SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

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

Device Trade Name: Prodigy, Proclaim XR, Proclaim Plus, and Externa Spinal Cord Stimulation (SCS) Systems

Device Product Codes: LGW, QRB

Applicant's Name and Address: Abbott Medical,
6901 Preston Road
Plano, Texas 75024

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P010032/S191

Date of Notice of Approval to the Applicant: May 10, 2023

Abbott's implantable neurostimulation system was first approved for spinal cord stimulation as an aid in the management of chronic, intractable pain of the trunk and/or limbs including unilateral or bilateral pain associated with any of the following: failed back surgery syndrome, and intractable low back and leg pain on December 3, 2001 (PMA P010032). This supplement was submitted to expand the indications to include non-surgical back pain (NSBP) for the tonic and BurstDR™ stimulation modes, and diabetic peripheral neuropathy (DPN) of the lower extremities for the tonic stimulation mode.

Table 1. SCS Indication History

No.	Submission	Approved Indications for Use
1	P010032 Approved on 12/03/2001	ANS (Advanced Neuromodulation Systems) Genesis Neurostimulation (IPG) 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 and leg pain.
2	P010032/S189	This spinal cord stimulation (SCS) systems is indicated as an aid in the management of chronic, intractable pain of

No.	Submission	Approved Indications for Use
	Approved on 01/24/2023	the trunk and/or limbs, including unilateral or bilateral pain associated with the following: failed back surgery syndrome, intractable low back and leg pain, and diabetic peripheral neuropathy of the lower extremities.

II. INDICATIONS FOR USE

Abbott Medical spinal cord stimulation (SCS) systems are indicated as an aid in the management of chronic, intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with the following: failed back surgery syndrome, non-surgical back pain (without prior surgery and not a candidate for back surgery), and diabetic peripheral neuropathy of the lower extremities.

III. CONTRAINDICATIONS

This system is contraindicated for patients who are unable to operate a system or who have failed to receive effective pain relief during trial stimulation.

IV. WARNINGS AND PRECAUTIONS

Warnings and precautions are provided in the associated Abbott neurostimulation system labeling. Safety information was updated in accordance with the most recent American Diabetes Association's Standard of Medical Care in Diabetes to address the increased risk and potential complications for diabetic peripheral neuropathy patients. Additional warnings were added to provide guidance for managing patients presenting with risk factors or sub-optimal glycemic control.

V. DEVICE DESCRIPTION

System Description

The Abbott SCS System utilizes a multi-programmable neurostimulation system to deliver electrical stimulation to specific neural targets within the human body. The system consists of the following components:

- External Pulse Generator (EPG) – The EPG provides stimulation for patients during an evaluation or during intraoperative testing.
- Implantable Pulse Generator (IPG) - The IPG is implanted and delivers electrical stimulation via leads/extensions in the epidural space to provide SCS therapy. The IPG is implanted in a subcutaneous pocket and receives programming signals from an external Patient Programmer. The IPG decodes the signals and delivers stimulation pulses to the patient via a selected combination of output electrodes. The IPG is

powered by a hermetically sealed battery enclosed within a hermetically sealed titanium case and uses an integrated circuit to generate electrical stimulation.

- Leads and Extensions - The lead delivers the stimulation to the targeted nerve through electrodes on the end of the lead. The extension connects the lead to the neurostimulator if necessary. The permanent and trial leads offer multiple lead configurations with variable lead body lengths and electrode spacing to satisfy placement preferences for the patient and implanting physician without compromising performance of the stimulator.
- Clinician Programmer (CP) - The CP interfaces with the IPG and is intended to be used by the clinician to noninvasively program and control device parameters.
- Patient Programmer - The Patient Programmer allows the patient to view, select, and control the programs that the clinician has prescribed.
- Patient recharger – Allows the patient to charge the battery of a rechargeable IPG. A plug-in charger recharges the patient recharger.

Principles of Operation

The Abbott SCS System is used 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, non-surgical back pain (without prior surgery and not a candidate for back surgery), and diabetic peripheral neuropathy of the lower extremities. The surgical procedure involves implanting a lead into the epidural space along the spinal cord to deliver low-intensity electrical pulses to the nerve fibers. The lead is connected to an implantable pulse generator, which is the power source of the system. When turned on, the stimulator sends mild electrical pulses to the nerve fibers of the spinal cord via a selected combination of output electrodes on the connected lead, modifying and masking the pain signals, as shown in Figure 1. The stimulation settings are established noninvasively via an external Clinician Programmer to create customized therapy for patients. The stimulation programs created by clinicians can be selected by patients via a Patient Programmer to assist the patient in managing their prescribed stimulation programs.

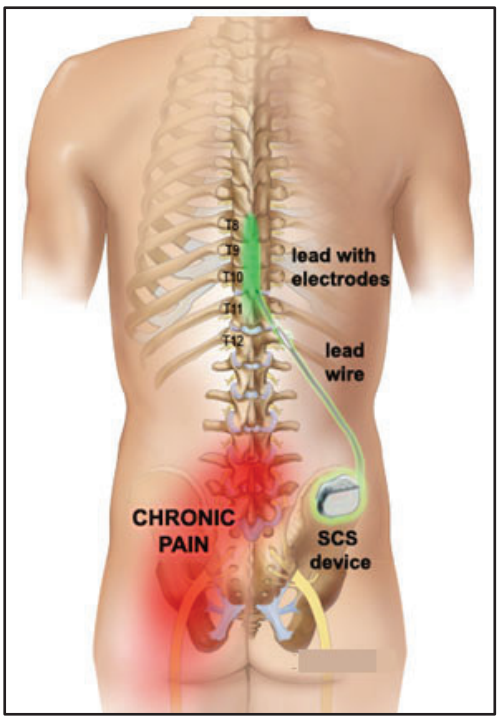

Figure 1. Representation of implanted SCS System

System Components

All the Abbott SCS System components within the scope of this submission are commercially available in the United States and have been approved by the FDA through supplements to PMA P010032. Table 2 lists all implantable system components and the associated document numbers. There are no changes proposed for these devices; the only changes proposed are to the labeling concerning the Indications for Use.

