A Study to Demonstrate the Value of Multiple Modalities using the Spectra WaveWriter™ Spinal Cord Stimulator System in the Treatment of Chronic Pain

VERITAS Study

CLINICAL INVESTIGATION PLAN

[redacted]

Sponsored By

Boston Scientific Neuromodulation Corporation

25155 Rye Canyon Loop

Valencia, CA 91355

United States of America

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E	May 10, 2019	90702637 Rev/Ver AL	All sections	• Updated the analysis • Updated study follow-up	• Updated the analysis • Updated study follow-up

2. Protocol Synopsis

VERITAS Study **A Study to Demonstrate the Value of Multiple Modalities using the Spectra WaveWriter™ Spinal Cord Stimulator System in the Treatment of Chronic Pain**	
Primary Objective	To demonstrate the value of multiple modalities and sustained clinically significant pain relief in patients with chronic pain when using the Boston Scientific Spectra WaveWriter Spinal Cord Stimulator (SCS) System.
Secondary Objectives	To determine the impact of Spectra WaveWriter SCS System on global patient outcomes including quality of life, patient preference, etc.
Indication(s) for Use	The Spectra WaveWriter Spinal Cord Stimulator (SCS) System is indicated as an aid in the management of chronic intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with the following: failed back surgery syndrome, Complex Regional Pain Syndrome (CRPS) Types I and II, intractable low back pain and leg pain.
Device	BSC Spectra WaveWriter™ SCS System
Study Design	Prospective, multi-center, open-label, single-arm study with an adaptive design
[redacted]	[redacted]
[redacted]	[redacted]
Primary Endpoint	Proportion of subjects with 50% or greater reduction from Baseline Visit in average overall pain intensity at 3 months post activation, with no increase in baseline average daily opioid medications used to treat pain.

VERITAS Study **A Study to Demonstrate the Value of Multiple Modalities using the Spectra WaveWriter™ Spinal Cord Stimulator System in the Treatment of Chronic Pain**	
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VERITAS Study **A Study to Demonstrate the Value of Multiple Modalities using the Spectra WaveWriter™ Spinal Cord Stimulator System in the Treatment of Chronic Pain**	
	[redacted]
[redacted]	[redacted]
Safety Parameters	Rates of occurrence of all device and procedure related non-serious adverse events, all serious adverse events, and unanticipated adverse events through the end of the study.

VERITAS Study **A Study to Demonstrate the Value of Multiple Modalities using the Spectra WaveWriter™ Spinal Cord Stimulator System in the Treatment of Chronic Pain**	
Follow-up Schedule	Study events occur at the following time points: • Screening • Opioid Medication Lock Visit (Up to 35 days following Informed Consent) • Baseline Period (14 days) • Baseline Visit (0 - 7 days post Baseline Period) • Implant Procedures (up to 90 days post Baseline Visit) • Healing Period (0 - 28 days) • Activation Visit (Day 0) • Programming Period (up to 70 days) • Programming Lock Visit (70 ± 14 days) • Evaluation Period • 3 Month Visit (90 + 14 days post Activation Visit) • 6-Month Visit (180 ± 30 days post Activation Visit) • 9-Month Visit (270 ± 30 days post Activation Visit) • Year 1 Visit (365 ± 30 days post Activation Visit)
[redacted]	[redacted]
Key Inclusion Criteria	IC1. Chronic pain of the trunk and/or limbs for at least 6 months [redacted] IC3. Average overall pain intensity (leg and/or low back pain) of 6 or greater on a 0-10 numerical rating scale at Baseline Visit based on 7-day recall [redacted]

VERITAS Study **A Study to Demonstrate the Value of Multiple Modalities using the Spectra WaveWriter™ Spinal Cord Stimulator System in the Treatment of Chronic Pain**	
	IC6. Willing and able to comply with all protocol-required procedures and assessments/evaluations [redacted] IC8. 22 years of age or older when written informed consent is obtained [redacted] IC10. Able to independently read and complete all questionnaires and assessments provided in English IC11. If female of childbearing potential: not pregnant, as evidenced by a negative pregnancy test at Screening IC12. Subject signed a valid, IRB-approved informed consent form (ICF) provided in English
Key Exclusion Criteria	[redacted] EC7. Any pain-related diagnosis or medical/psychological condition that, in the clinician's best judgment, might confound reporting of study outcomes (e.g. pelvic pain, anginal pain, chronic migraine, brain or spinal cord tumor) [redacted]

VERITAS Study **A Study to Demonstrate the Value of Multiple Modalities using the Spectra WaveWriter™ Spinal Cord Stimulator System in the Treatment of Chronic Pain**	
	EC9. Current systemic infection, or local infection in close proximity to anticipated surgical field, at Screening [redacted] EC13. Current condition associated with risk of immunocompromise that might increase risk of infection during study duration [redacted] EC15. Significant cognitive impairment at Screening that, in the opinion of the Investigator, would reasonably be expected to impair the study candidate's ability to participate in the study EC16. Participating (or intends to participate) in another drug or device clinical trial that may influence the data that will be collected for this study EC17. Previous spinal cord stimulation trial or is already implanted with an active implantable device(s) (e.g. pacemaker, drug pump, implantable pulse generator) EC18. A female who is breastfeeding EC19. A female of childbearing potential planning to get pregnant during the course of the study or not using adequate contraception [redacted] EC22. Any injury or medical/psychological condition that might be significantly exacerbated by the implant surgery or the presence of an implantable stimulator or otherwise compromise subject safety EC23. [redacted]

