A Randomized Controlled Study to Evaluate the Safety and Effectiveness of Boston Scientific Spinal Cord Stimulation (SCS) Systems in the Treatment of Chronic Low Back and/or Leg Pain with No Prior Surgeries

WaveWriter-SOLIS Study

SCS as an **O**ption for chronic **L**ow back and/or leg pain **I**nstead of **S**urgery

A4077

CLINICAL INVESTIGATION PLAN

Sponsored By

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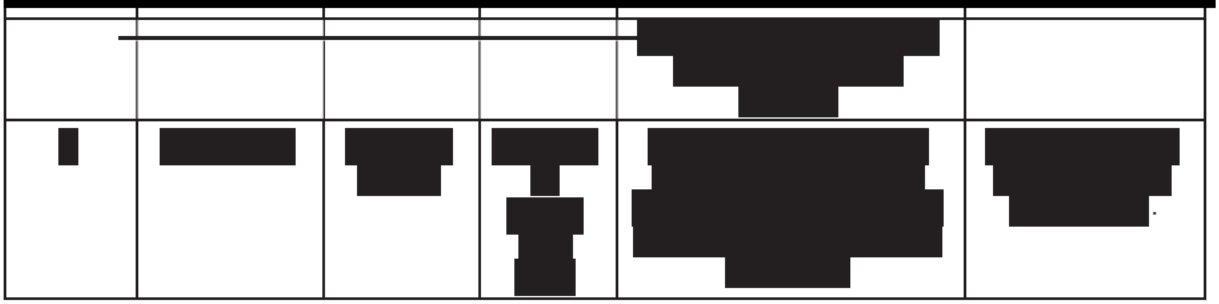

2. Protocol Synopsis

A Randomized Controlled Study to Evaluate the Safety and Effectiveness of Boston Scientific Spinal Cord Stimulation (SCS) Systems in the Treatment of Chronic Low Back and/or Leg Pain with No Prior Surgeries WaveWriter-SOLIS Study	
Study Objective(s)	To evaluate the safety and effectiveness of Spinal Cord Stimulation (SCS) with multiple modalities compared to Conventional Medical Management (CMM) in patients with chronic low back and/or leg pain who have not undergone spinal surgery when using the Boston Scientific WaveWriter SCS Systems.
Planned Indication(s) for Use	Boston Scientific Spinal Cord Stimulator Systems are indicated as an aid in the management of chronic intractable pain of the trunk and/or limbs including unilateral or bilateral pain associated with the following: failed back surgery syndrome, Complex Regional Pain Syndrome (CRPS) Types I and II, intractable low back pain and/or leg pain with or without prior surgery.
Test	Boston Scientific WaveWriter™ SCS Systems
Control	Conventional medical management (CMM)
Study Design	Prospective, multi-center, parallel-group randomized, controlled trial with an adaptive design
[redacted]	[redacted]
Safety Parameters	Rates of occurrence of: • Non-related, non-serious adverse events from the time of consent up to 3 months post-activation • All device hardware, device stimulation and/or procedure related non-serious adverse events, all serious adverse events, and unanticipated adverse events through the end of the study
Primary Effectiveness Endpoint	Proportion of subjects with 50% or greater reduction from Baseline in average overall (low back and/or leg) pain intensity at 3 months post-activation with no increase in baseline average daily opioid medications used to treat pain, compared between SCS and CMM.

A Randomized Controlled Study to Evaluate the Safety and Effectiveness of Boston Scientific Spinal Cord Stimulation (SCS) Systems in the Treatment of Chronic Low Back and/or Leg Pain with No Prior Surgeries WaveWriter-SOLIS Study	
Secondary Effectiveness Endpoints	All secondary endpoints will be analyzed as a comparison between SCS and CMM. Assessments required for deriving each endpoint are denoted in parentheses. [redacted] • Change in disability from Baseline Visit to 3 months post-Activation Visit (*ODIv2.1a*) • [redacted]
[redacted]	[redacted]

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	• [redacted]
[redacted]	[redacted]
[redacted]	[redacted]
Follow-up Schedule	Study events occur at the following time points: • Screening Period • Opioid Medication Lock Visit (Up to 35 days post Informed Consent) • Baseline/Randomization Visit (14 + 3 days post Opioid Medication Lock Visit) • Implant Procedures/CMM Optimization (up to 60 days post Randomization Visit) • Treatment Activation Visit (Day 0) • 1-Month Visit (30 ± 7 days) • 2-Month Visit (60 ± 7 days) • Treatment Lock Visit (70 -75 days post-Activation Visit) • 3-Month Visit (90 ± 7 days post-Activation Visit) • 6-Month Visit (180 ± 30 days post-Activation Visit) • 9-Month Visit (270 ± 30 days post-Activation Visit) • 12-Month Visit (365 ± 30 days post-Activation Visit) • 24-Month Visit (730 ± 30 days post-activation Visit)

A Randomized Controlled Study to Evaluate the Safety and Effectiveness of Boston Scientific Spinal Cord Stimulation (SCS) Systems in the Treatment of Chronic Low Back and/or Leg Pain with No Prior Surgeries

WaveWriter-SOLIS Study

[redacted]	[redacted]
[redacted]	[redacted]
Inclusion Criteria	IC1. Chronic low back pain, with or without leg pain, for at least 6 months with low back pain greater or equal to leg pain IC2. Received at least 90 days of documented pain management care to address the primary pain complaint, prior to Screening (e.g. medication, physical therapy) [redacted] IC12. If female of childbearing potential: not pregnant, as evidenced by a negative pregnancy test at Screening

A Randomized Controlled Study to Evaluate the Safety and Effectiveness of Boston Scientific Spinal Cord Stimulation (SCS) Systems in the Treatment of Chronic Low Back and/or Leg Pain with No Prior Surgeries WaveWriter-SOLIS Study	
	IC13. Subject signed a valid, IRB-approved informed consent form (ICF) provided in English
Exclusion Criteria	[redacted] EC5. Primary pain complaint of vascular origin (e.g. peripheral vascular disease) [redacted] EC11. Require implantation of lead(s) in the cervical epidural space [redacted]

A Randomized Controlled Study to Evaluate the Safety and Effectiveness of Boston Scientific Spinal Cord Stimulation (SCS) Systems in the Treatment of Chronic Low Back and/or Leg Pain with No Prior Surgeries WaveWriter-SOLIS Study	
	[redacted] EC18. Significant cognitive impairment at Screening that, in the opinion of the Investigator, would reasonably be expected to impair the study candidate's ability to assess pain intensity [redacted] EC20. Previous failed spinal cord stimulation trial or is already implanted with an active implantable device(s) (e.g. pacemaker, drug pump, implantable pulse generator) [redacted]
Statistical Methods	
Primary Statistical Hypothesis	The primary statistical null hypothesis is that the proportion of subjects with 50% or greater reduction from Baseline in average overall (low back and/or leg) pain intensity at 3-month visit with no increase in baseline average daily

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	opioid medications used to treat pain is equal between the Treatment (SCS) group and the Control (CMM) group: $H_0: \pi_t - \pi_c = 0$ $H_1: \pi_t - \pi_c \neq 0$ where π_t and π_c are the proportion of subjects with 50% or greater reduction from Baseline in average overall (low back and/or leg) pain intensity at 3-month visit with no increase in baseline average daily opioid medications in the Treatment and Control group, respectively.
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

A Randomized Controlled Study to Evaluate the Safety and Effectiveness of Boston Scientific Spinal Cord Stimulation (SCS) Systems in the Treatment of Chronic Low Back and/or Leg Pain with No Prior Surgeries WaveWriter-SOLIS Study	
	[redacted]

[redacted]

3. Table of Contents

[redacted]

[redacted]

[redacted]

4. Introduction

4.1. *Background / Report of Prior Investigations*

Chronic intractable pain is often defined as pain persisting for at least 6 months which has not responded to conservative treatment(s). The pain may be due to current or past nerve injury and causes significant disability, reduced work productivity, reduced quality of life, and significant cost burden.

The complexity of chronic pain and the diverse population it affects have resulted in varying results between the various treatment approaches including medications, physical therapy, stimulation etc. Early treatments for chronic pain typically include over the counter and prescription medications. Later treatments like physical therapy and interventional pain procedures (e.g. intraspinal injections, vertebroplasty, pulsed RF) are attempted, sometimes followed by chronic high dose opioids and back surgery, if indicated. If back surgery is unsuccessful in relieving the chronic pain, the patient can be labeled as having failed back surgery syndrome (FBSS). Spinal cord stimulation (SCS) is an option in well-selected patients with chronic low back and/or leg pain.

With SCS, an implanted pulse generator (IPG) delivers electrical current to electrode(s) implanted in the epidural space. This current stimulates nerves and can be programmed to direct stimulation to the nerves innervating the painful location, resulting in a reduction of the intensity of that pain (Kumar et al., 2006). Before an SCS system is implanted, a patient often undergoes a screening trial with an electrode that is connected to an external stimulator that the patient wears outside of the body. The results of the screening trial can predict the patient's outcome with an implanted system (Kumar et al., 2006).

SCS is effective for chronic intractable pain associated with a variety of conditions, including, but not limited to, FBSS ((Carter et al., 2004, Taylor et al., 2004), complex regional pain syndrome (Sears et al., 2011), and low back pain and leg pain (Cameron et al., 2004). Spinal cord stimulation (SCS) is a less invasive treatment option for FBSS but has generally been reserved for patients who have failed multiple, and indeed all possible, repeat operations. However, earlier neuromodulation intervention (a reversible treatment option) prior to spinal surgery may result in acceptable patient outcomes. Over the past decade, there have been studies that have documented success of neuromodulation in this patient population (Ahmadi, Vesper, Schu, & Slotty, 2017), (Deckers, et al., 2018).