Table 2. Abbott SCS components

Device	Model #	Relevant PMA-S File #
Rechargeable Neurostimulation System		
Prodigy IPG Prodigy MRI IPG	3799 3772	P010032/S109
Prodigy Patient Programmer	3855 3856	P010032/S109
Prodigy Charging System	3730	P010032/S074
Eterna SCS IPG	32400	P010032/S186
Patient Controller Application	55500	P010032/S186
Charger Kit	36000	P010032/S186
Primary Cell Neurostimulation System		

Device	Model #	Relevant PMA-S File #
Proclaim XR 5 IPG Proclaim XR 7 IPG Proclaim 5 IPG Proclaim 7 IPG	3660 3662 3661 3663	P010032/S096
Clinician Programmer App	3874	P010032/S096
Patient Controller App	3875	P010032/S096
Proclaim Plus 5 IPG Proclaim Plus 7 IPG Proclaim Plus 5 IPG Proclaim Plus 7 IPG	3670 3672 3671 3673	P010032/S187
Trial Neurostimulation System		
Trial EPG	3599	P010032/S092
SCS Permanent Percutaneous Leads		
Octrode™ Leads	3183 3186, 3189	P010032, P010032/S018
Quattrode™ Leads	3143, 3146, 3149, 3153, 3156, 3159	P010032, P010032/S018
SCS Permanent Paddle Leads		
Paddle Leads	3214, 3219, 3224, 3228, 3240, 3243, 3244, 3245, 3246, 3262, 3266, 3268, 3283, 3286, 3288, 3292	P010032, P010032/S010, P010032/S013, P010032/S018, P010032/S020, P010032/S026, P010032/S029 P010032/S193
SCS Trial Percutaneous Leads		
Octrode™ Leads	3086	P010032
Quattrode™ Leads	3046	P010032

In addition, accessory and extension kits are used in conjunction with Abbott SCS systems and are commercially available in the US.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Alternative practices to the use of totally implanted IPG for spinal cord stimulation to treat chronic pain of trunk and limbs include:

1. Non-surgical treatment options for chronic pain patients include:
    a. Oral medication
    b. Rehabilitative therapy

c. Transcutaneous electrical nerve stimulation (TENS);

d. Behavior modification

e. Neurolysis (i.e., Therapeutic nerve block, Cryoanalgesia Radiofrequency [RF] Lesioning)

2. Surgical treatment options for chronic pain patients include:

a. Sympathectomy- severing the nerve pathway

b. Partially Implanted SCS Systems – RF implantable spinal cord stimulators (the power source in this system is external).

c. Commercially available fully implanted SCS Systems.

The widely accepted treatment algorithm for back pain in an acute state begins with conservative care consisting of physiotherapy and medication optimization. Back pain persisting for more than three months is considered chronic. The majority of these patients do not have a diagnosis amenable to surgical intervention, thus we are considering these patients to have "non-surgical" back pain or NSBP. Patients with NSBP are likely to be offered non-operative algorithmic interventions such as physiotherapy, anesthetic or steroid injections, radiofrequency ablation, and analgesic therapy depending on the specific diagnosis. Those with a clear surgical indication may be offered surgery. Even with technically successful surgery, there is inconsistent clinical effectiveness, and significant pain can recur or persist from the original cause or from the post-surgical healing process[1,2,3]. This phenomenon is commonly referred to as Failed Back Surgery Syndrome (FBSS).

There are several alternatives for the treatment of DPN of the lower extremities. Generally, two different approaches are used to treat these patients: glycemic control and symptomatic pain treatment. Treatment of the underlying diabetes, if possible, is generally the primary approach to pain management through improved control of blood-sugar levels. In addition, pharmacologic treatments are delivered to address pain symptoms. These include tricyclic anti-depressants, anti-convulsants (α-2-δ modulators: gabapentin, pregabalin or valproate), and selective serotonin/norepinephrine re-uptake inhibitors (SSRI/SNRI). It is recommended that comorbidities should be evaluated before selecting a first-line therapy.

Subsequently, if a patient is refractory to one of the first-line therapies, a second or combination of other first-line drugs should be prescribed. Second- line therapies include opioid analgesics for acute rescue therapy. The recognition of dependence syndromes associated with the use of opioids complicates the treatment of symptoms refractory to first-line treatments. Non- pharmacologic treatments include physical therapy, cognitive therapy, and transcutaneous nerve stimulation (TENS). These therapies would be

[1] Fritzell, P., et al., 2001 Volvo Award Winner in Clinical Studies: Lumbar fusion versus nonsurgical treatment for chronic low back pain: a multicenter randomized controlled trial from the Swedish Lumbar Spine Study Group. Spine (Phila Pa 1976), 2001. 26(23): p. 2521-32; discussion 2532-4.

[2] Phillips, F.M., et al., Lumbar spine fusion for chronic low back pain due to degenerative disc disease: a systematic review. Spine (Phila Pa 1976), 2013. 38(7): p. E409-22

[3] Manchikanti, L. and J.A. Hirsch, An update on the management of chronic lumbar discogenic pain. Pain Manag, 2015. 5(5): p. 373-86

provided in conjunction or following first-line medical treatment, but before more invasive therapies are considered, and only under the direction of a pain management specialist. 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 Prodigy and Proclaim Spinal Cord Stimulation Systems for the treatment of chronic pain of trunk and limbs are currently approved for commercial distribution in Algeria, Argentina, Aruba, Australia, Brazil, Canada, Colombia, Costa Rica, Ecuador, El Salvador, Estonia, Ethiopia, European Union, Hong Kong, India, Israel, Japan, Kuwait, Mexico, Monaco, New Zealand, Norway, Panama, Puerto Rico, Russian Fed., Saudi Arabia, Singapore, South Africa, South Korea, Switzerland, Taiwan, Turkey, United Kingdom, USA, United Arab Emirates.

