NAVITAS Study

A Study to Characterize the Relationship between Select Objective Metrics and Clinical Outcomes in Chronic Pain Patients treated with Boston Scientific Neurostimulation Systems

CLINICAL INVESTIGATION PLAN

Sub-Study
TO THE RELIEF STUDY PROTOCOL
A7007

Sponsored By

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Neuromodulation
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United States of America

Contact Information

Role	Contact
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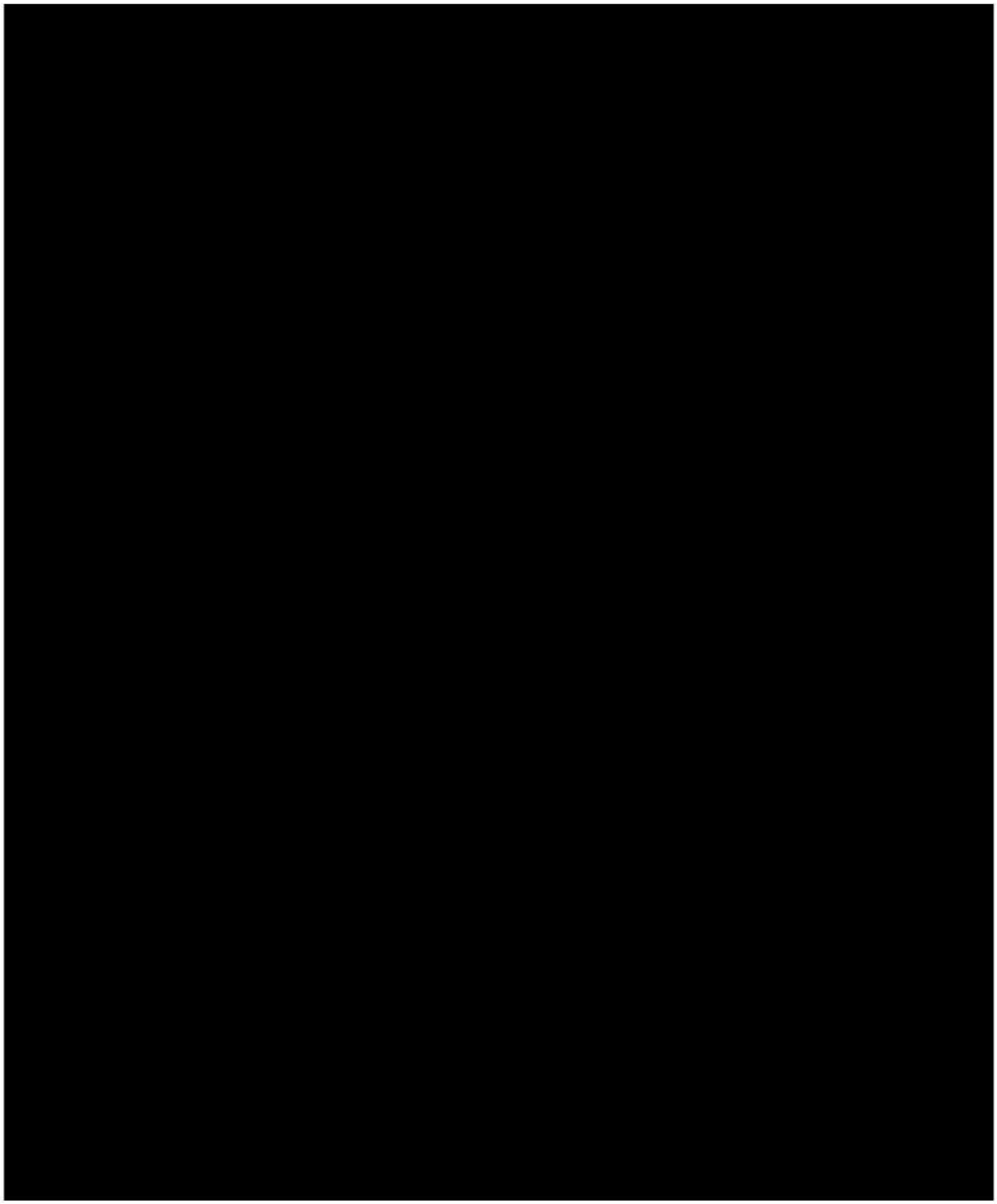
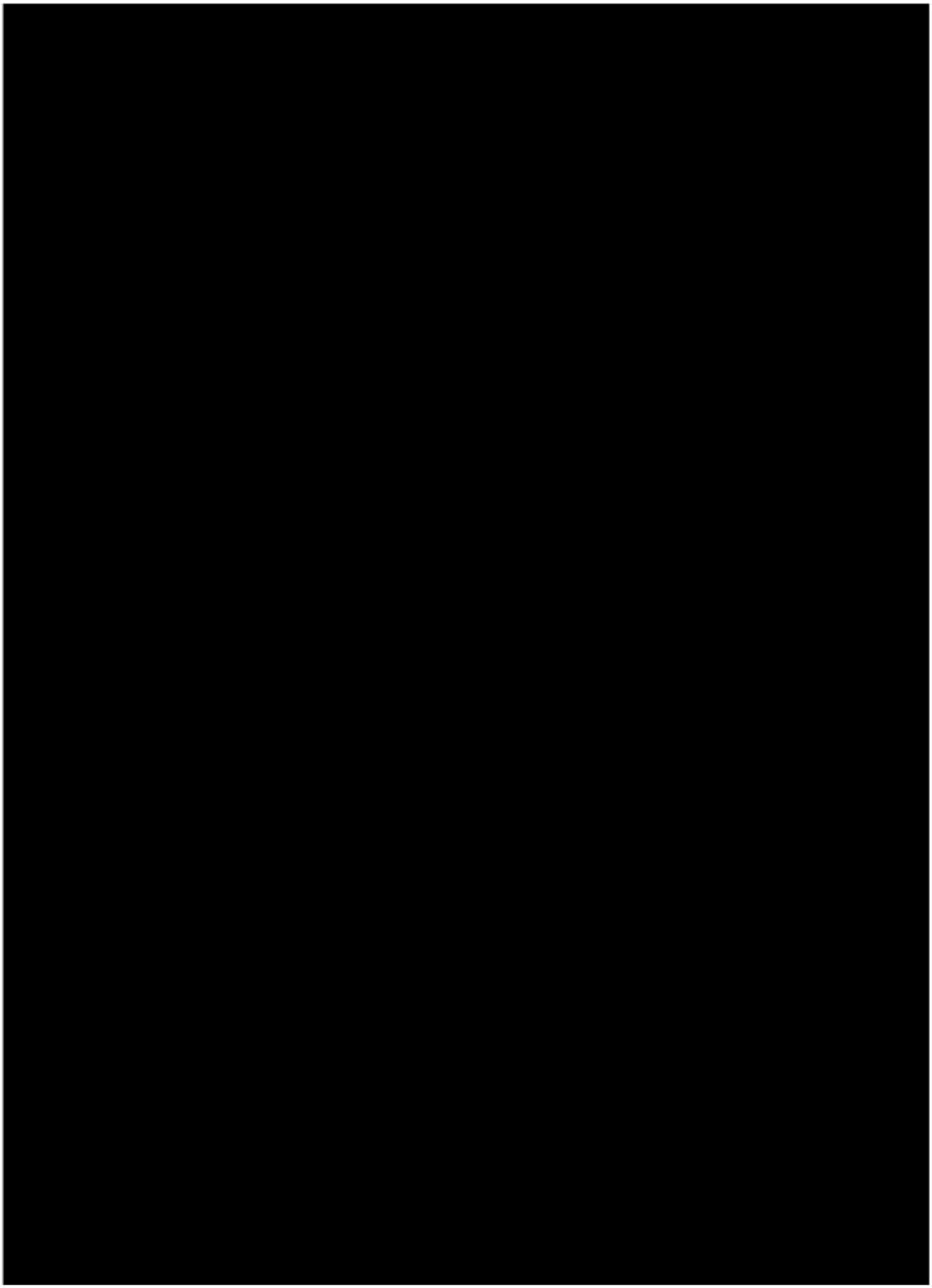
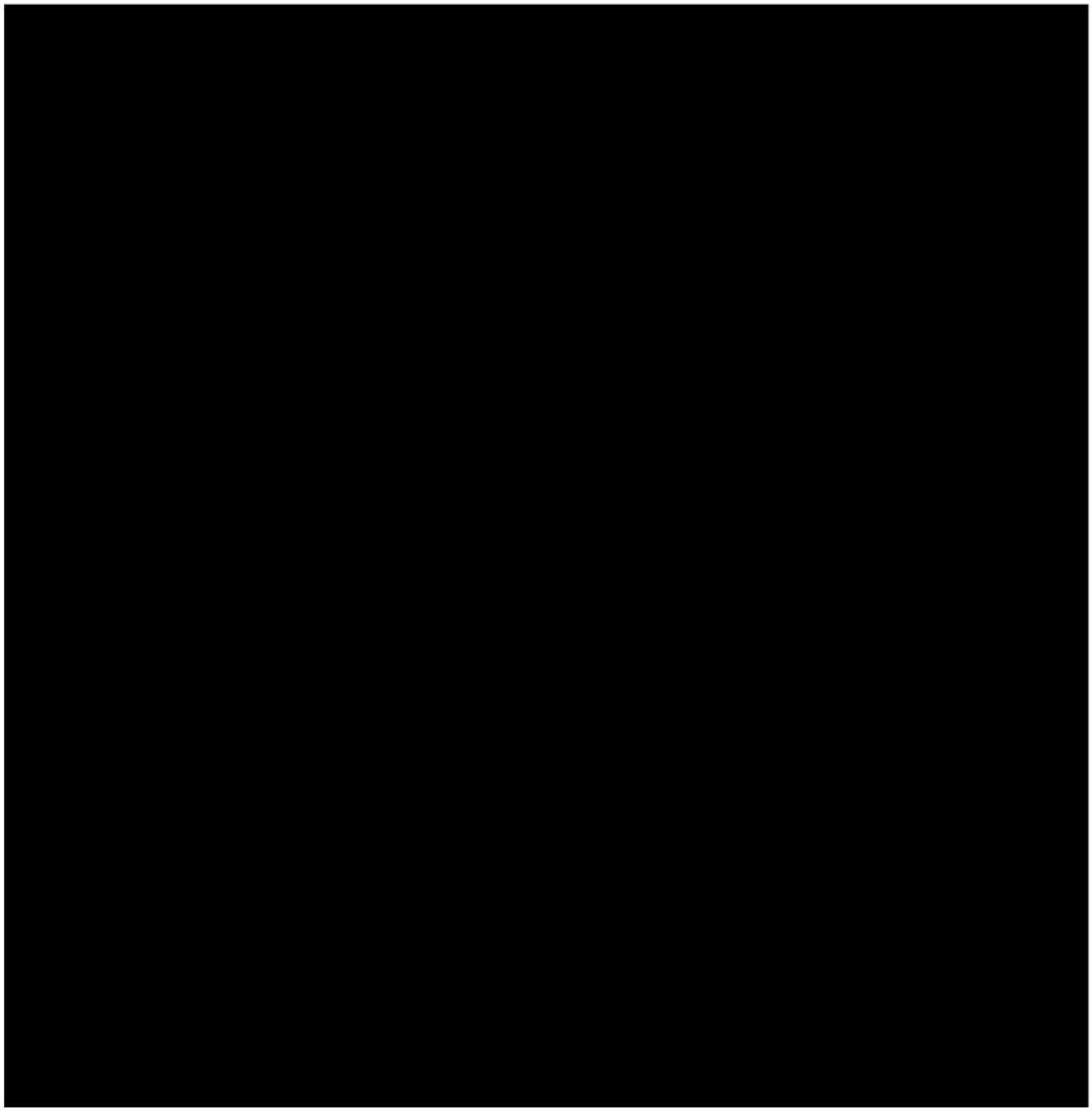
Original Release: 28APR2017