A single center study where 20 patients with no history of back surgery reported a 73% reduction in pain scores and 48% improvement in disability at 12 months with SCS. A similar trend was observed up to 3 years. Additionally, patients reported a reduction in the use of their opioid medications as well (Al-Kaisy 2018). Similar results were noted in a separate case-series (n = 8) evaluation (Ahmadi 2017). Pooled analysis (post-hoc) of 2 separate cohorts of patients with chronic non-surgical, refractory pain from two independently-conducted clinical studies (Kapural 2015, Kapural 2016) was recently reported (Al-Kaisy 2020). In a cohort of 26 patients, average back pain decreased by 70% at 3 months and overall responder rate of 73% was noted at 12 months. Improved functional

outcomes (improvement in disability as measured by ODI scores) and reduced opioid use was also reported.

Evidence related to real-world use of SCS in treatment of chronic pain in patients with no prior back surgery was recently reported (n = 186), as part of two ongoing real-world studies. Seventy-eight patients (as part of a multi-center retrospective chart review) were identified who reported a pre-trial pain score of 7.3. At last follow up (mean = 282 days), 40% (31 of 78) of subjects reported a pain score of 2 or lower. One hundred and eight subjects with no prior surgery, as part of on an ongoing, prospective, multi-center registry, were identified. Seventy-one percent (65 of 91) of participants reported being "much" or "very much improved" with SCS at 12 months and this was supported by improved functional outcomes (12.7 pt. improvement in ODI) (Rauck et al., 2020).

For Report of Prior Investigations, copies of the publications are not provided to sites and/or IRB unless requested. Instead publications are cited in the bibliography. Clinical Studies conducted in the United States and reference in this section were conducted in compliance with the relevant part of Good Clinical Practice (GCP) regulations, 21 CFR Part 50, 21 CFR Part 56 and 21 CFR Part 812. Clinical Studies conducted outside the United States and reference in this section were conducted in compliance with the relevant part of Good Clinical Practice (GCP) regulations, ISO 14155: Clinical Investigation of Medical Devices for the Human Subjects – Good Clinical Practice.

4.2. *Study Rationale*

Traditionally, SCS treatment has been reserved for patients who have undergone at least one prior spinal surgery. Using neurostimulation, a less invasive and reversible treatment, earlier in the treatment continuum before patients have undergone spinal surgery may result in acceptable outcomes, as demonstrated in previous small-scale studies.

This study will evaluate the safety and effectiveness of Spinal Cord Stimulation (SCS) with multiple modalities compared to Conventional Medical Management (CMM) in patients with chronic low back and/or leg pain who have not undergone spinal surgery when using the Boston Scientific WaveWriter SCS Systems.

5. Device Description

The WaveWriter™ Spinal Cord Stimulator (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, Complex Regional Pain Syndrome (CRPS) Types I and II, intractable low back pain and leg pain.

The System includes an Implantable Pulse Generator (IPG), External Trial Stimulator (ETS), Remote Control (RC), External Charger, and Clinician's Programmer (CP) and a portfolio of lead options. The IPG is rechargeable and is recharged transcutaneously by a charging unit. The System is capable of providing multiple waveforms.

The WaveWriter SCS Systems are approved by the Food and Drug Administration (FDA) and will be used per approved Directions for Use (DFU) and this study protocol.

6. Study Objectives and Endpoint

6.1. *Primary/Secondary Objective*

The primary objective of this study is to evaluate the safety and effectiveness of Spinal Cord Stimulation (SCS) with multiple modalities compared to Conventional Medical Management (CMM) in patients with chronic low back and/or leg pain who have not undergone spinal surgery when using the Boston Scientific WaveWriter SCS Systems.

The secondary objective of this study is to determine the impact of WaveWriter SCS Systems on global patient outcomes including quality of life, patient preference, etc.

6.2. *Primary Endpoint*

Proportion of subjects with 50% or greater reduction from Baseline in average overall (low back and/or leg pain) intensity at 3 months post-activation with no increase in baseline average daily opioid medications used to treat pain, compared between SCS and CMM.

6.3. *Secondary Endpoints*

[redacted]

- Change in disability from Baseline Visit to 3 months post-Activation Visit (*ODIv2.1a*)

[redacted]

6.5. *Primary Safety Parameters*

Rates of occurrence of:

- Non-related, non-serious adverse events from the time of consent up to 3 months post-activation
- All device hardware, device stimulation and/or procedure related non-serious adverse events, all serious adverse events, and unanticipated adverse events through the end of the study

[redacted]

7. Study Design

The study is a prospective, multi-center, randomized controlled trial with a parallel group design as shown in study schematic Figure 7.1-1.

[redacted]

[redacted]

[redacted]

[redacted]

- [redacted]
- [redacted]

[redacted]

7.2.1. Treatment and Control

Eligible subjects randomized to the Spinal Cord Simulation (SCS) group, will receive a WaveWriter Spinal Cord Stimulation System. Subjects with a positive trial will proceed to receive permanent implant, following by device activation to provide SCS therapy.

Subjects randomized to the Conventional medical management (CMM) group will continue with non-surgical, non-invasive treatment (e.g., medication management and interventional pain procedures) for the treatment of their pain.

[redacted]

8. Subject Selection

8.1. *Study Population and Eligibility*

Study candidates will be drawn from the population of patients, resident in pain management or surgical medical practices. The study eligibility criteria are listed below.

8.2. *Inclusion Criteria*

Subjects who meet all of the following criteria (see Table 8.2-1 Inclusion Criteria) may be given consideration for inclusion in this clinical investigation, provided no exclusion criterion (see Section 8.3) is met.

Table 8.2-1: Inclusion Criteria

Inclusion Criteria	IC1.	Chronic low back pain, with or without leg pain, for at least 6 months with low back pain greater or equal to leg pain
	IC2.	Received at least 90 days of documented pain management care to address the primary pain complaint, prior to Screening (e.g. medication, physical therapy)
	[redacted]	[redacted]

Table 8.2-1: Inclusion Criteria

	[redacted] all questionnaires and assessments provided in English IC12. If female of childbearing potential: not pregnant, as evidenced by a negative pregnancy test at Screening IC13. Subject signed a valid, IRB-approved informed consent form (ICF) provided in English

8.3. *Exclusion Criteria*

Subjects who meet any one of the following criteria (see Table 8.3-1 Exclusion Criteria) cannot be included in this study or will be excluded from this clinical study.

Table 8.3-1: Exclusion Criteria

Exclusion Criteria	[redacted]

Table 8.3-1: Exclusion Criteria

	EC5. Primary pain complaint of vascular origin (e.g. peripheral vascular disease) [redacted] EC11. Require implantation of lead(s) in the cervical epidural space [redacted] EC18. Significant cognitive impairment at Screening that, in the opinion of the Investigator, would reasonably be expected to impair the study candidate's ability to assess pain intensity [redacted] may influence the data that will be collected for this study EC20. Previous failed spinal cord stimulation trial or is already implanted with an active implantable device(s) (e.g. pacemaker, drug pump, implantable pulse generator) [redacted]

Table 8.3-1: Exclusion Criteria

	[redacted] litigation and/or an injury claim or workers compensation claim

9. Subject Accountability

9.1. *Point of Enrollment*

A subject will be considered enrolled in the study when the Informed Consent Form (ICF) is signed. If device implantation is unsuccessful, the subject will be followed for 2 weeks post implantation attempt to assess for procedure related adverse events.

9.2. *Withdrawal and Lost to Follow-up*

All subjects enrolled in the clinical study (including those withdrawn from the clinical study) shall be accounted for and documented. If a subject withdraws from the clinical investigation, the reason(s) shall be reported. If such withdrawal is due to problems related to investigational device safety or performance, the investigator shall ask for the subject's permission to follow his/her status/condition outside of the clinical study.

While study withdrawal is discouraged, subjects may withdraw from the study at any time, with or without reason and without prejudice to further treatment. In all cases of withdrawal or discontinuation, the Investigator will make all reasonable efforts to determine the reason for the subject's withdrawal. Subjects may be discontinued from the study for the various reasons, such as:

- Withdrawal of consent
- A safety concern defined by the Principal Investigator and/or Boston Scientific Neuromodulation (e.g., adverse event)
- Study non-compliance

- Subject did not meet inclusion criteria or met an exclusion criterion after signing informed consent
- Surgical intervention that affects the Implantable Pulse Generator (IPG) and/or leads
- Lost to follow-up
- Death of the subject

Before a subject is deemed lost to follow-up, the investigator or designee will make every effort to regain contact with the participant. Should the subject continue to be unreachable, he or she may be considered to be lost to follow-up. A subject is considered lost-to-follow-up after 3 unsuccessful contact attempts have been made to reach the subject (including those who relocate but cannot be transferred to another participating site). Staff at the participating site should make a good faith effort to contact the subject with three documented communication attempts, at least one of which must be in writing, sent via a traceable method to inform the subject of the end of study actions.

Data collected up to the point of subject withdrawal or lost to follow-up may be used for study analysis in accordance with applicable regulations.

Withdrawn subjects will be followed per the End of Study Action Plan as described below.

9.3. *Subject Status and Classification*

Subjects are considered enrolled in the study at the time written informed consent is provided. Subjects who sign the informed consent form but do not meet all study eligibility criteria (i.e., screen failure), or withdraw prior to completion of the Baseline Visit, will not be randomized. Subjects that are enrolled but not randomized will be deemed as "consented" and their reason for ineligibility will be documented.

Subjects who meet all study eligibility criteria will be "randomized" to receive either SCS or CMM. Subjects with a failed SCS trial will be withdrawn from the study.