The Eterna Spinal Cord Stimulation System for the treatment of chronic pain of trunk and limbs is currently approved for commercial distribution in USA.

The Prodigy, Proclaim, or Eterna SCS systems have not been withdrawn from marketing for reasons related to safety and effectiveness of the device.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

The implantation of a neurostimulation system involves risk. In addition to those risks commonly associated with surgery, the following risks are also associated with implantation, and/or use of a neurostimulation system.

- Undesirable changes in stimulation may occur over time. These changes in stimulation are possibly related to cellular changes in tissue around the electrodes, changes in the electrode position, loose electrical connections and/or lead failure.
- Placement of a lead in the epidural space is a surgical procedure that may expose the patient to risks of epidural hemorrhage, hematoma, infection, spinal cord compression, and/or paralysis.
- Patients on anticoagulation therapies may be at greater risk for postoperative complications such as hematomas that can result in paralysis.
- Battery failure and/or battery leakage may occur.
- Radicular chest wall stimulation.
- Cerebrospinal Fluid leakage.
- Persistent pain at the electrode or IPG site.
- Seroma at the implant site.
- Lead migration, which can result in changes in stimulation and subsequent reduction in pain relief.

- Allergic or rejection response to implant materials.
- Infection
- Implant migration and/or local skin erosion.
- Paralysis, weakness, clumsiness, numbness or pain below the level of implantation.
- Loss of pain relief return patients to their original pain condition.
- Stimulation-dependent gastrointestinal symptoms such as nausea, diarrhea, incontinence, or constipation.
- Stimulation-dependent bladder symptoms such as urinary retention, incontinence, or frequency.

For the specific adverse events that occurred in the supporting data, please see **Table 4** & **5** in **"Safety Results"** below.

IX. SUMMARY OF NONCLINICAL STUDIES

Pre-clinical studies previously submitted to FDA in the Original PMA application (P010032) and supplements continue to support the safety and effectiveness of the commercially available Abbott implantable neurostimulation system for treatment of chronic intractable pain of the trunk and/or limbs. No additional preclinical studies were required to evaluate the safety and effectiveness of Abbott SCS therapy for the treatment of non-surgical back pain or diabetic peripheral neuropathy. Table 2

X. SUMMARY OF PRIMARY CLINICAL STUDIES

An Abbott implantable neurostimulation system is indicated for spinal cord stimulation systems as an aid in the management of chronic, intractable pain of the trunk and/or limbs-including unilateral or bilateral pain. The safety and effectiveness of an Abbott implantable neurostimulation system has been previously established for the approved indications (see **Section I**, **Table 1**).

The clinical evidence supporting the safe and effective use of the Abbott implantable neurostimulation system in the diabetic neuropathy population has been previously submitted for the approval of P010032/S189. The data is a systematic review of published clinical scientific literature of commercially available SCS systems (manufactured by Abbott and others). Primary evidence comes from two randomized controlled trials in patients with DPN. Additional supplemental clinical evidence for safety was identified through the analysis of Medicare claims data, investigating adverse event data related to the use of Abbott SCS systems in patients with DPN, and included reports reflecting the experience of patients treated with SCS for any condition where a diagnosis of diabetes was considered. Please refer to S189 SSED for full information about the clinical evidence supporting the safe and effective use of the Abbott implantable neurostimulation system in the DPN population.

The clinical evidence supporting the safe and effective use of the Abbott implantable neurostimulation system in the NSBP population is based on the Abbott sponsored post-

market, prospective, multi-center, randomized, controlled clinical study with an optional crossover component that provides evidence for the subpopulation with BurstDR capable SCS devices.

A. Study Design

The safety and effectiveness of the Abbott implantable neurostimulation system to treat NSBP is based on the Abbott sponsored prospective, multicenter, randomized, controlled, clinical study (herein referred to as the DISTINCT study) with an optional crossover component. It was designed to evaluate the effectiveness of SCS that can be programmed with BurstDR™ therapy, in the treatment of chronic back pain, compared to conventional medical management (CMM). This clinical study (NCT04479787) enrolled subjects as patients with chronic back pain without an underlying surgically treatable pathology that have not had prior lumbar spine surgery. The study design outlined two phases of enrollment. Phase I included the first 200 randomized subjects and supported the primary endpoint analysis. This was predefined and outlined in the adaptive design plan. Phase II was the continued access phase and included up to 70 randomized subjects to add provide further high-quality evidence supporting SCS treatment in this population.

Only patients who met the inclusion/exclusion criteria were enrolled in the study. Any subject that did not meet all inclusion criteria or met any of the exclusion criteria was considered a screening failure. An independent board-certified spine surgeon acted as a medical monitor and evaluated each enrolled subject for suitability. After enrollment, subjects were randomized between two treatment arms:

- **Conventional medical management (CMM)**

  During the follow-up period, subjects in the CMM arm received supervised medical care, including medication optimization, and supervised non-interventional therapy. Medication optimizations include use of non-steroidal anti-inflammatories, muscle relaxants, anti-neuropathic agents, opioids, and other analgesics as appropriate. Supervised non-interventional therapy may include, but is not limited to, physical therapy, chiropractic care, cognitive behavioral therapy, and acupuncture. Interventional therapies such as injections and radiofrequency ablation were included.

- **Spinal cord stimulation (SCS)**

  Subjects randomized to receive spinal cord stimulation first undergo a trial of the therapy. A successful trial, defined as 50% decrease in pain recorded on the Numerical Rating Scale (NRS) for low back pain, is required for a subject to receive a permanent implant.

