of this study provide a reasonable assurance that the Senza System is effective, as defined by 21 CFR 860.7(e) (1). The study demonstrated clinically significant results in a significant portion of the target population for its intended uses and conditions of use, when accompanied by adequate directions for use.

3. Pediatric Extrapolation

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

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 clinical study included 18 investigators of which none were full-time or part-time employees of the sponsor and four 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: two investigators
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 sponsor provided data from a prospective, multicenter, randomized controlled trial (Senza-PDN) was comprised of 216 subjects in the ITT population and 184 subjects in the PP population. Ninety subjects in the HF10+CMM group received a permanent implant. With an average of over 7 years of peripheral neuropathy symptoms, subjects presented with moderate to severe neuropathic pain despite treatment with appropriate neuropathic pain medications, including antiepileptics, antidepressants, and even opiates despite lack of evidence for their efficacy. The subjects enrolled in the study suffer moderate to severe chronic pain of the limbs that does not adequately respond to other approved treatments. These patients typically have impaired quality of life including sleep disturbance to increased nighttime pain, reduced function and intolerable medication side-effects.
The primary objective of this study was to obtain evidence of safety and effectiveness of the Senza System for the treatment of chronic limb pain due to diabetic neuropathy (Painful Diabetic Neuropathy or PDN).

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

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

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The primary objective was accomplished by a composite endpoint of safety and effectiveness of the Senza System for the treatment of chronic limb pain. The composite endpoint is the percentage of subjects in the Intent to Treat analysis (ITT) who responded to SCS therapy, as assessed by pain VAS for lower limb pain and did not have a deterioration of their Baseline neurological deficits.
For the Per Protocol (PP) population, 85.1% of HF10+CMM subjects had an improvement of 50% or more in lower limb pain at 6 months. Furthermore, 60.2% of HF10+CMM subjects achieved remission with a sustained pain score of 3 or less over 6 consecutive months. Additionally, 86.2% of HF10+CMM subjects in the PP population achieved the composite primary endpoint at 3 months. All of these outcomes were statistically significantly different from the CMM alone group at a p-value < 0.001.

In addition to meeting the primary endpoint, secondary endpoints were assessed in a hierarchical manner and 7 of 8 prespecified secondary endpoints were met, supporting the conclusion that HF10 therapy results in a significant number of pain responders and remitters, improved sensation, and better quality of life for PDN patients. Findings from this study has been reported through 6 months of follow-up. Improvements on neurological examination in the HF10+CMM subjects was observed by investigators. At 6 months, in the HF10+CMM group, 61.9% of subjects showed improvements compared with 3.3% of CMM subjects ($p < 0.001$). Additionally, 49 of 84 (58.3%) HF10+CMM subjects demonstrated improvement specifically on the sensory portion of the neurological examination. This outcome has potential advantages for patients with diabetic neuropathy: improved sensation in the feet could aid in reduction of foot ulcers, reduction of infections and subsequently, reduction of lower limb amputations. Additionally, enhanced proprioception could reduce risk of falling and potential injury.

Another potential advantage for HF10 therapy for PDN is that the Senza System delivers paresthesia independent SCS. Typically, patients with PDN have numbness and tingling in their hands and feet as a result of their disease. Not only is paresthesia dependent SCS difficult to target into the distal limbs, it exacerbates a PDN patient's baseline tingling sensations. HF10 therapy provides pain relief without this side effect.

B. Safety Conclusions

The risks of the device are based on the data collected in a clinical study conducted to support PMA approval as described above. There were no stimulation-related neurological deficits reported in the study.

Among the 216 randomized subjects, 52 SAEs were reported in 31 subjects (31/216, 14.4%). There were 30 SAEs reported in 15 subjects (15/109, 13.8%) in the CMM alone group and 22 SAEs reported in 16 subjects (16/107, 15.0%) in the HF10+CMM group. There were 2 study related SAEs reported in 2 (1.9%) HF10+CMM subjects. Neither of the SAEs were classified as stimulation related. Also, the SAEs were not categorized as both unanticipated and device related; thus, neither were UADEs.

Regarding the AEs, there were 127 AEs reported in 55 subjects (55/109, 50.4%) in the CMM alone group and 190 AEs reported in 76 subjects (76/107, 71.0%) in the HF10+CMM group. Most events (86.8%) were categorized as mild or moderate and the

majority of events (83.3%) had resolved as of the data cutoff. there were 18 study-related AEs reported in 14 (13.1%) HF10+CMM subjects.

There were no study-related AEs reported in CMM subjects as the protocol did not require any specific treatments in this group. Eighteen study-related AEs were reported in 13.1% (14/107) of HF10+CMM subjects and stimulation-related AEs were reported in 2.8% (3/107).

C. Benefit-Risk Determination

Diabetes is quite common worldwide with peripheral neuropathy as a frequent complication that is both disabling and costly. Patients are typically managed with conservative therapies that often fail due to ineffectiveness or intolerable side effects. PDN patients with symptoms refractory to conservative care are left with a progressive neuropathic pain condition and without further treatment options.

The probable benefits and risks of the device are based on the post-market clinical study conducted to support PMA approval as described above.

The primary objective of this study was to obtain evidence of safety and effectiveness of the Senza System for the treatment of chronic limb pain due to diabetic neuropathy (Painful Diabetic Neuropathy or PDN). The primary objective was accomplished by a composite endpoint of safety and effectiveness of the Senza System for the treatment of chronic limb pain. The composite endpoint is the percentage of subjects who responded to SCS therapy, as assessed by pain VAS for lower limb pain and did not have a deterioration of their Baseline neurological deficits. The majority of subjects upon addition of HF10 therapy obtained at least a 50% reduction in pain that lasted through 6 months as compared to CMM alone subjects. It would be expected that subjects with chronic neuropathic limb pain would experience a similar benefit.

In addition to meeting the primary endpoint, 7 of 8 prespecified secondary endpoints were met, supporting the conclusion that HF10 therapy results in a significant number of pain responders and remitters, improved sensation, and better quality of life for PDN patients. Data reported through 6 months demonstrates the durability of the safety and effectiveness of HF10.

In addition to sustained pain relief, upon addition of HF10 therapy, there was significant improvement in a variety of assessments for neurological function, neuropathic pain severity, health- related quality of life, mental functioning, and sleep suggesting a broad impact of this treatment on patients' lives.

Senza therapy was also determined to be safe. There were no stimulation-related neurological deficits reported in the study. With addition of HF10, there were significantly more subjects with improvements in neurological assessments compared to CMM Alone. Most importantly, the subjects also showed improvements in protective sensation that has many advantages for patients with diabetic neuropathy.

The adverse events that were reported were consistent with the safety profile of all SCS systems including Senza SCS as described in the literature. Rates of study related AEs and SAEs reported in this study are consistent with adverse events reported in Senza-RCT (approved through P130022) and are anticipated of this device type. There are no new risks or new adverse events identified in this subset of the patient population.

Patient Perspective

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

In conclusion, given the available information above, the data support that for the use of the Senza SCS System when programmed to include a frequency of 10 kHz aids in the management of chronic intractable pain of the limbs due to PDN, and 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 support a reasonable assurance of the safety and effectiveness 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 based from a post- market clinical study. The analyses also support a clinical benefit to risk determination that is overall favorable to this patient population.

XIV. CDRH DECISION

CDRH issued an approval order on July 16, 2021.

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.