"Activated" subjects are those subjects who complete implant procedures (SCS) or treatment optimization (CMM) based on treatment assignment. All subjects who sign consent, meet all eligibility criteria, are randomized, and are activated will count towards the enrollment cap and cannot be replaced. Only activated subjects will be included for the analysis.

[redacted]

9.4. *End-of-Study Definition*

The study is considered complete when the last subject's last study visit has occurred.

9.5. *End of Study Action Plan*

The following End of Study Action plan will be implemented when the subject completes their study participation (i.e. 24-Month Visit or withdrawn). Boston Scientific Corporation will not pay for visits, devices and/or procedures that occur after a subject completes the 24-Month Visit, withdraws, or is determined to be lost to follow-up, except for the explant procedure. Reimbursement for the explant procedure will be covered by Boston Scientific if performed within 2 months from the end of study date.

If device implantation is unsuccessful, the subject will be followed for 2 weeks post implantation attempt to assess for procedure related adverse events. If the device is explanted prior to study completion, the subject will be followed for 30 days post explant to assess for related adverse events.

For those subjects whose device is explanted post-study completion, they will be followed per their physician's standard-of-care. If the subject is explanted, they (or their insurance) will be responsible for the cost of the explantation procedure. Boston Scientific will not pay for any visits that occur after the device has been deactivated/explanted.

Device related adverse events and/or deficiencies occurring after study participation, should be reported to BSN Patient Care at: 866-360-4747.

Subjects who received CMM will be followed per standard of care. Subjects who received SCS will be followed as described below.

[redacted]

[redacted]

10. Study Methods

10.1. *Data Collection*

The data collection schedule is shown in Table 10.1-1 Data Collection Schedule.

[redacted]

10.2. *Study Candidate Screening*

Subjects' eligibility for the study will be assessed based on study Inclusion and Exclusion criteria listed in Section 8.2 and 8.3, respectively. Subjects who have provided informed consent and who have been determined to not meet all eligibility requirements will be withdrawn.

10.3. *Informed Consent*

Written Informed Consent must be obtained for all patients who are potential study candidates. Study candidates will be asked to sign the Informed Consent form before any study-specific tests or procedures are performed.

- The context of the study must be fully explained to the patient and patients must be given an opportunity to ask questions and have those questions answered to their satisfaction.
- Study personnel should explain to each potential participant that even if he or she agrees to participate in the study and signs an informed consent form, further testing might demonstrate that he or she is not eligible for the study.
- Written informed consent must be recorded appropriately by means of the subject's dated signature.
- The consent process must be documented in the subject's medical chart.

Research study candidates in the State of California will also be provided with the California Experimental Patient's Bill of Rights

10.4. *Screening Period*

Subjects undergo screening related procedures to determine eligibility for the study. It will take up to the Baseline/Randomization Visit to complete all eligibility requirements.

[redacted]

[redacted]

10.5. *Opioid Medication Lock Visit (Up to 35 days post Screening Period)*

The Opioid Medication Lock Visit may occur the same day as informed consent and during the screening period, after informed consent is completed, or at a visit within 35 days following informed consent.

At this visit (or during the screening period), the investigator will convert the subject's opioid medication prescriptions from PRN to a fixed dose, as needed for the study. The subject's opioid pain medications will be locked, with no increase in type/dose/route/frequency, until the completion of Baseline/Randomization Visit.

Subjects will be reminded to use their mobile app., as applicable.

10.6. *Baseline/Randomization Visit (14 + 3 days post Opioid Medication Lock)*

At the Baseline/Randomization Visit, subjects will return to the clinic to complete all screening requirements. Any adverse event since the last study visit will be collected.

[redacted]

Subjects that meet all study criteria will be randomized in a 1:1 ratio to either:

- Spinal Cord Stimulation (SCS) with the WaveWriter SCS Systems
- Conventional Medical Management (CMM)

If a subject fails to meet all the eligibility criteria, they will be withdrawn from the study.

Subjects randomized to the SCS arm will proceed to receive the SCS implant (trial and permanent implant procedures.

Subjects randomized to CMM arm will continue to have their medical management regimen optimized.

Subjects will be reminded to use their mobile app., as applicable.

10.7. *Implant Procedures/CMM Optimization (Up to 60 days post Baseline/Randomization)*

Subjects will receive treatment based on assignment as shown below:

- SCS Arm: SCS Implant (Trial/Permanent Implant)
- CMM Arm: Optimization of conventional medical management

Subjects will remain in their treatment arm through completion of the 3-Month Visit.

10.8. *Implant Procedures (SCS Arm only)*

Subjects randomized to SCS will have up to 60 days following the Baseline/Randomization Visit to receive their WaveWriter SCS System.

[redacted]

Subjects will proceed to the Treatment Activation Visit upon completion of all implant procedures and healing as described above.

Subjects will be reminded to use their mobile app., as applicable.

10.9. *CMM Optimization (CMM Arm only)*

Subjects randomized to CMM arm will have their medical management regimen optimized for up to 60 days. Subjects will have as many office and/or phone visits as needed (unscheduled optimization visits) for optimization of therapy.

[redacted]

- Noninvasive interventional procedures (e.g., spinal injections/nerve blocks, [redacted]

[redacted]

Once the investigator deems that the subjects' medical management is fully optimized, their treatment plan will be finalized and documented accordingly. No increase in medical management treatments will be allowed once the subject's treatment plan is final until the subject completes the 3-Month post-activation visit.

Subjects will proceed to their Treatment Activation Visit to begin management under their final treatment plan.

Subjects will be reminded to use their mobile app., as applicable.

10.10. *Treatment Activation Visit (Day 0)*

At the Treatment Activation Visit, subjects' will have their treatment activated.

- [redacted]

Subjects are to contact the site in the event that any additional intervention is warranted, to report a complaint and/or a suspected adverse event, etc.

Subjects will be reminded to use their mobile app., as applicable.

10.11. *1-Month and 2-Month Post-Activation Visits (30 or 60 ± 7 days)*

Subjects will return to the office as described below. Any adverse events since their last study visit will be collected.

- [redacted]

10.12. *Treatment Lock Visit (70 – 75 days following Treatment Activation)*

At the Treatment Lock Visit, subjects will have their treatment locked until completion of the 3-Month Post-Activation Visit. Any adverse events since the last study visit will be collected.

- [redacted]

[redacted]

10.13. *3-Month Post-Activation Visit (90 ± 7 days)*

During the 3-Month Visit, subjects will return to the clinic for study evaluations. All study assessments must be completed prior to any programming/adjustment of treatments.

Any adverse events since their last study visit will be collected.

[redacted]

Following completion of assessments, subjects in the SCS arm will continue to use their SCS therapy as needed. CMM arm subjects may choose to crossover to receive SCS.

SCS subjects' device may be programmed as needed and programming information may be collected. In the event of suspected lead migration or to aid programming the subject's device, imaging may be performed to document lead position. Any additional instructions related to charging of the device and/or use of Remote Control may be provided.

Subjects' medications may be adjusted as needed upon completion of this visit.

Subjects will be reminded to use their mobile app., as applicable.

10.14. *6-Month Post-Activation Visit (180 ± 30 days)*

During the 6-Month Visit, subjects will return to the clinic for study evaluations. All study assessments must be completed prior to any programming/adjustment of treatments.

Any adverse events since their last study visit will be collected.

[redacted]

[redacted]

10.15. *9-Month Post-Activation Visit (270 ± 30 days)*

During the 9-Month Visit, subjects will return to the clinic for study evaluations. All study assessments must be completed prior to any programming/adjustment of treatments.

Any adverse events since their last study visit will be collected.

[redacted]

- [redacted]

[redacted]

10.16. ***12 and 24 Month Post-Activation Visits (365 ± 30 days and 730 ± 30 days post-activation Visit)***

During these visits, subjects will return to the clinic for study evaluations. All study assessments must be completed prior to any programming/adjustment of treatments.

[redacted]

6.

10.17. ***Unscheduled Visits***

Subjects may have as many unscheduled visits as required for device-related, treatment-related in-office or procedure visits (e.g., optimization of programming or conventional medical management during the programming period) or for evaluation of possible adverse events and if applicable, re-positioning, replacement or explant of a device component. Unscheduled visit information will be captured, as applicable.

10.18. *Revision or Replacement of Leads, Extensions and/or IPGs*

During the study, it is possible that leads may be placed incorrectly, migrate, or malfunction and require repositioning or replacement. It is also possible that the extensions or splitters or IPG may be uncomfortable or malfunction and may require repositioning or replacement. The decision to reposition or replace any device component will be made by the investigator and only if the subject agrees. Subjects not agreeing to a recommended lead revision will be withdrawn from the study but will be included in the intent-to-treat and safety analyses. Subjects agreeing to revision will continue in the study and will be followed according to the original study schedule. Effectiveness data from these subjects will be included in the intent to treat analysis. Lead revisions/replacements for the purpose of correcting for migration and/or malfunction must be performed as soon as is reasonably possible following determination of the need for revision/replacement.

The investigator should notify Boston Scientific prior to any study procedures. Any replacements or revisions performed during the course of the study should be recorded in the EDC system, including information about the procedure, device, and/or adverse event if applicable.

Information on assessing revisions or replacements of leads, extensions or IPGs as adverse events is described in Section 18.

10.19. *CMM to SCS Crossover post 3-Month Post-Activation Visit*

After completion of the 3-Month Visit, subjects in the Conventional Medical Management (CMM) group may choose to crossover. These subjects must have received their SCS implant by the 9-Month Post-Activation Visit.

CMM subjects who choose to crossover to SCS will be evaluated and per investigator discretion receive trial/permanent implant per standard of care.