Subjects are followed in-clinic at 1, 3, 6, 9, 12, 18, and 24 months and via phone call or optional clinic visit at 15 and 21 months. The primary endpoint was assessed at the 6-month follow-up visit. Upon completion of the 6-month follow-up visit, subjects who are dissatisfied with therapy and receiving inadequate improvement with their treatment

assignment could cross over to the other treatment arm, if desired. Below is a summary of the endpoints and analysis population from the study.

1. Primary Effectiveness Endpoint

   The primary effectiveness endpoint is the difference in responders between groups at 6 months. A subject is considered a responder for the primary endpoint if an improvement in back pain was reported, defined as a ≥ 50% decrease on NRS.

2. Secondary Effectiveness Endpoints

   Secondary endpoints are compared between the two treatment groups. Seven endpoints were pre-defined in the statistical analysis plan and are listed below:

   - Composite responder on NRS or Oswestry Disability Index (ODI, %)
     - 50% reduction on NRS 13-point reduction on ODI or score < 20
   - Relative NRS change (%)
   - ODI score change
   - Pain Catastrophizing Scale (PCS) responder (%)
     - No longer clinically catastrophizing or 40% reduction
   - Patient Global Impression of Change (PGIC) responder (%)
     - Better or Great deal better
   - Relative Pain Interference change (%)
   - Relative Physical Function change (%)

3. Descriptive Endpoints or Additional Data

   Descriptive endpoints include:

   - Proportion of patients who elect to cross-over after the primary endpoint
   - Change from baseline at each time point on the following:
     - ODI
     - PROMIS-29 questionnaire
     - PCS
     - Pain-condition related medication usage
     - Exercise frequency
     - Healthcare resource utilization
     - Patient satisfaction with therapy
     - PGIC
     - Serious device-related adverse events

- Device programming and usage
- Serious device-related adverse events

4. Responder Analysis
   - Proportion of subjects with ≥ 30% decrease on NRS
   - Proportion of subjects with ≥ 13% improvement, at least one category improvement or score ≤ 20% on ODI
   - Proportion of subjects within 1 Standard Deviation (SD) of population norm or reach MCID on PROMIS-29 domains
   - Proportion of subjects that are either clinically catastrophizing on PCS at baseline (PCS score ≥ 30) and report a score of < 30 at follow up or report a 40% decrease in score at follow-up compared to baseline.

5. Analysis Populations
   - Intention-to-Treat (ITT) Population: included all randomized subjects. Subjects were analyzed according to the treatment group they are randomized to. The ITT population was used as the primary analysis population for the primary endpoint.
   - Modified Intention-to-Treat (mITT) Population: included all randomized subjects except for those who are randomized to the SCS group who fail the trial period and did not receive a permanent system implant. Subjects were analyzed according to the treatment group they are randomized to.
   - Per-Treatment Evaluable (PTE) Population: included all subjects in the mITT population who either received permanent implant or received CMM. Subjects were analyzed according to the actual treatment received. The PTE population was used as the primary analysis population for the study except the primary endpoint analysis.

The following figure shows the flow of study design for the disposition of subjects followed to different time points.

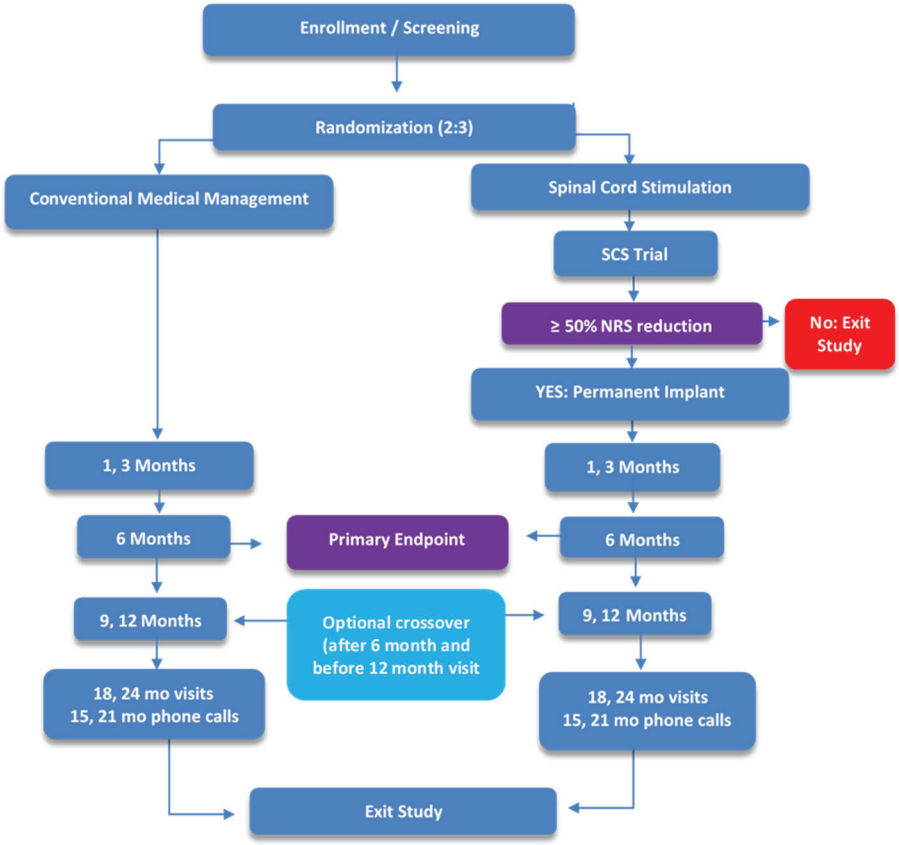

Figure 3 Disposition of 200 subjects at different follow-up time point

B. Safety and Effectiveness Results

1. Safety Results

The safety objective is to characterize the safety profile of SCS to treat NSBP.