Current Version: 24JUL2019







2. Protocol Synopsis

NAVITAS: A Study to Characterize the Relationship between Select Objective Metrics and Clinical Outcomes in Chronic Pain Patients treated with Boston Scientific Neurostimulation Systems The NAVITAS Sub-study is being conducted under the RELIEF Study however subjects enrolled in NAVITAS will follow protocol requirements within this document only. Subjects enrolled in the NAVITAS protocol will not be enrolled in the RELIEF study and should be withdrawn from RELIEF if they are already enrolled.	
Study Objective(s)	The objective of the study is to characterize the relationship between select objective metrics and clinical outcomes in chronic pain patients treated with Boston Scientific commercially approved neurostimulation systems.
Devices	All commercially approved Boston Scientific neurostimulation systems indicated for the treatment of chronic pain, with the exception of Precision™ and Precision™ Plus. All commercially approved VitalConnect™ Sensor indicated for continuous collection of physiological data in home and healthcare settings used as part of the physIQ VitaLink Solution ("Platform").
Study Design	Prospective, post-market, non-randomized, multi-center study
[redacted]	
Planned Number of Investigational Sites / Countries	The study will be conducted at up to 30 sites in the United States

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Exploratory Endpoints	This study does not have any pre-defined endpoints but may include ad-hoc exploratory endpoint(s) to explore the relationship between metrics and clinical outcomes. Exploratory endpoint(s) will be intended to generate hypotheses for future studies. Consequently, no correction for multiple testing will be performed for exploratory endpoint(s). Any exploratory endpoint(s) will be clearly identified as such in study reports, as applicable.
Safety Parameters	The rate of neurostimulator device and procedure-related adverse events (AEs), Serious Adverse Events (SAEs) from informed consent through study exit will be reported.