[redacted]

10.21. *Study Completion*

All activated subjects will be followed through completion of the 24-Month Visit or study withdrawal. The End of Study Action Plan (see Section 9.5) defines the actions to be taken when the subject reaches the end of their study participation.

10.22. *Source Documents*

Table 10.22-1 summarizes source data requirements for this study. Any information first captured on an electronic data collection platform or within the EDC system on eCRF evaluations, assessments or questionnaires, not initially documented in another record, is considered the source documentation.

It is preferable that original source documents are maintained, when available. In lieu of original source documents, certified copies are required to be maintained. A certified copy is a copy (irrespective of the type of media used) of the original record that has been verified (i.e., by a dated signature or by generation through a validated process) to have the same information, including data that describe the context, content, and structure, as the original.

Source documentation includes but is not limited to those items noted in Table 10.22-1.

Table 10.22-1: Source Documentation Requirements

Requirement	Disposition
Hospital records and/or clinical and office charts including the evidence of but not limited to inclusion/exclusion criteria, informed consent, procedures, exams, SCS System procedure(s) and devices used, evaluations, health economic assessments, laboratory results, medications, assessment of adverse events.	Retained at investigational site
Assessments and questionnaires	Retained at investigational site and/or electronic data collection platform/EDC
Programming information	Retained at investigational site and/or electronic data collection platform/EDC
Imaging films/prints documenting lead(s) location	Retained at investigational site

11. Statistical Considerations

11.1. *Endpoints*

11.1.1. Primary Effectiveness Endpoint

The primary effectiveness endpoint is the proportion of subjects with 50% or greater reduction from Baseline in average overall (low back and/or leg) pain intensity at 3 months

post-activation with no increase in baseline average daily opioid medications used to treat pain, compared between SCS and CMM.

[redacted]

A responder is defined as a subject who achieves 50% or greater reduction from Baseline in average daily overall (low back and/or leg) pain intensity at 3 months post-activation with no increase in baseline opioid medications used to treat pain. Specifically, a responder is defined as any subject meeting both following criteria:

- 50% or greater reduction
- No Increase in opioid pain medications

11.1.1.1. Hypotheses

The primary statistical null hypothesis is that the proportion of subjects with 50% or greater reduction from Baseline in average daily overall (low back and/or leg) pain intensity at the 3-month visit with no increase in baseline average daily opioid medications used to treat pain is equal between SCS and CMM:

$$H_0: \pi_t - \pi_c = 0$$

$$H_1: \pi_t - \pi_c \neq 0$$

where π_t and π_c are the proportion of subjects with 50% or greater reduction from Baseline in average daily overall (low back and/or leg) pain intensity at 3-month visit with no increase in baseline average daily opioid medications in the SCS and CMM groups, respectively.

[redacted]

Given the above assumptions, 66 subjects in each treatment group will be required. In order to account for 5% expected rate of attrition, 140 subjects need to be activated, 70 in each treatment group.

11.1.1.3. Statistical Methods

The 95% confidence interval of $\pi_t - \pi_c$ will be computed. The study will be considered a success if, using the Intent-To-Treat (ITT) analysis, the lower bound of the two-sided 95% confidence interval for the difference is great than 0.

[redacted]

11.2. *General Statistical Methods*

11.2.1. Analysis Sets

11.2.1.1. Intent-to-Treat (ITT)

In the intent-to-treat analysis, all subjects who are randomized and receive the treatment (activation in SCS group or medication in CMM group) will be included in the analysis. Subjects will be analyzed according to their randomization group, regardless of the treatment they receive.

11.2.1.2. Per-Protocol

In the per-protocol analysis, only subjects are randomized and receive the treatment with no major protocol deviations will be included in the analysis. [redacted]

11.2.1.3. Safety Analysis Set

In the safety analysis, all subjects who sign the IRB-approved written Informed Consent form will be included.

11.2.2. Control of Systematic Error/Bias

Selection of subjects will be made from the Investigator's usual patient load. All subjects meeting the inclusion/exclusion criteria and having signed the Informed Consent Form will be eligible for participation in the study. The reasons for exclusion, for subjects who sign an informed consent form but are not randomized, will be indicated in the screening log. Consequently, consecutively eligible subjects will be randomly allocated into the study, minimizing selection bias. Boston Scientific will report to the FDA any evidence of fraud, including deliberate tampering with the selection of subjects.

[redacted]

11.3. *Data Analyses*

All statistical analyses will be done using the SAS System software, version 8.2 or later (Copyright © 2000 SAS Institute Inc., SAS Campus Drive, Cary, North Carolina 27513, USA. All rights reserved). [redacted]

[redacted]

11.3.3. Justification of Pooling

Analyses will be performed using data pooled across various sites/institutions. Multivariate analysis techniques, including contingency tables and logistic regression for binary outcomes and analysis of variance for continuous measures, will be used to assess differences among study sites to justify pooling data across sites.

11.3.4. Multivariable Analyses

Multivariate analyses will be performed to assess the effect of possible covariates on the primary endpoint. [redacted]

[redacted]

[redacted]

12. Data Management

12.1. *Data Collection, Processing, and Review*

Subject data will be recorded in a limited access secure electronic data capture (EDC) system.

The clinical database will reside on a production server hosted by Medidata EDC System. All changes made to the clinical data will be captured in an electronic audit trail and available for review by the sponsor or its representative. The associated Rave software and database have been designed to meet regulatory compliance for deployment as part of a validated system compliant with laws and regulations applicable to the conduct of clinical studies pertaining to the use of electronic records and signatures. Database backups are performed regularly.

The Investigator provides his/her electronic signature on the appropriate electronic case report forms (eCRFs) in compliance with local regulations. A written signature on printouts of the eCRFs must also be provided if required by local regulation. Changes to data previously submitted to the sponsor require a new electronic signature by the Investigator acknowledging and approving the changes.

Visual and/or electronic data review will be performed to identify possible data discrepancies. Manual and/or automatic queries will be created in the Medidata EDC system and will be issued to the site for appropriate response. Site staff will be responsible for resolving all queries in the database.

[redacted]

[redacted]

12.1.1. Electronic Questionnaires

Questionnaires in electronic form may be collected directly using an electronic data collection platform at the clinical site (e.g. iPad). After completion by the subject or a clinician, data from the electronic questionnaires are transmitted directly into the EDC system.

12.1.2. Direct Data Uploads

For quality assurance purposes and validation, technical data on the SCS device will be collected using direct data upload to a secure BSC server. BSC Field personnel, who assist in programming the device settings per routine care, will upload the device files to a secure server stored in a restricted location at BSC.

Device files will also be uploaded into the EDC system.

[redacted]

[redacted]

[redacted]

[redacted]

12.2. *Data Retention*

The Principal Investigator or his/her designee or Investigational site will maintain all essential study documents and source documentation that support the data collected on the study subjects in compliance with applicable regulatory requirements.

The Principal Investigator or his/her designee will take measures to prevent accidental or premature destruction of these documents. If for any reason the Principal Investigator or his/her designee withdraws responsibility for maintaining these essential documents, custody must be transferred to an individual who will assume responsibility and BSC must receive written notification of this custodial change. Sites are required to inform Boston Scientific in writing where paper or electronic files are maintained in case files are stored off site and are not readily available.

[redacted]

13. Deviations

An Investigator must not make any changes or deviate from this protocol, except to protect the life and physical well-being of a subject in an emergency. An investigator shall notify the sponsor and the reviewing IRB, and the regulatory authority if applicable, of any deviation from the investigational plan to protect the life or physical well-being of a subject in an emergency, and those deviations which affect the scientific integrity of the clinical investigation. Such notice shall be given as soon as possible, but no later than 5 working days after the emergency occurred, or per prevailing local requirements, if sooner than 5 working days.

All deviations from the investigational plan, with the reason for the deviation and the date of occurrence, must be documented and reported to the sponsor using the EDC system. Sites

may also be required to report deviations to the IRB, and/or the regulatory authority, per local guidelines and/or national/government regulations.

Deviations will be reviewed and evaluated on an ongoing basis and, as necessary, appropriate corrective and preventive actions, site re-training, or site discontinuation/termination) will be put into place by the sponsor.

The sponsor will not approve protocol waivers.

Adherence to medication lock requirements will be assessed from the Medication Lock Visit through the 3-Month Visit. If a change to a medication(s) occurs, or subjects do not take medications as specified at the Medication Lock Visit, a protocol deviation will be issued.

Adherence to device programming lock requirements will be confirmed at all study follow-up visits, from the Treatment Lock Visit through the 3-Month Visit. A protocol deviation will be issued if device programming changes are made at any time other than required for replacement or revision procedures or to resolve a device and/or stimulation-related adverse event.

Adherence to conventional medical management treatment lock requirements will be confirmed at all study follow-up visits, from the Treatment Lock Visit through the 3-Month Visit. A protocol deviation will be issued if conventional interventions are increased at any time other than required to resolve an adverse event.

If eligibility was not confirmed with imaging as required, a protocol deviation will be issued.

[redacted]

15. Compliance

15.1. *Statement of Compliance*

This clinical investigation is financed by the study sponsor. Before the investigational site can be "Authorized to Enroll," the investigational site must enter into a Clinical Study Agreement with the sponsor that details the financing of the study as well as the rights and obligations of the investigational site and the investigator.

This study will be conducted in accordance with 21 CFR parts 50, 56, 54 and 812, EN ISO 14155: Clinical Investigation of Medical Devices for Human Subjects – Good Clinical

Practice, the relevant parts of the ICH Guidelines for Good Clinical Practices, ethical principles that have their origins in the Declaration of Helsinki, and applicable individual country laws and regulations. The study shall not begin until the required approval/favorable opinion from the IRB and/or regulatory authority has been obtained, if appropriate. Also, the study shall not begin prior to issuance of the site Authorization to Enroll, as provided by the sponsor. Any additional requirements imposed by the IRB or regulatory authority shall be followed, if appropriate.