The safety profile of Abbott implantable SCS systems to treat NSBP was characterized through the DISTINCT study. The safety profile for NSBP population using Abbott implantable SCS systems was deemed the same as the currently approved indications. The following were the observations from the study:

Three deaths, unrelated to treatment, were reported during the study. No stimulation-related SAEs or any events categorized as unanticipated adverse device effects (UADEs) were reported during the study. A total of 14 adverse events were reported in 14 subjects of the 200-subject cohort through the 6-month follow-up timepoint. Of these, 3 were device- or procedure-related SAEs while 8 were device- or procedure-related adverse events in the SCS treatment arm; these rates of observations were within expectations and considered acceptable.

Table 3. Summary of Safety Results for 200-subject cohort through 6-month follow-up timepoint

Event Description	Related to	Subjects with Events n/N (%)	Number of Events
Infection	Permanent Implant Procedure (1)	1/126 (0.8%)	1
Numbness below the level of implant	Trial implant Procedure (1)	1/126 (0.8%)	1
Post-Surgical Pain	Permanent Implant Procedure (1),	1/126 (0.8%)	1

A total of 14 adverse events were reported in the first 6 months up to the primary endpoint timepoint during the study. There were:

- Three (3) serious device-related adverse effects (SADEs), and
- Three (3) non-device-related serious adverse events (SAEs), and
- Eight (8) adverse device effects (ADEs).

The following tables summarizes adverse events. The AEs reported in this study were anticipated for the study population since the patient population evaluated in DISTINCT, NSBP, is a subpopulation of the currently indicated SCS patient population. The AEs are considered acceptable based on a risk assessment performed which concluded that all applicable patient hazards (risk) associated with the Adverse Events listed in the DISTINCT study are covered under the existing identified risks for the Abbott SCS systems. Device Related and Procedure related AE rates were also compared to SCS literature and determine to be within range of currently marketed SCS systems (Tables 4 and 5 below).

Table 4: Device related AEs for the DISTINCT Study

Adverse Events from DISTINCT Study	Count	Rate (Based on total Study population with SCS of N= 175)*	Range from Literature Reference Rates**[4,5,6,7,8,9]
ADE			
Changes In Stimulation Or Reduced Pain Relief Due To Lead Migration	**3**	**3/175 (1.7%)**	**1.4% - 13.6%**
Implant Migration	**1**	**1/175 (0.57%)**	**6.5%**
Movement Or Vibration Of The IPG Or Leads	**1**	**1/175 (0.57%)**	**6.5%**
Damage To The IPG Or Leads Causing The System To Fail Deliver Stimulation Or Causing The System To Deliver Overstimulation	**1**	**1/175 (0.57%)**	**1.7% - 9.1%**
Loss Of Analgesia	**1**	**1/175 (0.57%)**	**1.7% - 9.1%**

* The population is defined as those randomized to SCS and CMM subjects deciding to cross over to the SCS arm after 6-months.
** References (Not all events were reported in all Studies)

Procedure related risks are those related to the implantation procedure itself. These risks can include infection, healing pain, incision issues, and wound dehiscence.

Many of the clinical studies for SCS for this indication describe low incidences of procedure related events, primarily because of the longevity and familiarity that SCS has been used and on the market. There were 3 SADEs and 6 instances of ADEs. This AE analysis for procedure related AEs includes events for SCS randomized patients collected up to April 29, 2022, accounting for the Phase I 200-subject cohort at 6 months and any subjects from the CMM arm that had elected to cross over to the SCS arm after 6-months. Events observed to date show that procedure associated rates are below or within the expected ranges when compared to on market SCS devices as

[4] Deer 2014 [Deer TR, Krames E, Mekhail N, et al. The appropriate use of neurostimulation: new and evolving neurostimulation therapies and applicable treatment for chronic pain and selected disease states. Neuromodulation Appropriateness Consensus Committee. Neuromodulation : journal of the International Neuromodulation Society. 2014;17(6):599-615; discussion 615]
[5] Deer 2017 [Deer TR, Lamer TJ, Pope JE, et al. The Neurostimulation Appropriateness Consensus Committee (NACC) Safety Guidelines for the Reduction of Severe Neurological Injury. Neuromodulation : journal of the International Neuromodulation Society. 2017;20(1):15-30]
[6] Schulz 2016 [Schultz DM, Calodney AK, Mogilner AY, et al. Spinal Cord Stimulation (SCS)-The Implantable Systems Performance Registry (ISPR). Neuromodulation : journal of the International Neuromodulation Society. 2016;19(8):857-863
[7] Brinzeu 2019 [Brinzeu A, Cuny E, Fontaine D, et al. Spinal cord stimulation for chronic refractory pain: Long-term effectiveness and safety data from a multicentre registry. European journal of pain (London, England). 2019;23(5):1031-1044]
[8] Oakley 2007 [Oakley JC, Krames ES, Prager JP, et al. A new spinal cord stimulation system effectively relieves chronic, intractable pain: a multicenter prospective clinical study. Neuromodulation : journal of the International Neuromodulation Society. 2007;10(3):262-278]
[9] Kapural 2016 [Kapural L, Yu C, Doust MW, et al. Comparison of 10-kHz High-Frequency and Traditional Low-Frequency Spinal Cord Stimulation for the Treatment of Chronic Back and Leg Pain: 24-Month Results From a Multicenter, Randomized, Controlled Pivotal Trial. Neurosurgery. 2016;79(5):667-677]

reported by the literature. There were no unexpected AEs recorded in the DISTINCT study.

In general, the risk of a procedure related risk is minimal. While there is a risk of a procedure related event for any surgical procedure, the risk of an event for the implantation of SCS is minimal given the longevity and comfort of physicians implanting SCS over the last two decades. A summary of the procedure related risks described above is shown below.