VERITAS Study **A Study to Demonstrate the Value of Multiple Modalities using the Spectra WaveWriter™ Spinal Cord Stimulator System in the Treatment of Chronic Pain**	
Statistical Methods	
Primary Statistical Hypothesis	Proportion of subjects with 50% or greater reduction from Baseline Visit in average daily overall pain intensity at 3 months is non-inferior to the Objective Performance Criteria (OPC) of 40%. H_0: $\pi_{opc} - \pi_t \geq 0.20$ H_1: $\pi_{opc} - \pi_t < 0.20$ Where π_t is the proportion of subjects with 50% or greater reduction from Baseline in average daily overall pain intensity at 3 mos. post activation with no increase in baseline average daily pain medications using Spectra WaveWriter.
[redacted]	[redacted]
[redacted]	[redacted]
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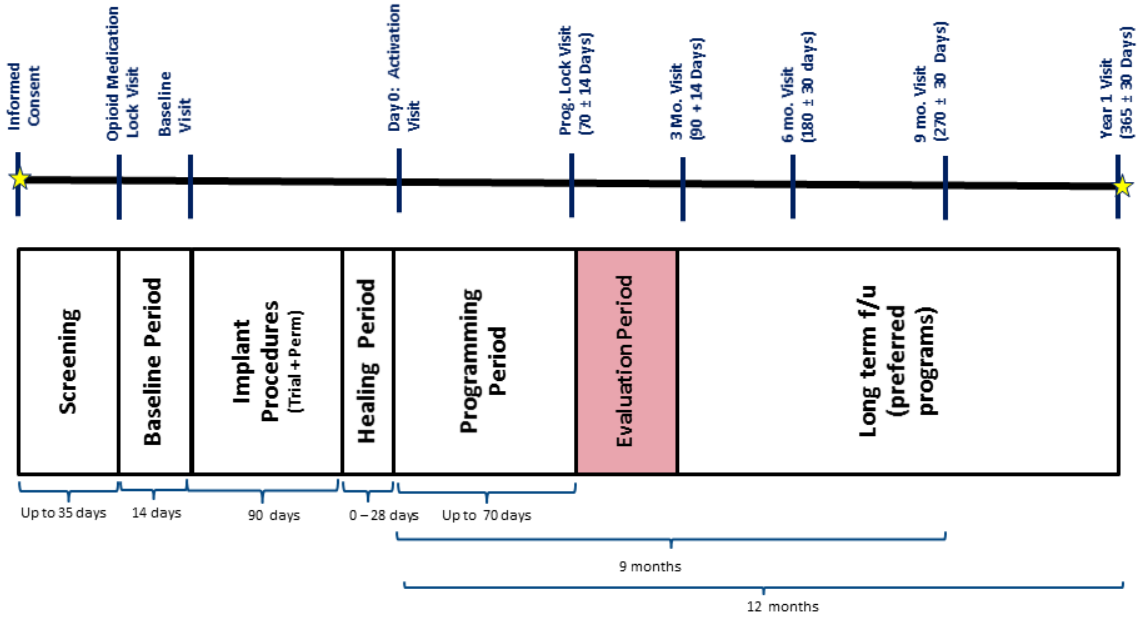
VERITAS Study

A Study to Demonstrate the Value of Multiple Modalities using the Spectra WaveWriter™ Spinal Cord Stimulator System in the Treatment of Chronic Pain

[redacted]

Study Schematic



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4. Introduction

4.1. *Chronic Intractable Pain*

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.

4.2. *Spinal Cord Stimulation*

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. 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).

In SCS pain relief is realized when the nerves that innervate the painful region(s) are electrically stimulated (North et al., 1990). To increase the chance of success, the electrode contacts are programmed based on the patient feedback to various combinations of contact polarities (anodes and cathodes), pulse rate (or frequency), pulse amplitude (or current), and pulse width.

Traditionally, Spinal Cord Stimulation (SCS) has relied on the understanding that to achieve pain relief, dorsal column stimulation-induced paresthesia has to be generated around the area of pain in order to successfully treat pain (North et al. 1991). However, recent studies indicate that effective pain relief may be obtained by employing stimulation without paresthesia (Van Buyten et al., 2012, De Ridder et al., 2010, Kapural et al 2015).

[redacted]

[redacted]

[redacted]

[redacted]

6. Study Objectives

6.1. *Primary Objective*

The primary objective of this study is to demonstrate the value of multiple modalities and sustained clinically significant pain relief in patients with chronic pain when using the Boston Scientific Spectra WaveWriter Spinal Cord Stimulator (SCS) System.

6.2. *Secondary Objective*

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

7. Study Endpoints

7.1. *Primary Endpoint*

The primary endpoint is the proportion of subjects with 50% or greater reduction from the Baseline Visit in average overall pain intensity at 3 months post activation, with no increase in baseline average daily opioid medications used to treat pain.

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

7.5. *Primary Safety Parameters*

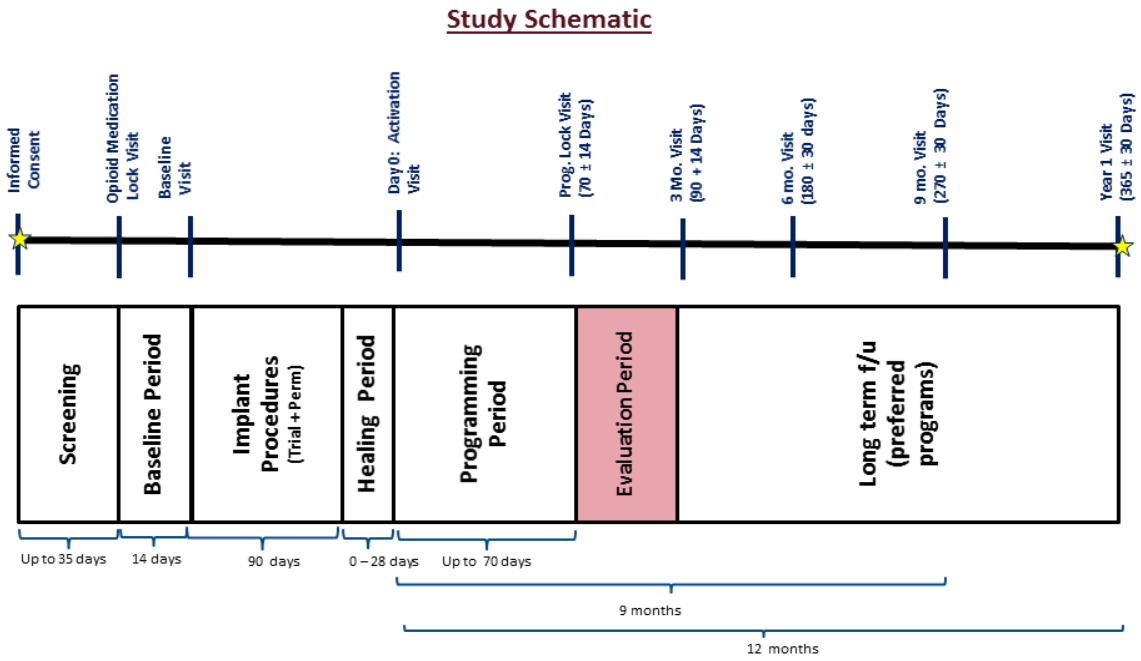
Safety parameters include the rates of occurrence of all device and procedure related non-serious adverse events, all serious adverse events, and unanticipated adverse events through the end of the study.

8. Study Design

The study is a prospective, multi-center, single-arm open-label study with an adaptive design. All participants will receive the Spectra WaveWriter Spinal Cord Stimulator (SCS) system and followed per the study schedule as shown in study schematic Figure 8.1-1.

[redacted]

Figure 8.1-1: VERITAS Study Design



8.1.1. Treatment

All enrolled subjects who pass eligibility criteria will receive a trial. Subjects with a positive trial will proceed to receive permanent implant. Following permanent implant, all subjects' device will be activated to provide therapy.

8.2. *Justification for the Study Design*

The study is a prospective, multi-center, open-label study with an adaptive design. The study is designed to demonstrate the value of multiple modalities and sustained clinically significant pain relief in patients with chronic pain when using the Boston Scientific Spectra WaveWriter SCS System. Additionally, the impact of the Spectra WaveWriter SCS System on global patient outcomes, quality of life and patient preference will also be evaluated.