15.2. *Investigator Responsibilities*

The Principal Investigator of an investigational site is responsible for ensuring that the study is conducted in accordance with the Clinical Study Agreement, the clinical investigation plan, ISO 14155, ethical principles that have their origins in the Declaration of Helsinki, any conditions of approval imposed by the reviewing IRB, and prevailing local and/or country laws and/or regulations, whichever affords the greater protection to the subject.

The Principal Investigator's responsibilities include, but are not limited to, the following.

- Prior to beginning the study, sign the Clinical Study Agreement and comply with the Investigator responsibilities as described in such Agreement.
- Prior to beginning the study, sign the Protocol Signature page documenting his/her agreement to conduct the study in accordance with the protocol.
- Provide his/her qualifications and experience to assume responsibility for the proper conduct of the study and that of key members of the site team through up-to-date curriculum vitae or other relevant documentation and disclose potential conflicts of interest, including financial, that may interfere with the conduct of the clinical study or interpretation of results.
- Make no changes in or deviate from this protocol, except to protect the life and physical well-being of a subject in an emergency; document and explain any deviation from the approved protocol that occurred during the course of the clinical investigation.
- Create and maintain source documents throughout the clinical study and ensure their availability with direct access during monitoring visits or audits; ensure that all clinical-investigation-related records are retained per requirements.
- Ensure the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor in the CRFs and in all required reports.
- Record, report, and assess (seriousness and relationship to the device/procedure) every adverse event, as applicable per the protocol, and observed device deficiency.
- Report to sponsor, per the protocol requirements, all reportable events.
- Report to the IRB and regulatory authorities any SAEs and device deficiencies that could have led to a SADE and potential/USADE or UADE, if required by applicable laws or regulations or this protocol or by the IRB, and supply BSC

with any additional requested information related to the safety reporting of a particular event.

- Ensure that the investigationally-labeled device is used only by authorized/designated users and in accordance with this protocol and instructions for use.
- Allow the sponsor to perform monitoring and auditing activities and be accessible to the clinical research monitor or auditor and respond to questions during monitoring visits or audit(s).
- Allow and support regulatory authorities and the IRB when performing auditing activities.
- Ensure that informed consent is obtained in accordance with applicable laws, this protocol and local IRB requirements.
- Provide adequate medical care to a subject during and after a subject's participation in a clinical study in the case of adverse events, as described in the Informed Consent Form (ICF).
- Inform the subject of the nature and possible cause of any adverse events experienced.
- As applicable, provide the subject with necessary instructions on proper use, handling, storage, and return of the investigational device when it is used/operated by the subject.
- Inform the subject of any new significant findings occurring during the clinical investigation, including the need for additional medical care that may be required.
- Provide the subject with well-defined procedures for possible emergency situations related to the clinical study, and make the necessary arrangements for emergency treatment, including decoding procedures for blinded/masked clinical investigations, as needed.
- Ensure that clinical medical records are clearly marked to indicate that the subject is enrolled in this clinical study.
- Ensure that, if appropriate, subjects enrolled in the clinical investigation are provided with some means of showing their participation in the clinical investigation, together with identification and compliance information for concomitant treatment measures (contact address and telephone numbers shall be provided).
- Inform, with the subject's approval or when required by national regulations, the subject's personal physician about the subject's participation in the clinical investigation.
- Make all reasonable efforts to ascertain the reason(s) for a subject's premature withdrawal from clinical investigation while fully respecting the subject's rights.

- Ensure that an adequate investigation site team and facilities exist and are maintained and documented during the clinical investigation.

All investigators will provide their qualifications and experience to assume responsibility for their delegated tasks through up-to-date curriculum vitae or other relevant documentation and disclose potential conflicts of interest, including financial, that may interfere with the conduct of the clinical study or interpretation of results.

15.2.1. Delegation of Responsibility

When specific tasks are delegated by an investigator, including but not limited to conducting the informed consent process, the Principal Investigator is responsible for providing appropriate training, ensuring they are competent to perform the tasks they have been delegated and providing adequate supervision of those to whom tasks are delegated. Where there is a sub investigator at a site, the sub investigator should not be delegated the primary supervisory responsibility for the site. The investigator is accountable for regulatory violations resulting from failure to adequately supervise the conduct of the clinical study.

15.3. *Institutional Review Board*

The investigational site will obtain the written and dated approval/favorable opinion of the IRB for the clinical investigation before recruiting subjects and implementing all subsequent amendments, if required.

A copy of the written IRB and/or competent authority (CA) approval of the protocol (or permission to conduct the study) and ICF, must be received by the sponsor before recruitment of subjects into the study and shipment of investigational product/equipment. Prior approval must also be obtained for other materials related to subject recruitment or which will be provided to the subject.

Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. All changes to the ICF will be IRB approved; a determination will be made regarding whether a new ICF needs to be obtained from participants who provided consent, using a previously approved ICF. Annual IRB approval and renewals will be obtained throughout the duration of the study as required by applicable local/country laws or regulations or IRB requirements. Copies of the study reports and the IRB continuance of approval must be provided to the sponsor.

15.4. *Sponsor Responsibilities*

All information and data sent to BSC concerning subjects or their participation in this study will be considered confidential by BSC and will be kept confidential in accordance with all applicable laws and regulations. Only authorized BSC personnel and/or a BSC representative including, but not limited to Contract Research Organization (CRO), will have access to this information. Authorized regulatory personnel have the right to inspect and copy all records pertinent to this study. Study data collected during this study may be used by BSC for the purposes of this study, publication, and to support future research and/or other business purposes, such as overseeing and improving the performance of its device, new medical

research and proposals for developing new medical products and procedures. All data used in the analysis and reporting of this study or shared with a third-party researcher will be without identifiable reference to specific subjects.

Information received during the study will not be used to market to subjects; subject names will not be placed on any mailing lists or sold to anyone for marketing purposes.

[redacted]

[redacted]

16. Monitoring

Monitoring will be performed during the study to assess continued compliance with the protocol and applicable regulations. In addition, the clinical research monitor verifies that study records are adequately maintained, that data are reported in a satisfactory manner with respect to timeliness, adequacy, and accuracy, and that the Principal Investigator continues to have sufficient staff and facilities to conduct the study safely and effectively. The Principal Investigator/institution guarantees direct access to original source documents by BSC personnel, their designees, and appropriate regulatory authorities.

The sponsor will put a plan in place to document the specific monitoring requirements. The study may also be subject to a quality assurance audit by BSC or its designees, as well as inspection by appropriate regulatory authorities. It is important that the Principal Investigator and relevant study personnel are available during on-site monitoring visits or audits and that sufficient time is devoted to the process.

17. Potential Risks and Benefits

17.1. *Anticipated Adverse Events*

The following anticipated adverse events (AE) have been identified for this study:

Very Common:

- Minor bruising
- Post-operative pain and swelling

Common:

- Nausea associated with anesthesia

Less Common:

- Infection such as cellulitis or subcutaneous abscess
- Pain

Uncommon:

- Swelling
- Worsened back pain

Rare:

- Abnormal healing or failure to heal
- Allergic, immune, or inflammatory response or reaction to medication or surgical materials
- Death
- Deep vein thrombosis/thrombophlebitis
- Depression due to unmet expectations of treatment
- Dural tear with or without CSF leak
- Headache
- Hematoma of a serious type, e.g. an epidural hematoma resulting in paralysis
- Hemorrhage requiring transfusion
- Infection that is severe or life-threatening, such as epidural abscess, meningitis or sepsis
- Nerve injury, which can result in symptoms such as tingling, numbness, pain, loss of bladder or bowel control, weakness, or paralysis
- Pneumothorax, Pneumocephalus, or injury to other tissues during surgery
- Pulmonary embolism
- Radiation exposure (harm from this is rare)
- Respiratory arrest, e.g. apnea during surgical procedure
- Risks associated with anesthesia and any type of surgery, e.g. exposure to biohazardous materials

17.2. *Anticipated Adverse Device Effects*

From the Anticipated Adverse Events listed above, the following anticipated adverse device effects (ADE) have been identified for use of SCS as described in this protocol. The risks listed include those associated with the procedure to implant the SCS device system, the presence of the device (whether activated or not) within the body, and the use of SCS stimulation[1]. Potential risks not already identified may exist.

The following anticipated adverse device effects (ADE) have been identified for the SCS device.

[1] Note that some of these symptoms may be resolved or reduced by current steering, changing stimulation parameters, or by repositioning of the lead.

Very Common:

- Minor bruising

Common:

- Additional surgical procedure such as explant, revision, or reimplantation of the leads, extensions, or IPG, or revision of the IPG pocket
- Pain, including pain at IPG
- Stimulation in non-target areas, which can include undesired sensations of pain, pressure, or numbness
- Undesired sensations at stimulation target areas, which can include feelings of pain, pressure, numbness, or dislike of paresthesia
- Overstimulation of tissue, which can include feeling sensations such as jolts or shocks, and potential injuries arising from this causing distraction or loss of muscle control (e.g. fall)

Less Common:

- Infection, such as cellulitis or subcutaneous abscess

Uncommon:

- Discomfort, which can include minor tenderness, uncomfortable awareness of the device, or anxiety
- Skin erosion, including pressure sores, over the device
- Swelling, including seroma, at the IPG site or other locations
- Weight gain or loss

Rare:

- Abnormal healing or failure to heal
- Allergic, immune, or inflammatory response or reaction to the presence of the device or its materials
- Burns due to charger misuse
- Death
- Dural tear with or without Cerebrospinal Fluid (CSF) leak
- Error during implantation of device, e.g. faulty connection of extension to the IPG, which can lead to additional surgery
- Headache
- Hematoma of a serious type, e.g. an epidural hematoma resulting in paralysis

- Hemorrhage requiring transfusion
- Inability to change stimulation, e.g. the remote control stops working
- Infection that is severe or life-threatening, such as epidural abscess, meningitis or sepsis
- Muscle spasms
- Musculoskeletal stiffness
- Nausea
- Nerve injury arising from the electrodes, which can result in symptoms such as unintended tingling, numbness, pain, loss of bladder or bowel control, weakness, or paralysis
- Pneumothorax, pneumocephalus, or injury to other tissues during surgery
- Seizure
- Stimulation-related symptoms in other body systems, e.g. changes to urinary function, priapism
- Tissue damage at implant site from exposure to MRI

17.3. *Risks Associated with the Study Device(s)*

There are no known incremental risks associated with the study device above those of market-available products.