Table 5: Procedure related AEs for the DISTINCT Study

Adverse Events from DISTINCT Study	Count	Rate (Based on total Study population with SCS of N = 175)*	Range from Literature Reference Rates**[6,7,8,9,10,11]
SADEs			
Infection	1	1/175 (0.57%)	2-4%
Numbness Below The Level Of Implant	1	1/175 (0.57%)	0-1%
Post Surgical Pain	1	1/175 (0.57%)	1-3%
ADEs			
Dermatitis And Desquamation	1	1/175 (0.57%)	< 1 %
Infection	1	1/175 (0.57%)	3.0% - 10.0%
Persistent Pain At The IPG Site	2	2/175 (1.1%)	0.9% - 13.4%
Skin Reaction	1	1/175 (0.57%)	< 1 %
Seroma At The Lead Incision Site	1	1/175 (0.57%)	0.87% - 2.5%

* The population is defined as those randomized to SCS and CMM subjects deciding to cross over to the SCS arm after 6-months.
** References (Not all events were reported in all Studies)

2. Effectiveness Results

The effectiveness objective is to characterize the clinical benefits related to pain relief for SCS used to treat NSBP when compared to the standard-of-care.

The effectiveness of Abbott implantable SCS systems to treat NSBP was demonstrated through analysis of DISTINCT clinical study results. Effectiveness was demonstrated by the probability of treatment success. The probability of treatment success (i.e., Responder Rate or proportion of successfully treated subjects) was defined by a specified percent reduction in pain rating or Patient Global Impression of Change (PGIC) rating and the magnitude of pain relief as measured through reduction in pain scores from a Numeric Rating Scale (NRS) were considered in determining effectiveness.

The primary endpoint successfully demonstrated greater effectiveness in those treated with SCS compared to CMM; 72.6% of SCS subjects reported 50% pain relief or greater compared to 7.1% in the CMM arm in an ITT analysis population. The Per

[10] Rigoard 2019 [Rigoard P, Basu S, Desai M, et al. Multicolumn spinal cord stimulation for predominant back pain in failed back surgery syndrome patients: a multicenter randomized controlled trial. Pain. 2019;160(6):1410-1420]

Treatment Analysis (PTE) reported 85.2% responders in the SCS arm. Hierarchical testing of the 7 secondary endpoints was initiated and was completed for all 7 as each reported statistically significant greater effectiveness in the SCS group. These endpoints support greater improvements in back pain (NRS), back pain-related disability (ODI), pain-related emotional suffering (PCS), patient satisfaction (PGIC), pain interference on day-to-day living, and physical function (PROMIS-29).

The primary endpoint of the study was designed to show a superior responder rate in the SCS group compared to CMM. The endpoint was met, and analysis results are shown in the following table.

Table 6: Primary Efficacy Endpoint and Sensitivity analysis - Difference in Response Rates at 6 Months

	SCS (N= 126)	**CMM (N= 74)**	**Difference [95% CI][3]**	**P-Value[4]**	**Conclusion[5]**
Primary Endpoint Response Rate, Complete Case + Trial Failure [95% Confidence Interval][1]	72.6% (69/95)[2] [62.5%, 81.3%]	7.1% (4/56) [2.0%, 17.3%]	65.5% [54.3%, 76.7%]	<0.0001	Endpoint met
Sensitivity Analyses					
ITT Analysis Population, Multiple imputation [95% Confidence Interval][3]	82.6% [74.5%, 90.8%]	6.7% [0.2%, 13.2%]	75.9% [65.7%, 86.1%]	<0.0001	Endpoint met
mITT Analysis Population, Complete Case [95% Confidence Interval][1]	85.2% (69/81) [75.6%, 92.1%]	7.1% (4/56) [2.0%, 17.3%]	78.0% [67.8%, 88.3%]	<0.0001	Endpoint met
PTE Analysis Population, Complete Case [95% Confidence Interval][1]	85.2% (69/81) [75.6%, 92.1%]	7.1% (4/56) [2.0%, 17.3%]	78.0% [67.8%, 88.3%]	<0.0001	Endpoint met

[1] Exact Clopper-Pearson.
[2] Trial failures are imputed as non-responders.
[3] By normal approximation.
[4] Two-sided Z-Test with unpooled variance.
[5] P-value < 0.05 indicates endpoint is met.

Seven statistically powered and pre-defined secondary endpoints were tested on the per- treatment evaluable (PTE) population. The PTE analysis is the same as the modified intent to treat analysis as all subjects received the treatment assigned at randomization. Statistical testing was executed in a pre-defined order and only carried

out if the previous endpoint reached significance. All secondary endpoints were successfully met for the SCS arm with a statistically significant difference compared to the CMM arm, as shown in the following table. Together, this supports superior improvements in pain (NRS), back pain-related function (ODI), emotional suffering (PCS), patient satisfaction (PGIC), pain interference and physical function (PROMIS-29 domains), achieved by SCS when compared with CMM.

Table 7: Summary of Secondary Endpoints at 6 months

Secondary Endpoints	SCS (N= 91)	CMM (N= 74)	Difference [95% CI][2]	P-Value	Conclusion[5]
#1. Composite Responder Rate [95% Confidence Interval][1]	91.4% (74/81) [83.0%, 96.5%]	19.6% (11/56) [10.2%, 32.4%]	71.7% [59.6%, 83.8%]	< 0.0001[3]	Endpoint met
#2. NRS Relative change from Baseline to 6 Months Mean ± SD (n) Median (Q1, Q3) Range (Min, Max) [95% Confidence Interval][2]	69.7 ± 25.0 (81) 75.0 (57.1, 87.5) (0.0, 100.0) [64.2, 75.2]	3.6 ± 22.7 (56) 0.0 (-11.1, 12.5) (-42.9, 77.8) [-2.5, 9.7]	66.1 [57.9, 74.2]	<0.0001[4]	Endpoint met
#3. ODI Change from Baseline to 6 Months Mean ± SD (n) Median (Q1, Q3) Range (Min, Max) [95% Confidence Interval][2]	30.6 ± 19.8 (78) 28.2 (17.8, 42.0) (-8.0, 79.6) [26.2, 35.1]	0.7 ± 14.4 (56) 0.0 (-8.0, 9.2) (-46.0, 34.0) [-3.1, 4.6]	29.9 [24.1, 35.8]	<0.0001[4]	Endpoint met
#4. PCS Responder Rate [95% Confidence Interval][1]	86.4% (70/81) [77.0%, 93.0%]	21.4% (12/56) [11.6%, 34.4%]	65.0% [51.9%, 78.1%]	< 0.0001[3]	Endpoint met
#5. PGIC Responder Rate [95% Confidence Interval][1]	77.8% (63/81) [67.2%, 86.3%]	3.6% (2/56) [0.4%, 12.3%]	74.2% [63.9%, 84.5%]	< 0.0001[3]	Endpoint met