A prospective study design will eliminate the bias associated with case selection in a retrospective review and will ensure that identical procedures are followed for data capture and review.

A multi-center design will minimize the impact on treatment outcome that may potentially result from differences in patient selection, regional differences in the patient demographic, and differences in investigator technique and patient management.

The primary endpoint is the proportion of subjects with 50% or greater reduction (responder rate) from the Baseline Visit in average overall pain intensity at 3 months post activation, with no increase in baseline average daily opioid medications used to treat pain. A 3 month endpoint was chosen as 3 months provides adequate time for a subject to have their programming parameters optimized.

9. Subject Selection

9.1. *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 in Sections 9.2 and 9.3.

9.2. *Inclusion Criteria*

Subjects who meet all of the following criteria (see Table 9.2-1) may be given consideration for inclusion in this clinical investigation, provided no exclusion criterion (see Section 9.3) is met.

Table 9.2-1: Inclusion Criteria

Clinical Inclusion Criteria	IC1. Chronic pain of the trunk and/or limbs for at least 6 months [redacted] IC3. Average overall pain intensity (leg and/or low back pain) of 6 or greater on a 0-10 numerical rating scale at Baseline Visit based on 7-day recall [redacted] [redacted] IC6. Willing and able to comply with all protocol-required procedures and assessments/evaluations [redacted] IC8. 22 years of age or older when written informed consent is obtained [redacted] IC10. Able to independently read and complete all questionnaires and assessments provided in English

	IC11. If female of childbearing potential: not pregnant, as evidenced by a negative pregnancy test at Screening IC12. Subject signed a valid, IRB-approved informed consent form (ICF) provided in English

Abbreviations: Spinal Cord Stimulation (SCS), Directions for Use (DFU), Milligram (mg), Institutional Review Board (IRB), Informed Consent Form (ICF)

9.3. *Exclusion Criteria*

Subjects who meet any one of the following criteria (Table 9.3-1) will be excluded from this clinical study.

Table 9.3-1: Exclusion Criteria

Clinical Exclusion Criteria	[redacted] EC7. Any pain-related diagnosis or medical/psychological condition that, in the clinician's best judgment, might confound reporting of study outcomes (e.g. pelvic pain, anginal pain, chronic migraine, brain or spinal cord tumor) [redacted] EC9. Current systemic infection, or local infection in close proximity to anticipated surgical field, at Screening [redacted] EC13. Current condition associated with risk of immunocompromise that might increase risk of infection during study duration

	[redacted] EC15. Significant cognitive impairment at Screening that, in the opinion of the Investigator, would reasonably be expected to impair the study candidate's ability to participate in the study EC16. Participating (or intends to participate) in another drug or device clinical trial that may influence the data that will be collected for this study EC17. Previous spinal cord stimulation trial or is already implanted with an active implantable device(s) (e.g. pacemaker, drug pump, implantable pulse generator) EC18. A female who is breastfeeding EC19. A female of childbearing potential planning to get pregnant during the course of the study or not using adequate contraception [redacted] [redacted] EC22. Any injury or medical/psychological condition that might be significantly exacerbated by the implant surgery or the presence of an implantable stimulator or otherwise compromise subject safety EC23. [redacted]

Abbreviations: Implantable Pulse Generator (IPG), Magnetic Resonance Imaging (MRI).

10. Subject Accountability

10.1. *Point of Enrollment*

A subject will be considered enrolled in the study when the Informed Consent Form (ICF) is signed. All enrolled and activated subjects will be included in the study analyses.

If device implantation is unsuccessful, the subject will be followed for 2 weeks post implantation attempt to assess for procedure related adverse events.

10.2. *Withdrawal*

All subjects enrolled in the clinical study (including those withdrawn from the clinical study or lost to follow-up) 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
- Inadequate use of device that may impact study outcomes 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

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 that the device must programmed per standard of care with commercially approved settings.

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 in Section 10.5.

10.3. *Subject Status and Classification*

Subjects who provide written informed consent but do not meet all of the study eligibility criteria will not be implanted or activated. These subjects will be deemed as "enrolled but not activated" and their reason for ineligibility will be documented.

Enrolled subjects who are not activated will not count towards the enrollment cap. Subjects who sign consent, meet all eligibility criteria, undergo permanent implant and are activated cannot be replaced.

[redacted]

10.5. *End-of-Study Action Plan*

When each subject completes the 1-Year Visit or withdraws, the subject exits the study and ends study participation. Subjects may continue to use their system per the applicable Directions for Use and will be followed according to standard of care.

If the study is terminated early due to sponsor discretion or due to the discovery of an unexpected, significant, or unacceptable risk/safety concern regardless of how far along the subject has reached in their study follow-up, subjects will be followed according to standard of care. Sites will have 30 days to notify all subjects of study closure.

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, the subject will be followed for 30 days post explant to assess for related adverse events.

Device related adverse events and/or deficiencies occurring after study participation, withdrawal from the study, or after the specified timeframe following unsuccessful trials, implant failures, and explants, should be reported to BSN Patient Care at: 866-360-4747. Such complications should not be captured as adverse events in the study.

11. Study Methods

11.1. *Data Collection*

There are a number of different study assessments required at each visit. The data collection schedule is provided in Table 11-1. Full descriptions for all assessments are provided in Section 13.

Table 11.1-1: Data Collection Schedule

	Screening	Opioid Medication Lock Visit	Baseline Period	Baseline Visit	Implant Procedures *(Trial and Permanent)*		Activation Visit	Programming Period	Programming Lock Visit	Evaluation Period	3-Month Visit	6-Month Visit	9-Month Visit	1-Year Visit *End of Study*	Unscheduled Visit
		Up to 35 days	14 days post-Medication Lock		Up to 90 days post-Baseline Visit		Day 0	Up to 70 days post-Activation Visit	70 ± 14 days		90 + 14 days	180 ± 30 days	270 ± 30 days	365 ± 30 days	
Informed Consent (ICF)	X														
Inclusion/Exclusion Criteria Evaluation	→	→	→	→											
Demography				X											
Medical History				X											
Beck Depression Inventory (BDI-II)				X							X			X	
Oswestry Disability Index (ODI v2.1a)				X							X	X	X	X	
Short Form Health Survey 36 item (SF-36v2)				X							X	X	X	X	
EQ-5D-5L				X							X	X	X	X	
Resource Utilization Inventory (RUI)				X							X	X	X	X	
Work Productivity (WPAI-SHP v2.0)				X							X	X	X	X	
Pain Intensity (NRS)				X							X	X	X	X	
Pain Intensity (VRS)				X							X	X	X	X	
Procedure Information					X[ᵀ]										X**
End of Trial Assessment					X										
Programming Parameters* **					X		X	X	X	X	X	X	X	X	X
Therapy Rating					X			→	→	→	→	→	→	→	→
Clinician Global Impression of Change (CGI-C)											X	X	X	X	
Patient Global Impression of Change (PGI-C)											X	X	X	X	
Percent Pain Relief (PPR)											X	X	X	X	
Preference Questionnaire											X	X	X	X	
Treatment Satisfaction Questionnaire (TSQM-9m)											X	X	X	X	
Concomitant Medications (opioid pain medications)		X		X	X		X		X		X	X	X	X	X
Adverse Event (AE)	X[¥]	X[¥]	X[¥]	X[¥]	X[¥]		X[¥]	X[¥]	X[¥]	X[¥]	X[¥]	X[¥]	X[¥]	X[¥]	X[¥]

Healing Period (0-28 days)

← **Opioid Medications Locked** →

[**] For unscheduled visits where procedures are performed.
[***] Only when device programming is performed.
[ᵀ] The device will remain off until the Activation Visit.
[¥] A follow up neurological assessment may be performed to determine if neurological deficit is noted.