17.4. *Risks associated with Participation in the Clinical Study*

The subject might find it difficult, uncomfortable, or tiresome to complete study visits, evaluate the device, and/or questionnaires.

17.4.1. Magnetic Resonance Imaging (MRI) Risk

Subjects, especially those who are claustrophobic or anxious, may become uncomfortable with the enclosed space or knocking sounds made by the MRI.

Typically, MRI is contraindicated in subjects who have electrically, magnetically, or mechanically activated implants, or metal in or on their bodies. Subject should inform their physician of any implanted metal or electronic devices before an MRI is performed, as the interaction could cause serious injury.

Women should always inform their physician and MRI technologist if there is any possibility that they are pregnant. The effects of an MRI on a fetus are not well understood.

It is also possible imaging may show an unexpected abnormal finding. This information could cause subjects anxiety as well as suggest the need for additional tests and financial costs.

17.5. *Possible Interactions with Concomitant Medical Treatments*

No possible interactions have been identified for use of the SCS system concomitant with any specific medications. However, there may be some risk that is unknown.

The following medical treatments should not be used while the SCS System remains implanted.

Magnetic Resonance Imaging (MRI).

Refer to the MRI Guideline manuals for guidance before proceeding with any MRI to understand the possible interactions. MRI may be performed in subjects as applicable, if conditions set in those manuals are met accordingly.

- Potential Interactions with MRI Environment: During an MRI examination there are potential interactions with the system that may result in heating, magnetic field effects, induced stimulation, or damage to the device, requiring its replacement.
    - Heating – The MRI fields may interact with the Spinal Cord Stimulation System causing warming of the IPG and Leads. This may cause discomfort, pain, or burns.
    - Mechanical effects – The MRI magnetic field may exert force or torque on the Spinal Cord Stimulation System. Patients may feel a tugging or vibration sensation. Patients with recent implant incisions may feel surgical wound discomfort.
    - Induced stimulation – An MRI may induce energy onto the implanted Leads, potentially causing unintended or uncomfortable sensations (e.g., tingling, shocking, or jolting).

Following the safety conditions designated in the MRI Guidelines manual will minimize potential interactions described in this section.

If these interactions cause the patient discomfort, stop the MRI scan.

Full-Body MRI (Spectra WaveWriter System only): Study participants implanted with the Spectra WaveWriter SCS System should not have an MRI for any part of the body other than the head only under specific conditions. Exposure may result in movement of the stimulator or lead(s), heating of the stimulator, damage to the stimulator electronics and/or power going through the leads or stimulator which can cause an uncomfortable or "jolting" sensation.

Diathermy. SCS subjects should not have any form of diathermy either as treatment for a medical condition or as part of a surgical procedure. The high energy and heat generated by diathermy can be transferred through the stimulator system, causing tissue damage at the lead site and, possibly, severe injury or death. The Stimulator, whether it is turned on or off, may be damaged.

Implanted Stimulation Devices. Spinal cord stimulators may interfere with the operation of implanted sensing stimulators such as pacemakers or cardioverter defibrillators. The effects of implanted stimulation devices on neurostimulators are unknown.

Medical Devices/Therapies. The following medical therapies or procedures may turn stimulation off or may cause permanent damage to the Stimulator, particularly if used in close proximity to the device:

- Lithotripsy
- Electrocautery (See "Instructions for the Physician" in the Information for the Prescriber Manual)
- External defibrillation
- Radiation therapy
- Ultrasonic scanning
- High-output ultrasound

17.6. *Risk Minimization Actions*

Additional risks may exist. Risks can be minimized through compliance with this protocol, performing procedures in the appropriate hospital environment, adherence to subject selection criteria, close monitoring of the subject's physiologic status during research procedures and/or follow-ups and by promptly supplying BSC with all pertinent information required by this protocol.

17.7. *Anticipated Benefits*

The reported benefits of the WaveWriter SCS Systems may include:

- Reduction in the intensity of chronic low back pain
- Reduction in the intensity of chronic leg pain
- Reduction in overall chronic low back and/or leg pain
- Improvement in physical functioning (disability)
- Improvement in sleep
- Improvement in quality of life
- Improvement in depression
- Reduction in pain-related medication use
- Reduction in the occurrence of side-effects of pain-related medications accompanied by reduction in opioid use (e.g. sleep disturbances, constipation, reduction in mental acuity)

17.8. *Risk to Benefit Rationale*

The risk evaluation for the WaveWriter SCS Systems determined that all hazards attributed to the SCS Systems and overall remaining residual risks after implementations of the required mitigations have been evaluated. Based on the risk evaluation results, the benefit

provided by the WaveWriter SCS Systems to treat chronic intractable pain of the trunk and limbs outweighs the remaining residual risk. As the overall residual risk meets BSN's criteria, the WaveWriter SCS Systems are acceptable for use in a clinical setting.

18. Safety Reporting

18.1. *Reportable Events by investigational site to Boston Scientific*

It is the responsibility of the investigator to assess and report to BSC any event which occurs in any of following categories:

- All Serious Adverse Events, regardless of relationship
- All Device Deficiencies
- Unanticipated Adverse Device Effects
- All Device Related (Device hardware and/or stimulation) Non-Serious Adverse Events
- All Procedure Related Non -Serious Adverse Events
- Non-serious AEs which are neither device/procedure related from the time of informed consent through 3 months post activation.
- New findings/updates in relation to already reported events

When possible, the medical diagnosis should be reported as the Event Term instead of individual symptoms.

If it is unclear whether or not an event fits one of the above categories, or if the event cannot be isolated from the device or procedure, it should be submitted as an adverse event and/or device deficiency.

Any reportable event, experienced by the study subject after informed consent and once considered enrolled in the study (as defined in study subject classification section), whether prior to, during or subsequent to the study procedure, must be recorded in the eCRF.

Underlying diseases and chronic conditions are not reported as AEs unless there is an increase in severity or frequency during the course of the investigation. Death should not be recorded as an AE but should only be reflected as an outcome of one (1) specific SAE (see Table 18.2-1 for AE definitions).

Refer to Section 17 for the known risks associated with the study device(s).

18.2. *Definitions and Classification*

Adverse event definitions are provided in Table 18.2-1. Administrative edits were made on the safety definitions from applicable regulations and guidance including (but not limited to) 21 CFR Part 812, ISO 14155 and EU MDR 2017/745/MDCG 2020-10/1 Guidance on Safety Reporting in Clinical Investigations for clarification purposes.

Table 18.2-1: Safety Definitions

Term	Definition
Adverse Event (AE) *Ref: ISO 14155* *Ref: MDCG 2020-10/1*	Any untoward medical occurrence, unintended disease or injury, or any untoward clinical signs (including an abnormal laboratory finding) in subjects, users or other persons, in the context of a clinical investigation, whether or not related to the investigational medical device and whether anticipated or unanticipated. **NOTE 1**: This includes events related to the investigational medical device or comparator. **NOTE 2**: This definition includes events related to the procedures involved. **NOTE 3**: For users or other persons, this definition is restricted to events related to the investigational medical device.
Adverse Device Effect (ADE) *Ref: ISO 14155* *Ref: MDCG 2020-10/1*	Adverse event related to the use of an investigational medical device **NOTE 1**: This includes any adverse event resulting from insufficiencies or inadequacies in the instructions for use, the deployment, the implantation, the installation, the operation, or any malfunction of the investigational medical device. **NOTE 2**: This definition includes any event resulting from use error or from intentional misuse of the investigational medical device. **NOTE 3**: This includes 'comparator' if the comparator is a medical device.
Serious Adverse Event (SAE) *Ref: ISO 14155* *Ref: MDCG 2020-10/1*	Adverse event that led to any of the following: a) death, b) serious deterioration in the health of the subject, users or other persons as defined by either: 1) a life-threatening illness or injury, or 2) a permanent impairment of a body structure or a body function, including chronic diseases, or 3) in-patient hospitalization or prolongation of existing hospitalization, or 4) medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function c) foetal distress, foetal death, or a congenital abnormality or birth defect including physical or mental impairment. **NOTE 1:** Planned hospitalization for a pre-existing condition, or a procedure required by the clinical investigational plan, without a serious deterioration in health, is not considered a serious adverse event.
Serious Adverse Device Effect (SADE) *Ref: ISO 14155* *Ref: MDCG 2020-10/1*	Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.
Unanticipated Adverse Device Effect (UADE) *Ref: 21 CFR Part 812*	Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