Secondary Endpoints	SCS (N= 91)	CMM (N= 74)	Difference [95% CI][2]	P-Value	Conclusion[5]
#6. PROMISE-29 Pain Interference Relative change from Baseline to 6 Months Mean ± SD (n) Median (Q1, Q3) Range (Min, Max) [95% Confidence Interval][2]	18.1 ± 11.4 (81) 17.3 (9.2, 25.5) (-2.1, 45.0) [15.6, 20.6]	1.1 ± 10.6 (56) 0.0 (-4.5, 6.2) (-32.4, 45.0) [-1.8, 3.9]	17.0 [13.3, 20.8]	<0.0001[4]	Endpoint met
#7. PROMISE-29 Physical function Relative change from Baseline to 6 Months Mean ± SD (n) Median (Q1, Q3) Range (Min, Max) [95% Confidence Interval][2]	28.0 ± 25.1 (81) 26.2 (8.9, 40.7) (-3.7, 153.3) [22.5, 33.6]	1.3 ± 13.1 (56) 0.0 (-6.4, 5.5) (-26.2, 42.6) [-2.2, 4.8]	26.7 [20.2, 33.2]	<0.0001[4]	Endpoint met

[1] Exact Clopper-Pearson.
[2] By normal approximation.
[3] Two-sided Z-Test with unpooled variance.
[4] Two-sample t-test.
[5] P-value < 0.05 indicates endpoint is met.

The average age of subjects was 59 years. Fifty eight percent (58%) of the subjects were female. Most subjects were Caucasian (83.5%). Fifty percent (50%) reported chronic pain for over 10 years (average of 13.03 ± 12.21 years).

3. Subgroup Analysis

No analyses were performed for sex-, gender-, age-, race-, ethnicity-, or any other relevant characteristic- specific subgroups.

4. Pediatric Extrapolation

We believe that existing clinical data can be leveraged to support a reasonable assurance of safety and effectiveness of the subject device in a pediatric sub-population of adolescents aged 18-21.

In accordance with section 515A of the Federal Food, Drug, and Cosmetic Act (the FD&C Act), an analysis was conducted on the available information about pediatric subpopulations who suffer from chronic, intractable pain of the trunk and/or limbs. The pediatric population is defined as patients 21 years of age or younger. While FDA considers patients aged 18-21 to still be pediatric in nature, this is a population that requires no special considerations and is treated the same as an adult population 22 and older ("Transitional adolescent B"). The discussion below follows the decision tree in the FDA Guidance Document "Leveraging existing clinical data for extrapolation to pediatric uses of medical devices", issued June 21, 2016.

To the best of our knowledge, there is no requirement that the prevalence meet or exceed a certain percentage in order to qualify for extrapolation.

The Abbott SCS system is implanted and there are no differences between the adult and pediatric populations in the location or duration of implantation that could affect safety or effectiveness in a clinically meaningful way.

The Abbott SCS system is a permanent implant, as noted previously. The positioning of the device is the same for adults 22 and older as would be for patients aged 18-21. There is no need for specific instructions related to the implantation of the device for the 18-21 age range relative to the older than 22 population. Therefore, there are no differences in these attributes that could affect the safety or effectiveness of the device in a clinically meaningful way.

Additionally, there are no differences in device characteristics between pediatric and adult use that could affect safety or effectiveness in a clinically meaningful way. The Abbott SCS system needs no modifications to be used for a patient aged 18-21 compared to those patients 22 and older. Both adults aged 22 and older and patients aged 18-21 will use the same hardware, with the specific hardware selections being individualized according to the particular needs of the patient, as it is done currently. Similarly, the stimulation is set on an individual basis, and is not calibrated any differently for the 18-21 subpopulation. Therefore, there are no differences in device characteristics that could affect the safety or effectiveness of the device in a clinically meaningful way.

There are no unique characteristics of the device that could affect safety or effectiveness in a clinically meaningful way when used in the pediatric population. As mentioned above, the type of population to which we seek to extrapolate data includes transitional adolescents who are treated like adults. In that regard, there is no evidence to suggest that there are substantial differences between patients who are 18-21 with NSBP and those who are 22 and older. Skeletal maturity is achieved by age 18, for example, and relative to a patient who is 22 any group differences are negligible. Therefore, there are no characteristics that are unique to the intended pediatric subpopulation that could affect the safety or effectiveness of the device in a clinically meaningful way.

XI. 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 104 investigators of which 76 participated in a procedure or study visit. None of the investigators were full-time or part-time employees of the Sponsor; of the 76 participating, 5 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: Five
- Proprietary interest in the product tested held by the investigator: None
- Significant equity interest held by investigator in sponsor of covered study: None

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.