11.2. *Study Candidate Screening*

Subjects' eligibility for the study will be assessed based on study Inclusion and Exclusion criteria listed in Sections 9.2 and 9.3, respectively. Subjects who have provided informed consent and who have been determined to not meet all eligibility requirements will be withdrawn.

11.2.1. 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

11.2.2. Screening Period

Subjects undergo screening related procedures to determine eligibility for the study. It may take up to the end of Baseline Period to complete all eligibility requirements.

All enrolled subjects who are women of child-bearing potential must undergo a pregnancy test at screening. Women with positive pregnancy test results will be withdrawn from the study. The results of the test result must be documented in the subject's medical chart.

Subjects taking prescription opioids for primary chronic pain complaint (low back and/or leg pain), whose pain medications are not stable for 30 days prior to informed consent, will be withdrawn. However these subjects may be re-consented/rescreened once 30 days have passed since the last change.

Any adverse event occurring after the subject is enrolled (i.e. signing the Informed Consent Form) will be documented.

11.3. *Opioid Medication Lock Visit (Up to 35 days following informed consent)*

The in-office Opioid Medication Lock Visit will occur within 35 days following informed consent, after completion of some screening requirements as described in Section 11.2. At this visit, the subject's opioid pain medications will be locked, with no change in type/dose/route/frequency, until the 3-Month post-Activation Visit.

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.

11.4. *Baseline Period (14 days)*

The Baseline Period will last for 14 consecutive days following the Medication Lock Visit. At the end of the Baseline Period, subjects will return to the clinic for their Baseline Visit.

Subjects are to not make any changes to their opioid pain medications during this period.

11.5. *Baseline Visit (0 – 7 days post Baseline Period)*

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

The following assessments, as outlined in Table 11.1-1, will be conducted:

- Demographics
- Medical history
- Beck Depression Inventory (BDI-II)
- Oswestry Disability Index (ODIv2.1a)
- Short Form Health Survey 36 (SF-36v2)
- EQ-5D 5-Level
- Resource Utilization Inventory (RUI)
- Work Productivity (WPAI-SHP v2.0)
- Pain Intensity: VRS
- Pain Intensity: NRS

Subjects that meet all study criteria will be scheduled for the device implant procedures (trial and permanent implant of the SCS system). If a subject fails to meet all the eligibility criteria, they will be withdrawn from the study.

End of Visit Information:

- Subjects should be reminded not to make any changes to their opioid medications.

11.6. *Implant Procedures (Up to 90 days following the Baseline Visit)*

Subjects will have up to 90 days following the Baseline Visit to receive their Spectra WaveWriter System. Subjects will undergo a trial procedure per standard of care. Following a successful trial, i.e. at least 50% pain reduction in their overall pain as compared with Baseline, the subject will proceed to permanent implantation. Subjects with an unsuccessful implant procedure will be followed for 2 weeks for procedure related adverse events then withdrawn from the study. Acute opioid pain medications may be taken.

11.7. *Healing Period (0 - 28 days following Implant Procedures)*

The subject's device will remain inactivated (device OFF) for up to 28 days following the permanent implantation procedure to allow for healing. Acute opioid pain medications may be taken during this period. No additional scheduled assessments will be completed during this period.

11.8. *Activation Visit (Day 0)*

At the Activation Visit, the subject's Spectra WaveWriter SCS System will be activated. Any adverse events since the last study visit will be collected.

Subjects must stop taking acute opioid pain medications, as applicable, and are not to make any changes to their opioid pain medications up to the 3-Month Visit.

Information regarding programming parameters will be documented. To aid in programming it is recommended that thoracic and/or lumbar imaging is obtained at this visit or up to 7 days prior to the visit to show the position(s) of the study device lead(s). In the event of suspected lead migration, imaging may be performed to document lead positions.

End of Visit Information:

- Subjects will receive instructions on the use of the device including the Remote Control and charging system.
- Subjects should be instructed to evaluate all programs saved on the Remote Control prior to their next visit as applicable.
- Subjects are to contact the site in an event that any additional intervention is warranted, to report a complaint and/or a suspected adverse event, reprogramming, etc.
- Subjects should be reminded not to make any changes to their opioid pain medications.

11.9. *Programming Period (Up to 70 days following the Activation Visit)*

Following device activation, subjects' device will be optimized to achieve effective therapy during the Programming Period of up to 70 days post-activation.

During this period, subjects may return as many times as needed (unscheduled visits) for optimization of programming.

Information regarding programming parameters and device information may be collected and documented.

11.10. *Programming Lock Visit (Day 70 ± 14 days)*

At the Programming Lock Visit, subjects will return to the clinic to have their programs locked. Any adverse events since the last study visit will be collected.

It is recommended that their final settings be documented in the study records. No further changes to the subjects programs such as electrode configuration will be allowed except to resolve a device and/or stimulation-related AE.

At this Visit, subjects will choose their preferred programs (or modalities) to be evaluated during the Evaluation Period. Subjects' choice will be documented.

Information regarding programming parameters and device information may be collected and documented.

End of Visit Information:

- Subjects will receive instructions on the use of the device including the Remote Control and charging system, as needed.
- Subjects should be instructed to evaluate their preferred programs (or modalities) prior to their next visit.
- Subjects are to contact the site in an event that any additional intervention is warranted, to report a complaint and/or a suspected adverse event, reprogramming, etc.
- Subjects should be reminded not to make any changes to their opioid medications.

11.11. *Evaluation Period*

During the Evaluation Period, subjects will evaluate each of the programs (or modalities) previously chosen at the Programming Lock Visit.

11.12. *3-Month Visit (90 + 14 days)*

During the 3-Month Visit, subjects will return to the clinic for study evaluations and programming. Any adverse events since their last study visit will be collected.

The following assessments will be completed as summarized in Table 11.1-1:

- Beck Depression Inventory (BDI-II)
- Oswestry Disability Index version 2.1a (ODI v2.1a)
- Short Form Health Survey 36 items (SF-36 v2)
- EQ-5D 5-Level
- Resource Utilization Inventory (RUI)
- Work Productivity (WPAI-SHP v2.0)
- Pain Intensity: VRS
- Pain Intensity: NRS
- Clinical Global Impression of Change (CGI-C)
- Patient Global Impression of Change (PGI-C)
- Percent Pain Relief (PPR)

- Preference Questionnaire
- Treatment Satisfaction Questionnaire for Medication - modified (TSQM-9m)

Following completion of assessments, subjects' device will 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.