Table 18.2-1: Safety Definitions

Term	Definition
Unanticipated Serious Adverse Device Effect (USADE) *Ref: ISO 14155* *Ref: MDCG 2020-10/1*	Serious adverse device effect which by its nature, incidence, severity, or outcome has not been identified in the current risk assessment. **NOTE 1**: Anticipated serious adverse device effect (ASADE) is an effect which by its nature, incidence, severity or outcome has been identified in the risk assessment.
Serious Health Threat *Ref: ISO 14155*	Signal from any adverse event or device deficiency that indicates an imminent risk of death or a serious deterioration in the health in subjects, users or other persons, and that requires prompt remedial action for other subjects, users or other persons. **NOTE 1**: This would include events that are of significant and unexpected nature such that they become alarming as a potential serious health hazard or possibility of multiple deaths occurring at short intervals.
Device Deficiency *Ref: ISO 14155* *Ref: MDCG 2020-10/1*	An inadequacy of a medical device related to its identity, quality, durability, reliability, usability, safety or performance. **NOTE 1**: Device deficiencies include malfunctions, use errors, and inadequacy in the information supplied by the manufacturer including labelling. **NOTE 2**: This definition includes device deficiencies related to the investigational medical device.
The following definitions will be used for defining hospitalization or prolongation of hospitalization for SAE classification purposes:	
Hospitalizations	Hospitalization does not include: • emergency room visit that does not result in in-patient admission Note: although an emergency room visit does not itself meet the definition for hospitalization, it may meet other serious criteria (e.g. medical or surgical intervention to prevent permanent impairment or damage) • elective and pre-planned treatment/surgery for a pre-existing condition that is documented in the subject's record at the time of consent/enrollment • admission for social reasons and/or respite care in the absence of any deterioration in the subject's general condition (e.g. subject is homeless, caregiver relief) • pre-planned, protocol-specified admission related to the clinical study (e.g. procedure required by protocol)
Prolongation of hospitalization	In-patient admission to the hospital that is prolonged beyond the expected standard duration for the condition under treatment. **Note:** new adverse events occurring during the hospitalization are evaluated to determine if they prolonged hospitalization or meet another SAE criteria.

NOTES:

1. For the purposes of this study, hospitalization is defined as any in-patient admission except as noted in Table 18.2-1.
2. Hospitalizations occurring for the purpose of performing a planned procedure as per routine care such as implant procedures, or follow-up visits, are not to be reported as a SAE. However, complications or adverse events that occur during the planned

procedure should be reported as (S)AEs if they meet the protocol specified definitions.

3. Elective/planned hospitalization(s) need not be reported as an SAE. However, complications or adverse events that occur during an elective/planned hospitalization, should be reported as (S)AEs if they meet the protocol specified definitions.
4. In the event of subject death during the conduct of the study, efforts should be made to perform an autopsy.
5. Sensations or side effects that occur during the programming session should not be reported as AEs. However, undesired sensations or side effects caused by the final programming parameters (including active contact, pulse width, frequency, and amplitude) that persist or occur after the completion of the programming should be reported as AEs.
6. Lack of efficacy/decreased therapeutic response should not be reported as AEs. Clinical sequelae, other than pain, that occur as a result of lack of efficacy/decreased therapeutic response should be reported as AEs
7. Clinically significant worsening of the pattern of intensity or distribution of Baseline pain symptoms should be reported as an AE.
8. Device deficiencies, including, but not limited to device/lead migrations, which are not associated with an adverse clinical outcome should only be reported as device deficiencies. However, if a device deficiency precipitates an AE, the AE should be reported in the *Adverse Event* eCRF and the device deficiency should be documented in the *Device Deficiency* eCRF.

18.3. *Relationship to Study Device(s) and/or Study Procedure*

The Investigator must assess the relationship of the reportable AE to the study device, (hardware and/or stimulation) and/or study procedure. See criteria in Table 18.3-1.

Table 18.3-1: Criteria for Assessing Relationship of Study Device or Procedure to Adverse Event

Classification	Description
Not Related *Ref: MDCG 2020-10/1*	Relationship to the device, comparator or procedures can be excluded when: - the event has no temporal relationship with the use of the investigational device or the procedures related to the use of the investigational device; - the serious event does not follow a known response pattern to the medical device (if the response pattern is previously known) and is biologically implausible; - the discontinuation of medical device application or the reduction of the level of activation/exposure - when clinically feasible – and reintroduction of its use (or increase of the level of activation/exposure), do not impact on the serious event; - the event involves a body-site or an organ that cannot be affected by the device or procedure; - the serious event can be attributed to another cause (e.g. an underlying or concurrent illness/ clinical condition, an effect of another device, drug, treatment or other risk factors);

Table 18.3-1: Criteria for Assessing Relationship of Study Device or Procedure to Adverse Event

	- the event does not depend on a false result given by the investigational device used for diagnosis, when applicable; - In order to establish the non-relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the serious event.
Possibly Related *Ref: MDCG 2020-10/1*	The relationship with the use of the investigational device or comparator, or the relationship with procedures is weak but cannot be ruled out completely. Alternative causes are also possible (e.g. an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment). Cases where relatedness cannot be assessed or no information has been obtained should also be classified as possible.
Probably Related *Ref: MDCG 2020-10/1*	The relationship with the use of the investigational device or comparator, or the relationship with procedures seems relevant and/or the event cannot be reasonably explained by another cause.
Causal Relationship *Ref: MDCG 2020-10/1*	The serious event is associated with the investigational device or comparator or with procedures beyond reasonable doubt when: - the event is a known side effect of the product category the device belongs to or of similar devices and procedures; - the event has a temporal relationship with investigational device use/application or procedures; - the event involves a body-site or organ that -the investigational device or procedures are applied to; -the investigational device or procedures have an effect on; - the serious event follows a known response pattern to the medical device (if the response pattern is previously known); - the discontinuation of medical device application (or reduction of the level of activation/exposure) and reintroduction of its use (or increase of the level of activation/exposure), impact on the serious event (when clinically feasible); - other possible causes (e.g. an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment) have been adequately ruled out; - harm to the subject is due to error in use; - the event depends on a false result given by the investigational device used for diagnosis, when applicable; - In order to establish the relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the serious adverse event.

The Investigator must assess the potential relationship of all adverse events to the **study device (hardware and stimulation) and study procedure.**

All **study device** related adverse events will be assessed according to their relationship to one of the following sub-categories:

- **Device Hardware-Related AEs:** AEs that can reasonably be attributed to the mere physical presence of the device or to deficiency of the device (i.e., an allergic response to device materials).

- **Stimulation-Related AEs:** AEs that can reasonably be attributed to the effects of stimulation. A relationship to stimulation may be determined by demonstrating a predictable response to the alternating between stimulation-on and stimulation-off settings. However, a relationship to stimulation may also be reported without demonstrating a predictable response to the alternating between the stimulation-on and stimulation-off settings if in the opinion of the Investigator the AE is potentially related to stimulation.

18.4. *Investigator Reporting Requirements*

The communication requirements for reporting to BSC are as shown in Table 18.4-1.

Table 18.4-1: Investigator Reporting Requirements

Event Classification	**Communication Method**	**Communication Timeline pre-market studies** (*21 CFR Part 812, MDCG 2020-10/1*)
Unanticipated Adverse Device Effect / Unanticipated Serious Adverse Device Effect	Complete AE eCRF page with all available new and updated information.	• Within 1 business day of first becoming aware of the event. • Terminating at the end of the study
	Provide all relevant source documentation (de-identified/ pseudonymized) for reported event.	• Upon request of sponsor.
Serious Adverse Event	Complete AE eCRF page with all available new and updated information.	• Immediately, but not later than 3 calendar days of first becoming aware of the event or as per local/regional regulations. • Reporting required through the end of the study
	Provide all relevant source documentation (de-identified/ pseudonymized) for reported event, as requested by sponsor.	• Upon request of sponsor
Serious Adverse Device Effects	Complete AE eCRF page with all available new and updated information.	• Immediately, but not later than 3 calendar days of first becoming aware of the event or as per local/regional regulations. • Reporting required through the end of the study
	Provide all relevant source documentation (de-identified/ pseudonymized) for reported event.	• When documentation is available • Upon request of sponsor
Device Deficiencies (including but not limited to malfunctions, use errors and inadequacy in information supplied by the manufacturer, including labeling)	Complete eCRF pages/fields with all available new and updated information.	• Immediately, but not later than 3 calendar days of first becoming aware of the event. • Reporting required through the end of the study
	Provide all relevant source documentation (de-identified/ pseudonymized) for reported event.	• Upon request of sponsor

Table 18.4-1: Investigator Reporting Requirements

Event Classification	**Communication Method**	**Communication Timeline pre-market studies** (*21 CFR Part 812, MDCG 2020-10/1*)
Note: Any Device Deficiency that might have led to a serious adverse event if appropriate action had not been taken, intervention had not occurred, or circumstances had been less fortunate is considered a reportable event.		
Adverse Event including Adverse Device Effects	Complete AE eCRF page, which contains such information as date of AE, treatment of AE resolution, assessment of seriousness and relationship to the device.	• In a timely manner (e.g. Recommend within 10 business days) after becoming aware of the information • Reporting of non-related adverse events are required up to 3 months post activation. • Reporting of device hardware, stimulation and/or procedure related adverse events are required through the end of the study • Upon request of sponsor
	Provide all relevant source documentation (de-identified/pseudonymized) for reported event, as requested by sponsor.	

* Please note that pre-market studies are clinical studies with investigational devices or with medical devices that bear the regulatory approval and are not being used for the same approved indications.

18.5. *Device Deficiencies*

Device deficiencies (including but not limited to failures, malfunctions, use errors, product nonconformities, and inadequacy in the information supplied by the manufacturer) will be documented and reported to BSC. If possible, the investigational device(s) should be returned to BSC for analysis. Instructions for returning the investigational device(s) will be provided to study sites. Device deficiencies should also be documented in the subject's source records.