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 Neurology Review 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

All primary and secondary endpoints were met in the DISTINCT study. The powered endpoints demonstrate that Abbott BurstDR enabled SCS systems compared to CMM in NSBP patient population provide:

- superior pain relief
- superior pain relief or functional improvement
- a superior reduction in pain-related emotional distress
- superior improvements in quality of life

The DISTINCT study incorporated specific outcome measures and associated clinically meaningful improvements based on the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) guidelines. Similar to other SCS studies[11] [12], core outcomes that assess multiple components of chronic pain, particularly pain intensity, emotional suffering, and physical function[13] were evaluated and shown to have clinically meaningful outcomes with improvements above MCID values.

B. Safety Conclusions

Three deaths, unrelated to treatment, were reported during the study. No stimulation-related SAEs or any events categorized as unanticipated adverse device effects (UADEs) were reported during the study. A total of 14 adverse events were reported in 14 subjects of the 200 subject cohort through the 6 month follow-up time point. Of these, 3 were device- or procedure-related SAEs while 8 were device- or procedure-related AEs in the SCS treatment arm; these rates of observations were below or within expected ranges based on historical literature of SCS therapy and considered to be acceptable.

C. Benefit-Risk Determination

Per FDA guidance, there are many factors to consider when assessing the benefits and risks of a medical device compared to the current standard. The presence and extent of the benefits of the device compared to both pre-implantation and standard of care need to be considered. For the risks associated with the device, the severity and types of harmful events, severity of adverse events, as well as the probability of a harmful event and duration of harmful events need to be compared between the treatment and the control. Having evaluated the extent of the probable benefits to health, the probable risks to health, and the uncertainty associated with both the benefits and the risks, the conclusion is that the benefits outweigh the risks. This assessment is similar to the risk vs benefit of the overall SCS patient population.

D. Overall Conclusions

Spinal cord stimulation (SCS) has been used to treat chronic pain for more than 50 years. The current SCS labeling includes patients with intractable pain of the trunk and/or limbs. Throughout this PMA Supplement, Abbott has presented clinical data from the DISTINCT

[11] Deer, T., et al., Success Using Neuromodulation With BURST (SUNBURST) Study: Results From a Prospective, Randomized Controlled Trial Using a Novel Burst Waveform. Neuromodulation, 2018. 21(1): p. 56-66.
[12] Falowski, S.M., et al., Improved Psychosocial and Functional Outcomes and Reduced Opioid Usage Following Burst Spinal Cord Stimulation. Neuromodulation, 2020
[13] Dworkin RH, Turk DC, Wyrwich KW, Beaton D, Cleeland CS, Farrar JT, et al. Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. J Pain. 2008;9(2):105-21.

study that demonstrates a reasonable assurance of safety and effectiveness in subjects with NSBP.

The benefits include everything from pain reduction to quality-of-life improvement. The level of benefit experienced by the SCS group exceeded the control group in all aspects, and with a reasonable degree of certainty. The risks include device and procedure related risks such as lead migration or breakage, device malfunction, or infection. The risk profile for NSBP was evaluated and is considered to be similar to the overall SCS patient population. SCS has been used for chronic pain for over 50 years and has been approved for over 30 years. Many of these commercially available SCS systems have subsequently undergone extensive post-market clinical evaluation and have long-term safety and effectiveness data reported in a large body of published clinical studies. associated with the therapy.

XIV. CDRH DECISION

CDRH issued an approval order on May 10, 2023.

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

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

1. Fritzell, P., et al., 2001 Volvo Award Winner in Clinical Studies: Lumbar fusion versus nonsurgical treatment for chronic low back pain: a multicenter randomized controlled trial from the Swedish Lumbar Spine Study Group. Spine (Phila Pa 1976), 2001. 26(23): p. 2521-32; discussion 2532-4.

2. Phillips, F.M., et al., Lumbar spine fusion for chronic low back pain due to degenerative disc disease: a systematic review. Spine (Phila Pa 1976), 2013. 38(7): p. E409-22

3. Manchikanti, L. and J.A. Hirsch, An update on the management of chronic lumbar discogenic pain. Pain Manag, 2015. 5(5): p. 373-86

4. Deer 2014 [Deer TR, Krames E, Mekhail N, et al. The appropriate use of neurostimulation: new and evolving neurostimulation therapies and applicable treatment

for chronic pain and selected disease states. Neuromodulation Appropriateness Consensus Committee. Neuromodulation : journal of the International Neuromodulation Society. 2014;17(6):599-615; discussion 615]

5. Deer 2017 [Deer TR, Lamer TJ, Pope JE, et al. The Neurostimulation Appropriateness Consensus Committee (NACC) Safety Guidelines for the Reduction of Severe Neurological Injury. Neuromodulation : journal of the International Neuromodulation Society. 2017;20(1):15-30]

6. Schulz 2016 [Schultz DM, Calodney AK, Mogilner AY, et al. Spinal Cord Stimulation (SCS)-The Implantable Systems Performance Registry (ISPR). Neuromodulation : journal of the International Neuromodulation Society. 2016;19(8):857-863

7. Brinzeu 2019 [Brinzeu A, Cuny E, Fontaine D, et al. Spinal cord stimulation for chronic refractory pain: Long-term effectiveness and safety data from a multicentre registry. European journal of pain (London, England). 2019;23(5):1031-1044]

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

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

10. Rigoard 2019 [Rigoard P, Basu S, Desai M, et al. Multicolumn spinal cord stimulation for predominant back pain in failed back surgery syndrome patients: a multicenter randomized controlled trial. Pain. 2019;160(6):1410-1420]

11. Deer, T., et al., Success Using Neuromodulation With BURST (SUNBURST) Study: Results From a Prospective, Randomized Controlled Trial Using a Novel Burst Waveform. Neuromodulation, 2018. 21(1): p. 56-66.

12. Falowski, S.M., et al., Improved Psychosocial and Functional Outcomes and Reduced Opioid Usage Following Burst Spinal Cord Stimulation. Neuromodulation, 2020

13. Dworkin RH, Turk DC, Wyrwich KW, Beaton D, Cleeland CS, Farrar JT, et al. Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. J Pain. 2008;9(2):105-21.