End of Visit Information:

- Subjects will receive instructions on the use of the device including the Remote Control and charging system, as needed.
- Subjects are to contact the site in an event that any additional intervention is warranted, to report a complaint and/or a suspected adverse event, reprogramming, etc.
- Changes to opioid pain medications are allowed up to End of Study Visit.

11.13. *6-Month Visit (180 ± 30 days)*

During the 6-Month Visit, subjects will return to the clinic for study evaluations and programming. Any adverse events since their last study visit will be collected.

The following assessments will be completed as summarized in Table 11.1-1:

- Oswestry Disability Index version 2.1a (ODI v2.1a)
- Short Form Health Survey 36 items (SF-36 v2)
- EQ-5D 5-Level
- Resource Utilization Inventory (RUI)
- Work Productivity (WPAI-SHP v2.0)
- Pain Intensity: NRS
- Pain Intensity: VRS
- Clinical Global Impression of Change (CGI-C)
- Patient Global Impression of Change (PGI-C)
- Percent Pain Relief (PPR)
- Preference Questionnaire
- Treatment Satisfaction Questionnaire for Medication - modified (TSQM-9m)

Following completion of assessments, subjects' device will 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.

End of Visit Information:

- Subjects will receive instructions on the use of the device including the Remote Control and charging system, as needed.
- Subjects are to contact the site in an event that any additional intervention is warranted, to report a complaint and/or a suspected adverse event, reprogramming, etc.
- Changes to opioid pain medications are allowed up to End of Study Visit.

11.14. *9-Month Visit (270 ± 30 days)*

During the 9-Month Visit, subjects will return to the clinic for study evaluations and programming. Any adverse events since their last study visit will be collected.

The following assessments will be completed as summarized in Table 11.1-1:

- Oswestry Disability Index version 2.1a (ODI v2.1a)
- Short Form Health Survey 36 items (SF-36 v2)
- EQ-5D 5-Level
- Resource Utilization Inventory (RUI)
- Work Productivity (WPAI-SHP v2.0)
- Pain Intensity: NRS
- Pain Intensity: VRS
- Clinical Global Impression of Change (CGI-C)
- Patient Global Impression of Change (PGI-C)
- Percent Pain Relief (PPR)
- Preference Questionnaire
- Treatment Satisfaction Questionnaire for Medication - modified (TSQM-9m)

Following completion of assessments, subjects' device will 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.

End of Visit Information:

- Subjects will receive instructions on the use of the device including the Remote Control and charging system, as needed.
- Subjects are to contact the site in an event that any additional intervention is warranted, to report a complaint and/or a suspected adverse event, reprogramming, etc.

11.15. *Year 1 Visit (365 ± 30 days)*

During the 1 Year Visit, subjects will return to the clinic for study evaluations and programming. Any adverse events since their last study visit will be collected.

The following assessments will be completed as summarized in Table 11.1-1:

- Beck Depression Inventory (BDI-II)
- Oswestry Disability Index version 2.1a (ODI v2.1a)
- Short Form Health Survey 36 items (SF-36 v2)
- EQ-5D 5-Level
- Resource Utilization Inventory (RUI)
- Work Productivity (WPAI-SHP v2.0)
- Pain Intensity: NRS
- Pain Intensity: VRS
- Clinical Global Impression of Change (CGI-C)
- Patient Global Impression of Change (PGI-C)
- Percent Pain Relief (PPR)
- Preference Questionnaire
- Treatment Satisfaction Questionnaire for Medication - modified (TSQM-9m)

Following completion of assessments, subjects' device will 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.

The 1 Year Visit is the End of Study Visit and End of Study Action Plan (ESAP) will be followed as described in Section 10.5.

11.16. *Unscheduled Visit*

Subjects may have as many unscheduled visits as required for device-related in-office or procedure visits (e.g., optimization of programming 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.

11.16.1. Revision or Replacement of Leads, Extensions and/or IPGs

During the course of 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 on 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 20.

11.16.2. Interventional Pain Procedures

No interventional pain procedures to treat the SCS-targeted pain are allowed through the 3-Month Visit. Procedures associated with the SCS device (e.g. IPG Revision, Lead revision, CSF leak interventions and interventions associated with SCS procedure related adverse event management) are allowed. Excluded procedures include, but are not limited to, the following:

- Epidural steroid injection
- Facet joint injection
- Selective nerve root block
- Radiofrequency ablation
- Spine surgery (e.g., discectomy, vetebroplasty, fusion)

11.17. *Medication Requirements*

Opioid Medication Lock Period (Medication Lock visit to 3-Month Visit):

Investigators/Subjects will not be allowed to change opioid pain medications from the Medication Lock visit until completion of the 3-Month Visit. Type/dose/route must remain unchanged.

The use of acute opioid pain medication for procedural discomfort is allowed during the Procedures and Healing Period and in the event of the revision or replacement of leads, extensions and/or IPG, per site's routine care.

Opioid Medication Open Period (3-Month Visit to End of Study visit)

Investigators/Subjects may change opioid pain medications during the pain medication open period, from the 3-Month Visit to the 1-Year, End of Study Visit as needed.

11.18. *Study Completion*

All activated subjects permanently implanted will be followed through completion of the 1-Year Visit or study withdrawal. The End of Study Action Plan (see Section 10.5) defines the actions to be taken when the subject reaches the end of their study participation.

11.19. *Source Documents*

Table 11.17-1 summarizes all 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.

Table 11.17-1: 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

12. Statistical Considerations

12.1. *Endpoints*

12.1.1. Primary Endpoint

The primary endpoint for this study is the proportion of subjects with 50% or greater reduction from Baseline Visit in average overall pain intensity at 3 months post activation with no increase in baseline average opioid medications used to treat pain.

[redacted]

12.1.1.1. Hypotheses

The primary statistical hypothesis in this study is that the proportion of subjects with 50% or greater reduction from Baseline Visit in average daily overall pain intensity at 3 months post activation is non-inferior to an Objective Performance Criteria (OPC) of 40%.

H_0: $\pi_{opc} - \pi_t \geq 0.20$

H_1: $\pi_{opc} - \pi_t < 0.20$

Where π_t is the proportion of subjects with 50% or greater reduction from Baseline in average daily overall pain intensity at 3 months post activation with no increase in baseline average daily opioid pain medications using Spectra WaveWriter. π_{opc} is the responder rate of an OPC based on Kumar paper (Kumar 2008).

[redacted]

[redacted]

12.2. *General Statistical Methods*

12.2.1. Analysis Sets

- **Intent-to-Treat (ITT) Population**: All subjects who receive the study device and are activated.
- **Per Protocol (PP) Population**: All subjects who receive the study device, with no major protocol deviations.