Device deficiencies are not adverse events. However, an adverse event that results from a device deficiency would be recorded as an adverse event on the appropriate eCRF.

18.6. *Reporting to Regulatory Authorities / IRBs / Investigators*

BSC is responsible for reporting adverse event information to all participating Principal Investigators, IRBs and regulatory authorities, as applicable.

The Principal Investigator is responsible for informing the IRB, and regulatory authorities of UADEs and SAEs as required by local/regional regulations.

18.7. *Subject Death Reporting*

Death should not be recorded as an adverse event but should only be reflected as an outcome of one (1) specific SAE.

19. Informed Consent

Subject participation in this clinical study is voluntary. Informed Consent is required from each subject. The Investigator is responsible for ensuring that Informed Consent is obtained prior to the use of any study devices, study-required procedures and/or testing, or data collection.

The obtaining and documentation of Informed Consent must be in accordance with the principles of the Declaration of Helsinki, ISO 14155, any applicable national regulations, and local Ethics Committee and/or Regulatory authority, as applicable. The ICF must be accepted by BSC or its delegate (e.g. CRO), and approved by the site's IRB, or central IRB, if applicable.

Boston Scientific will provide a study-specific template of the ICF to investigators participating in this study. The ICF template may be modified to meet the requirements of the investigative site's IRB. Any modification requires acceptance from BSC prior to use of the form. The ICF must be in a language understandable to the subject and privacy language shall be included in the body of the form or as a separate form as applicable.

The process of obtaining Informed Consent shall at a minimum include the following steps, as well as any other steps required by applicable laws, rules, regulations and guidelines:

- be conducted by the Principal Investigator or designee authorized to conduct the process,
- include a description of all aspects of the clinical study that are relevant to the subject's decision to participate throughout the clinical study,
- avoid any coercion of or undue influence of subjects to participate,
- not waive or appear to waive subject's legal rights,
- use native language that is non-technical and understandable to the subject,
- provide ample time for the subject to consider participation and ask questions if necessary,
- ensure important new information is provided to new and existing subjects throughout the clinical study.

The ICF shall always be signed and personally dated by the subject competent to sign the ICF under the applicable laws, rules, regulations and guidelines and by the investigator and/or an authorized designee responsible for conducting the informed consent process. The original signed ICF will be retained by the site and a copy of the signed and dated document and any other written information must be given to the subject signing the form.

Failure to obtain subject consent will be reported by BSC to the applicable regulatory authority according to their requirements (e.g., FDA requirement is within 5 working days of learning of such an event). Any violations of the informed consent process must be reported as deviations to the sponsor and local regulatory authorities (e.g. IRB), as appropriate.

If new information becomes available that can significantly affect a subject's future health and medical care, that information shall be provided to the affected subject(s) in written form

via a revised ICF or, in some situations, enrolled subjects may be requested to sign and date an addendum to the ICF. In addition to new significant information during the course of a study, other situations may necessitate revision of the ICF, such as if there are amendments to the applicable laws, protocol, a change in Principal Investigator, administrative changes, or following annual review by the IRB. The new version of the ICF must be approved by the IRB. Acceptance by Boston Scientific is required if changes to the revised ICF are requested by the site's IRB. The IRB will determine the subject population to be re-consented.

20. Committees

20.1. *Safety Monitoring Process*

The BSC personnel from the Medical Safety and Safety Trial Operation Teams review safety data as it is reported by the sites throughout the duration of the study. During scheduled monitoring activities, clinical research monitors further support this review through their review of source documents and other data information.

20.2. *Independent Safety Reviewer*

An independent Safety Reviewer, expert in pain management, will review accumulating safety data to monitor for incidence of pre-specified key safety events that may warrant modification or termination of the trial.

21. Suspension or Termination

21.1. *Premature Termination of the Study*

Boston Scientific reserves the right to terminate the study at any stage but intends to exercise this right only for valid scientific or business reasons and reasons related to protection of subjects. Investigators, associated IRBs, and regulatory authorities, as applicable, will be notified in writing in the event of study termination.

21.1.1. Criteria for Premature Termination of the Study

Possible reasons for premature study termination include, but are not limited to, the following.

- Suspicion of an unacceptable risk. In this case, the sponsor shall suspend the clinical investigation while the risk is assessed. The sponsor shall terminate the clinical investigation if an unacceptable risk which cannot be controlled is confirmed.
- Instructions by the IRB or regulatory authorities to suspend or terminate the clinical investigation.
- An enrollment rate far below expectation that prejudices the conclusion of the study.
- A decision on the part of Boston Scientific to suspend or discontinue development of the device.

[redacted]

21.2. *Termination of Study Participation by the Investigator or Withdrawal of IRB Approval*

Any investigator, or associated IRB or regulatory authority may discontinue participation in the study or withdraw approval of the study, respectively, with suitable written notice to Boston Scientific. Investigators, associated IRBs, and regulatory authorities, as applicable, will be notified in writing in the event of these occurrences.

21.3. *Requirements for Documentation and Subject Follow-up*

In the event of premature study termination, a written statement as to why the premature termination has occurred will be provided to all participating sites by Boston Scientific. The IRB and regulatory authorities, as applicable, will be notified. Detailed information on how enrolled subjects will be managed thereafter will be provided.

In the event an IRB terminates participation in the study, participating investigators, associated IRBs, and regulatory authorities, as applicable, will be notified in writing. Detailed information on how enrolled subjects will be managed thereafter will be provided by Boston Scientific.

In the event a Principal Investigator terminates participation in the study, study responsibility will be transferred to another investigator, if possible. In the event there are no opportunities to transfer Principal Investigator responsibility, detailed information on how enrolled subjects will be managed thereafter will be provided by Boston Scientific.

The Principal Investigator or his/her designee must return all study-related documents and investigational product to Boston Scientific, unless this action would jeopardize the rights, safety, or welfare of the subjects.

21.4. *Criteria for Suspending/Terminating a Study Site*

Boston Scientific reserves the right to stop the inclusion of subjects at a study site at any time after the study initiation visit or if the site has multiple or severe protocol violations/noncompliance without justification and/or fails to follow remedial actions.

In the event of termination of site participation, all study devices and testing equipment, as applicable, will be returned to BSC unless this action would jeopardize the rights, safety or well-being of the subjects. The IRB and regulatory authorities, as applicable, will be notified. Study participants will be contacted, as applicable, and be informed of changes to study visit schedule.

22. Study Registration and Results

22.1. *Study Registration*

To comply with applicable laws and regulations, the study will be registered on a publicly accessible database.

22.2. *Clinical Investigation Report*

Study results will be made available in accordance with the legal requirements and the recognized ethical principles, in accordance with the Boston Scientific Policy. A Clinical Investigation Report will be made available to all investigators, IRB and regulatory authorities, as applicable in accordance with the Boston Scientific Policy and local requirements. As applicable an abbreviated Clinical Investigation Report will be made available on a publicly accessible database.

22.3. *Publication Policy*

BSC requires disclosure of its involvement as a sponsor or financial supporter in any publication or presentation relating to a BSC study or its results. BSC may submit study results for publication (regardless of study outcome) following the conclusion or termination of the study. Boston Scientific adheres to the Contributorship Criteria set forth in the Uniform Requirements of the International Committee of Medical Journal Editors (ICMJE; http://www.icmje.org). In order to ensure the public disclosure of study results in a timely manner, while maintaining an unbiased presentation of study outcomes, BSC personnel may assist authors and investigators in publication preparation provided the following guidelines are followed:

- All authorship and contributorship requirements as described above must be followed.
- BSC involvement in the publication preparation and the BSC Publication Policy should be discussed with the Coordinating Principal Investigator(s) and/or Executive/Steering Committee at the onset of the project.
- The First and Senior authors are the primary drivers of decisions regarding publication content, review, approval, and submission.

The data, analytic methods, and study materials for this clinical trial may be made available to other researchers in accordance with the Boston Scientific Data Sharing Policy (https://www.bostonscientific.com/).

23. Bibliography

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24. Abbreviations and Definitions

24.1. *Abbreviations*

Abbreviations are shown in Table 24.1-1.

Table 24.1-1: Abbreviations

Abbreviation/Acronym	Term
ADE	Adverse device effect
AE	Adverse event
BSC	Boston Scientific Corporation
BSN	Boston Scientific Neuromodulation
CGI-C	Clinical Global Impression of Change
CFR	Code of Federal Regulations
CRPS	Complex Regional Pain Syndrome
CP	Clinician programmer
CRF	Case report form
CRO	Contract research organization
DFU	Directions for use
eCRF	Electronic case report form
ESAP	End of study action plan
FBSS	Failed back surgery syndrome
FDA	Food and Drug Administration
GCP	Good clinical practice
HCP	Health care personnel
ICF	Informed Consent Form
ICH	International Conference on Harmonisation

Table 24.1-1: Abbreviations

Abbreviation/Acronym	Term
IPG	Implantable Pulse Generator
IRB	Institutional Review Board
ISO	International Organization for Standardization
Mg	Milligram
MRI	Magnetic Resonance Imaging
NRS	Numerical rating scale
ODI	Oswestry Disability Index
PGI-C	Patient Global Impression of Change
PPR	Percent Pain Relief
PSQI	Pittsburg Sleep Quality Index
SADE	Serious adverse device effect
SAE	Serious adverse event
SCS	Spinal cord stimulation
SF-36v2	Short Form 36 Health Survey (version 2)
TSQM-9m	Treatment Satisfaction Questionnaire for Medication - modified
UADE	Unanticipated adverse device effect
VRS	Verbal rating scale

24.2. *Definitions*

Detailed definitions or descriptions are provided in applicable sections of the protocol.