Follow-up Schedule	NAVITAS Study assessments will be required, as appropriate, at the following time points (the additional visits included as part of the NAVITAS Study are denoted by italicized text):
	• **<u>Baseline Visit (In-office)</u>**
	  ○ De Novo and Existing
	  ○ *≥8 – 14 days prior to Stimulation Trial Procedure for De Novo Cohort only.*
	  ○ *Day 0 for Existing Cohort only*
	• Baseline Period (At Home) 8 – 14 days*:
	  ○ De Novo and Existing
	  ○ *After the Baseline Visit and ≥ 8 – 14 days prior to the Stimulation Trial Procedure for De Novo Cohort only*
	  ○ *≥ 8 – 14 days for Existing Cohort only*
	Chest-worn biosensor patch worn for 8 – 14 total* days.
	Wrist-worn biosensor, Pain Log, and eDiary application daily
	• **<u>Neurostimulation Trial Procedure Visit (In-office, Day 0 for De Novo Cohort)</u>**
	De Novo Cohort only
	• Trial Period (At Home)
	  ○ *De Novo Cohort only, Day 0*
	  ▪ *Chest-worn biosensor patch during trial period*

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	▪ *Wrist-worn biosensor, Pain Log, and eDiary application daily* • **End of Neurostimulation Trial Period Visit (In-office)** • **IPG Implantation and Activation Visit (In-office)** Up to 12-Month Post neurostimulation trial procedure visit • *Month 1 Post Neurostimulation Trial Procedure Visit (De Novo Cohort)/Post Enrollment (Existing Cohort) Period (At Home, 30 days ± 14 days)* Chest-worn biosensor patch for five total* days. Wrist-worn biosensor, Pain Log, and eDiary application daily • Month 2 Post Neurostimulation Trial Procedure Visit (De Novo Cohort)/Post Enrollment (Existing Cohort) Period (At Home, 60 days ± 14 days) Chest-worn biosensor patch for five total* days Wrist-worn biosensor, Pain Log, and eDiary application daily • *Month 3 Post Neurostimulation Trial Procedure Visit (De Novo Cohort)/Post Enrollment (Existing Cohort) Period (At Home, 90 days ±14 days)* Chest-worn biosensor patch for five total* days Wrist-worn biosensor, Pain Log, and eDiary application daily • **3-Month Post Neurostimulation Trial Procedure Visit[1] (De Novo Cohort only, In-office, 90 days ± 10 days)/Post Enrollment (Existing Cohort) Visit (In-office, 90 days ± 10 days)** • *Month 4 Post Neurostimulation Trial Procedure Visit (De Novo Cohort)/Post Enrollment (Existing Cohort) Period (At Home, 120 days ± 14 days)*

* Chest-worn biosensor patch wear reflects total days. Subjects are encouraged to wear the patch for consecutive days however one day breaks are allowed in between patch changes. Breaks do not count towards the total.

[1] Only for De Novo cohort subjects who have undergone IPG Implantation prior to this visit

	Chest-worn biosensor patch for five total* days Wrist-worn biosensor, Pain Log, and eDiary application daily • *Month 5 Post Neurostimulation Trial Procedure Visit (De Novo Cohort)/Post Enrollment (Existing Cohort) Period (At Home, 150 days ± 14 days)* Chest-worn biosensor patch for five total* days Wrist-worn biosensor, Pain Log, and eDiary application daily • *Month 6 Post Neurostimulation Trial Procedure Visit (De Novo Cohort)/Post Enrollment (Existing Cohort) Period (At Home, 180 days ± 14 days)* Chest-worn biosensor patch for five total* days Wrist-worn biosensor, Pain Log, and eDiary application daily • **6-Month Post Neurostimulation Trial Procedure Visit (De Novo Cohort Existing Cohort, as applicable) Visit (In-office, 180 days ± 30 days)** • *Month 7 Post Neurostimulation Trial Procedure Visit (De Novo Cohort)/ Post Enrollment (Existing Cohort) Period (At Home, 210 days ± 14 days)* Chest-worn biosensor patch for five total* days Wrist-worn biosensor, Pain Log, and eDiary application daily • *Month 8 Post Neurostimulation Trial Procedure Visit (De Novo Cohort)/ Post Enrollment (Existing Cohort) Period (At Home, 240 days ± 14 days)* Chest-worn biosensor patch for five total* days Wrist-worn biosensor, Pain Log, and eDiary application daily • *Month 9 Post Neurostimulation Trial Procedure Visit (De Novo Cohort)/ Post Enrollment (Existing Cohort) Period (At Home, 270 days ± 14 days)* Chest-worn biosensor patch for five total* days Wrist-worn biosensor, Pain Log, and eDiary application daily