- **Safety Population**: All subjects who sign the IRB-approved written Informed Consent form

12.2.2. Control of Systematic Error/Bias

Selection of patients will be made from the Investigator's usual patient load. All patients 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 implanted, will be indicated in EDC. Boston Scientific will report to the ethic committee any evidence of fraud, including deliberate tampering with the selection of subjects.

[redacted]

[redacted]

12.3. *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]

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12.3.3. 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.

[redacted]

12.3.5. Changes to Planned Analyses

[redacted] Changes from the planned statistical methods after performing the analyses will be documented in the clinical study report along with a reason for the deviation.

13. Data Management

13.1. *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 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 EDC system and will

be issued to the site for appropriate response. Site staff will be responsible for resolving all queries in the database.

13.1.1. 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.

13.1.2. Direct Data Upload

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.

13.2. *Study Assessments*

13.2.1. Adverse Events

Adverse event evaluation will be conducted to identify adverse events occurring during the study and classify them in regards to seriousness, relationship to the implant procedure and/or device, action taken and outcome. Safety events will be reported as specified in Table 20.4-1.

All device and procedure related non-serious adverse events, all serious adverse events, and unanticipated adverse events will be collected from the time of consent through the end of the study.

13.2.2. Beck Depression Inventory (BDI-II)

BDI-II measures the intensity, severity, and depth of depression. It includes a long form of 21 questions, each evaluating a specific depression symptom (e.g., sadness, pessimism, irritability, loss of energy, concentration difficulty, indecisiveness, changes in sleep pattern, fatigue, etc.).

13.2.3. Concomitant Medications

All opioid pain-related medications will be collected throughout the study in order to obtain a full record of medication-related resource utilization. Information will include medication name, dates of prescription, indication or purpose, dose, frequency, and route of administration.

13.2.4. Clinical Global Impression of Change (CGI-C)

CGI-C is a seven-point scale that requires the clinician to assess how much the subject's condition has improved or worsened relative to the subject's enrollment in the study. The clinician will rate the subject's change as: very much improved; much improved; minimally improved; no change; minimally worse; much worse; or very much worse.

13.2.5. Demography

Demographic information will include date of birth, gender, and race/ethnicity.

13.2.6. EQ-5D 5 Level (EQ-5D-5L)

EQ-5D-5L is a standardized measure of health status developed by the EuroQol Group in order to provide a simple, generic measure of health for clinical and economic appraisal. Applicable to a wide range of health conditions and treatments, it provides a simple descriptive profile and a single index value for health status that can be used in the clinical and economic evaluation of health care as well as in population health surveys.

EQ-5D-5L is comprised of a descriptive system and a visual analog scale. The descriptive system measures quality of life along five dimensions, including mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, with five levels for each dimension from which subjects are asked to select one. The visual analog scale is used to record the subject's self-rated health on a 20cm vertical line with endpoints labeled 'the best health you can imagine' and 'the worst health you can imagine'.

13.2.7. Medical History

Medical history will include medical and procedural history relating to pain management, onset of chronic pain, all pain-related diagnoses and medical/psychological conditions, medication use etc.

13.2.8. Oswestry Disability Index Version 2.1a (ODI v2.1a)

ODI v2.1a assesses the degree of subject disability due to pain, measuring the impact of pain on activities of daily living. ODI v2.1a is composed of 10 questions that describe the pain and its impact on daily life on a 0 - 5 scale, with higher values indicating the more severe impact.

13.2.9. Pain Intensity: NRS

Pain Intensity: NRS is a questionnaire that assesses the intensity of the subject's pain intensities, including overall, leg, and low back pain over the past 7 days. Pain intensity is expressed on a 0 – 10 numerical rating scale (NRS), where 0 indicates "no pain" and 10 indicates "pain as bad as you can imagine" as self-reported by the subject.

13.2.10. Pain Intensity: VRS

Pain Intensity: VRS is a questionnaire that verbally assesses the intensity of the subject's pain intensities, including overall, leg, and low back pain over the past 7 days. This is done based on a clinician interview (e.g. study personnel such as physician or study coordinator) with the subject.

Pain intensity is expressed on a 0 – 10 verbal rating scale (VRS), where 0 indicates "no pain" and 10 indicates "pain as bad as you can imagine", verbally reported by the subject to study personnel.

13.2.11. Procedure Information

General information will be collected regarding the SCS procedures performed during the study, including implant, explant and revision procedures.

13.2.12. Patient Global Impression of Change (PGI-C)

PGI-C is a seven-point scale that requires the subject to assess how much their condition has improved or worsened relative to their baseline. Subjects will rate themselves as: very much improved; much improved; minimally improved; no change; minimally worse; much worse; or very much worse.

13.2.13. Percent Pain Relief (PPR)

PPR is a questionnaire assessing how much of the subject's low back pain and leg pain has been relieved by the SCS treatment. Pain relief is expressed as a percentage from 0 – 100%.

13.2.14. Preference Questionnaire

The Preference Questionnaire assesses the subjects' preference for treatment based on the options offered during the study.

13.2.15. Programming Parameters

Standard information regarding the programming parameters used to program the subject's IPG, as well as measurements taken using the device (e.g. contact impedances) will be collected from the Clinician Programmer (CP).

13.2.16. Resource Utilization Inventory (RUI)

Health-related resource utilization data will be collected to support the health economic analyses. Resource utilization categories include: office/hospital visits, diagnostic tests, and non-surgical procedures.

13.2.17. Short-Form Health Survey 36 Item (SF-36v2)

The SF-36v2 measures subjects' functional health and well-being from their own point of view. SF-36v2 is comprised of 36 questions spanning eight health domains: physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. All health domain scales contribute to the scoring of two component summary measures: physical health and mental health.

13.2.18. Therapy Rating

The Remote Control has a therapy rating feature. Subjects may be instructed to perform therapy ratings at a frequency that may be up to daily. Information regarding therapy ratings will be collected from the Clinical Programmer, as applicable.

13.2.19. Treatment Satisfaction Questionnaire for Medication – modified (TSQM-9m)

TSQM-9 is a 9-item instrument validated for the assessment of subjects' satisfaction with a medication across three domains: effectiveness, convenience, and global satisfaction. TSQM-9m is a slightly modified version developed for this study in which the term 'medication' is substituted for 'device' to be applicable with a medical device treatment.

13.2.20. Work Productivity (WPAI-SHP v2.0)

WPAI:SHP v2.0 assesses the amount of absenteeism, presenteeism, and daily activity impairment attributable to a specific health problem. The specific health problem in this study is chronic pain. WPAI:SHP v2.0 consists of six questions addressing the subject's employment status, true work status, productivity while working, and ability to carry out regular daily activities.

13.3. *Data Retention*

The Principal Investigator or his/her designee or Investigational site will maintain, at the investigative site, all essential study documents and source documentation that support the data collected on the study subjects in compliance with ICH/GCP guidelines. Documents must be retained for at least 2 years after the last approval of a marketing application or until at least 2 years have elapsed since the formal discontinuation of the clinical investigation of the product. These documents will be retained for a longer period of time by agreement with BSC or in compliance with other country/regional/local regulations.

The Principal Investigator or his/her designee will take measures to ensure that these essential documents are not accidentally damaged or destroyed. 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.

14. Amendments

If a protocol revision is necessary which affects the rights, safety or welfare of the subject or scientific integrity of the data, an amendment is required. Appropriate approvals (e.g., IRB) of the revised protocol must be obtained prior to implementation.

15. 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 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, per local guidelines and government regulations.

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

[redacted]

16. Device/Equipment Accountability

Commercially approved Spectra WaveWriter SCS Systems are used in this study per the Directions for Use; no investigational devices are used.

17. Compliance

17.1. *Statement of Compliance*

This study will be conducted in accordance with 21 CFR 50 and 56, 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 pertinent 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. Any additional requirements imposed by the IRB or regulatory authority shall be followed, if appropriate.

17.2. *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 Investigational Plan/Protocol, ISO 14155, applicable Code of Federal Regulations, 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 Investigational Plan/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 study.
- Report protocol deviations to the sponsor, IRB and/or regulatory authorities, as required by the protocol, IRB guidelines, and/or national/regulatory regulations.
- 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 the sponsor, per the protocol requirements, all SAEs and device deficiencies that could have led to a SADE and potential/USADE or UADE.
- 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 the national 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.
- Maintain device disposition records and ensure that the device components are used only by authorized/designated users and in accordance with this protocol and Directions 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 device.
- Inform the subject of any new significant findings occurring during the clinical study, 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.
- 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 study are provided with some means of showing their participation in the clinical study, 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 study.

- Make all reasonable efforts to ascertain the reason(s) for a subject's premature withdrawal from clinical study 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 study.
- Ensure that maintenance and calibration of the equipment relevant for the assessment of the clinical study is appropriately performed and documented, where applicable.

17.2.1. 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 and adequate supervision of those to whom tasks are delegated. The investigator is accountable for regulatory violations resulting from failure to adequately supervise the conduct of the clinical study.

17.3. *Institutional Review Board*

Prior to gaining Approval-to-Enroll status, the investigational site will provide to the sponsor documentation verifying that their IRB is registered or that registration has been submitted to the appropriate agency, as applicable according to national/regulatory requirements.

A copy of the written IRB approval of the protocol (or permission to conduct the study) and Informed Consent Form, must be received by the sponsor before recruitment of subjects into the study. Prior approval must also be obtained for other materials related to subject recruitment or which will be provided to the subject.

Annual IRB approval and renewals will be obtained throughout the duration of the study as required by local/country or IRB requirements. Copies of the Investigator's reports and the IRB continuance of approval must be provided to the sponsor.

17.4. *Sponsor Responsibilities*

All information and data sent to BSC concerning subjects or their participation in this study will be considered confidential by BSC. Only authorized BSC personnel or a BSC representative including, but not limited to Contract Research Organization (CRO) will have access to these confidential records. 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. All data used in the analysis and reporting of this study will be without identifiable reference to specific subject name.

Boston Scientific will keep subjects' identifiable health information confidential in accordance with all applicable laws and regulations. Boston Scientific may use subjects' health information to conduct this research, as well as for additional purposes, such as overseeing and improving the performance of its device, new medical research and proposals for developing new medical products or procedures, and other business purposes.

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]

18. 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, the IRB, and appropriate regulatory authorities.

The study may also be subject to a quality assurance audit by BSC or its designees, as well as inspection by the IRB and/or 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.

19. Potential Risks and Benefits

19.1. *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

19.2. *Anticipated Adverse Device Effects*

The risks summarized below are anticipated during 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.

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

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

- 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

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

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

19.4. *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.

19.5. *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 lead remains implanted.

Magnetic Resonance Imaging (MRI). The subject should not be exposed to Magnetic Resonance Imaging (MRI). Exposure to this diagnostic technology may result in dislodgement of the Stimulator or lead(s), heating of the Stimulator, damage to the Stimulator electronics and/or voltage induction 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

19.6. *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.

19.7. *Anticipated Benefits*

The reported benefit of the Spectra WaveWriter SCS System 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 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)

19.8. *Risk to Benefit Rationale*

The risk evaluation for the Spectra WaveWriter SCS System determined that all hazards attributed to the Spectra WaveWriter SCS System 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 Spectra WaveWriter SCS System 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 Spectra WaveWriter SCS System is acceptable for use in a clinical setting.

20. Safety Reporting

20.1. *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
- All Investigational Device Deficiencies
- Unanticipated Adverse Device Effects
- Non-serious device and/or procedure related adverse events
- 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 AE event required by the protocol, experienced by the study subject after informed consent and once considered enrolled in the study (as defined in study subject classification section), whether during or subsequent to the procedure, must be recorded in the eCRF.

Underlying diseases are not reported as AEs unless there is an increase in severity of 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 20.2-1 for AE definitions).

Refer to Section 19 for the known risks associated with the study device(s).

20.2. *Definitions and Classification*

Adverse event definitions are provided in Table 20.2-1. Administrative edits were made on the definition of serious adverse event from ISO 14155 and MEDDEV 2.7/3 for clarification purposes.

Table 20.2-1: Safety Definitions

Term	Definition
Adverse Event (AE) *Ref: ISO 14155*	Any untoward medical occurrence, unintended disease or injury, or any untoward clinical signs (including an abnormal laboratory finding) in subjects, users or other persons, whether or not related to the investigational medical device. NOTE 1: This includes events related to the investigational medical device or comparator.

Table 20.2-1: Safety Definitions

Term	Definition
Ref: MEDDEV 2.7/3	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: MEDDEV 2.7/3*	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 intentional abnormal use of the investigational medical device.
Serious Adverse Event (SAE) *Ref: ISO 14155* *Ref: MEDDEV 2.7/3*	Note: This definition meets the reporting objectives and requirements of ISO 14155 and MEDDEV 2.7/3. Adverse event that: a) Led to death, b) Led to serious deterioration in the health of the subject as defined by either: 1) a life-threatening illness or injury, or 2) a permanent impairment of a body structure or a body function, 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) Led to fetal distress, fetal death, or a congenital abnormality or birth defect. **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: MEDDEV 2.7/3*	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.
Device Deficiency *Ref: ISO 14155*	An inadequacy of an investigational medical device related to its identity, quality, durability, reliability, safety or performance. This may include malfunctions, use error, or inadequacy in the information supplied by the manufacturer.

Table 20.2-1: Safety Definitions

Term	Definition
Ref: MEDDEV 2.7/3	

Abbreviations: IRB=Institutional Review Board

Underlying diseases 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 a specific SAE.

Any AE experienced by the study subject after informed consent, whether during or subsequent to the procedure, must be recorded in the eCRF.

Refer to Section 19 for the known risks associated with the study device(s).

NOTES:

1. For the purposes of this study, hospitalization is defined as any in-patient admission.
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.

20.3. *Relationship to Study Device(s)*

The Investigator must assess the relationship of the AE to the study device or procedure. See criteria in Table 20.3-1.

Table 20.3-1: Criteria for Assessing Relationship of Study Device or Procedure to Adverse Event

Classification	Description
Not Related	Relationship to the device or procedures can be excluded when: - the event is not a known side effect of the product category the device belongs to or of similar devices and procedures; - the event has no temporal relationship with the use of the investigational device or the procedures; - 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 not expected to 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, or treatment or other risk factors); - the event does not depend on a false result given by the investigational device used for diagnosis, when applicable; harms to the subject are not clearly due to use error; - 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.
Unlikely Related	The relationship with the use of the device seems not relevant and/or the event can be reasonably explained by another cause, but additional information may be obtained.
Possibly Related	The relationship with the use of the investigational device 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	The relationship with the use of the investigational device seems relevant and/or the event cannot reasonably explained by another cause, but additional information may be obtained.
Causal Relationship	The serious event is associated with the investigational device 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 o the investigational device or procedures are applied to; o 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 event.

Abbreviations: IRB=Institutional Review Board

The Investigator must assess the potential relationship of all adverse events to the **study device 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.

20.4. *Investigator Reporting Requirements*

The communication requirements for reporting to BSC are as shown in Table 20.4-1.

Table 20.4-1: Investigator Reporting Requirements

Event Classification	**Communication Method**	**Communication Timeline post-market studies**** (MEDDEV 2.12/2: GUIDELINES ON A MEDICAL DEVICE VIGILANCE SYSTEM)
Unanticipated 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
Serious Adverse Event	Complete AE eCRF page with all available new and updated information.	• Within 10 business days after becoming aware of the event or as per local/regional regulations. Reporting required through the end of the study

Table 20.4-1: Investigator Reporting Requirements

Event Classification	**Communication Method**	**Communication Timeline post-market studies**** (MEDDEV 2.12/2: GUIDELINES ON A MEDICAL DEVICE VIGILANCE SYSTEM)
	Provide all relevant source documentation (unidentified) for reported event upon request of the sponsor.	• When documentation is available
Serious Adverse Device Effects	Complete AE eCRF page with all available new and updated information.	• Within 2 business 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 (unidentified) for reported event	• When documentation is available
Device Deficiencies (including but not limited to failures, malfunctions, and product nonconformities) Note: Any Investigational Device Deficiency that might have led to a serious adverse event if a) suitable action had not been taken or b) intervention had not been made or c) if circumstances had been less fortunate is considered a reportable event.	Complete Device Deficiency eCRF with all available new and updated information.	• Within 2 business days of first becoming aware of the event. • Reporting required through the end of the study
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 30 business days) after becoming aware of the information • Reporting of Adverse events which are device/procedure related will be required through the end of the study.

Abbreviations: AE=adverse event; CRF=case report form; IDE=Investigational Device Exemption; UADE=unanticipated adverse device effect

20.5. *Boston Scientific Device Deficiencies*

All 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 device(s) should be returned to BSC for analysis. Instructions for returning the investigational device(s) will be provided to study sites. If it is not possible to return the device, the investigator should document why the

device was not returned and the final disposition of the device. Device failures and malfunctions should also be documented in the subject's medical record.

Device deficiencies (including but not limited to failures, malfunctions, and product nonconformities) are not adverse events. However, an adverse event that results from a device failure or malfunction should be recorded as an adverse event on the appropriate eCRF.

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

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

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

21. 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 devices, study-required procedures and/or testing, or data collection.

The obtaining and documenting Informed Consent must be in accordance with the principles of the Declaration of Helsinki, ISO 14155, any applicable national regulations, and local IRB and/or regulatory authority body, as applicable. The ICF must be accepted by Boston Scientific (BSC), 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. 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 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.

Failure to obtain subject consent will be reported by BSC to the applicable regulatory body 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.

Study personnel should explain that even if a subject agrees to participate in the study and signs an Informed Consent form, screening procedures may demonstrate that the subject is not a suitable candidate for the study.

22. Suspension or Termination

23.1 Premature Termination of the Study

Boston Scientific Corporation reserves the right to terminate the study at any stage but intends to exercise this right only for valid scientific or administrative 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.

23.1.1 Criteria for Premature Termination of the Study

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

- The occurrence of unanticipated adverse device effects that present a significant or unreasonable risk to subjects enrolled in the study.
- 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.

23.2 Termination of Study Participation by the Investigator or Withdrawal of IRB Approval

Any investigator or IRB in the VERITAS Study may discontinue participation in the study or withdrawal 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.

23.3 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 products to Boston Scientific, unless this action would jeopardize the rights, safety, or welfare of the subjects.

23.4 Criteria for Suspending/Terminating a Study Site

Boston Scientific Corporation reserves the right to stop the inclusion of subjects at a study site at any time after the study initiation visit if no subjects have been enrolled 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-related products, 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. All subjects enrolled in the study at the site will continue to be followed according to the protocol and the end of study action plan. The Principal Investigator at the site must make provision for these follow-up visits unless BSC notifies the investigational site otherwise.

BSC may also consider transferring active subjects from the site that is being closed to another approved study site within geographic area.

Possible reasons for suspending/terminating a study center include:

- Persistent non-compliance with protocol;
- Repeated failure to complete CRFs in a timely manner;
- Failure to obtain written Informed Consent;
- Failure to report UADE within 1 business day after "becoming aware date" and SAE within 2 business days after becoming aware date to BSC;
- Loss of study product inventory;
- Failure to enroll subjects.

23. 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 will submit study results for publication (regardless of study outcome) following the conclusion or termination of the study. Boston Scientific Corporation 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.

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- BSC involvement in the publication preparation and the BSC Publication Policy should be discussed with the Coordinating Principal Investigator(s) at the onset of the project.
- The First and Senior authors are the primary drivers of decisions regarding publication content, review, approval, and submission.

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25. Abbreviations and Definitions

25.1. *Abbreviations*

Abbreviations are shown in Table 27.1-1. Detailed definitions or descriptions are provided in applicable sections of the protocol.

Table 27.1-1: 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
IPG	Implantable pulse generator
IRB	Institutional review board
ISO	International Organization for Standardization
Mg	Milligram
MRI	Magnetic Resonance Imaging
NRS	Numerical rating scale
ODI	Oswetry Disability Index
PGI-C	Patient Global Impression of Change
PPR	Percent pain relief
SADE	Serious adverse device effect
SAE	Serious adverse event
SCS	Spinal cord stimulation
SF-36v2	Short Form 36 Health Survey ver 2
TSQM-9m	Treatment Satisfaction Questionnaire for Medication - modified

Table 27.1-1: Abbreviations

Abbreviation/Acronym	Term
UADE	Unanticipated adverse device effect
VRS	Verbal rating scale