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	• **<u>9-Months Post Neurostimulation Trial Procedure Visit[1] (De Novo Cohort only, In-office, 270 days ± 30 days)</u>** • *Month 10 Post Neurostimulation Trial Procedure Visit (De Novo Cohort)/ Post Enrollment (Existing Cohort) Period (At Home, 300 days ± 14 days)* Chest-worn biosensor patch for five total* days Wrist-worn biosensor, Pain Log, and eDiary application daily • *Month 11 Post Neurostimulation Trial Procedure Visit (De Novo Cohort)/ Post Enrollment (Existing Cohort) Period (At Home, 330 days ± 14 days)* Chest-worn biosensor patch for five total* days Wrist-worn biosensor, Pain Log, and eDiary application daily • *Month 12 Post Neurostimulation Trial Procedure Visit (De Novo and Existing Cohort) Period (At Home, 360 days ± 14 days)* Chest-worn biosensor patch for five total* days Wrist-worn biosensor, Pain Log, and eDiary application daily • **<u>12-months Post Neurostimulation Trial Procedure (De Novo and Existing, as applicable) (In-office, 365 ± 60 days Post Neurostimulation Trial Procedure Visit)/Post Enrollment (Existing) Visit (In-office, 365 ± 60 days)</u>** • *Months 13-15 Post Neurostimulation Trial Procedure Visit Period (Optional De Novo and Optional Existing Cohort[2]) Period (At Home, 410 days ± 44 days)* Wrist-worn biosensor, Pain Log, and eDiary application daily for ≥ seven total* days • Months 16-18 Post Neurostimulation Trial Procedure Visit Period (Optional De Novo and Optional Existing Cohort[2]) Period (At Home, 500 days ±*44 days*)

[2] For Subjects that have not ended study participation and opted to continue NAVITAS Study follow up for > 12 months

	Wrist-worn biosensor, Pain Log, and eDiary application daily for ≥ seven total* days • *Months 19-21 Post Neurostimulation Trial Procedure Visit Period (Optional De Novo and Optional Existing Cohort[2]) Period (At Home, 590 days ± 44 days)* Wrist-worn biosensor, Pain Log, and eDiary application daily for ≥ seven total* days • *Months 22-24 Post Neurostimulation Trial Procedure Visit Period (Optional De Novo and Optional Existing Cohort[2]) Period (At Home, 680 days ±44 days)* o *Wrist-worn biosensor, Pain Log, and eDiary application daily for ≥ seven total* days* • **Optional 24-months Post Neurostimulation Trial Procedure Visit[2] (In-office, 720 ± 60 days Post Neurostimulation Trial Procedure Visit)** • Months 25-27 Post Neurostimulation Trial Procedure Visit Period (Optional De Novo and Optional Existing Cohort[3]) Period (At Home, 765 days ±*44 days*) Wrist-worn biosensor, Pain Log, and eDiary application daily for ≥ seven total* days • *Months 28-30 Post Neurostimulation Trial Procedure Visit Period (Optional De Novo and Optional Existing Cohort[3]) Period (At Home, 855 days ± 44 days)* Wrist-worn biosensor, Pain Log, and eDiary application daily for ≥ seven total* days • Months 31-33 Post Neurostimulation Trial Procedure Visit Period (Optional De Novo and Optional Existing Cohort[3]) Period (At Home, 945 days ±*44 days*) Wrist-worn biosensor, Pain Log, and eDiary application daily for ≥ seven total* days

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- Months 34-36 Post Neurostimulation Trial Procedure Visit Period (Optional De Novo and Optional Existing Cohort[3]) Period (At Home, 1035 days *±44 days*)
  - *Wrist-worn biosensor, Pain Log, and eDiary application daily for ≥ seven total* days*
- **Optional 36-months Post Neurostimulation Trial Procedure Visit[2] (In-office, 1095 ± 60 days Post Neurostimulation Trial Procedure Visit)**

NAVITAS Study De Novo subjects who did not have a successful neurostimulation trial will complete their participation in the NAVITAS Study after completion of the End of Neurostimulation Trial Period visit and all trial leads/extensions have been explanted. NAVITAS Study De Novo Subjects who have not proceeded to IPG implantation with a BSC IPG by the 12-Months Post neurostimulation trial procedure visit will complete their participation in the NAVITAS Study after completion of the 12-Months Post neurostimulation trial procedure visit.

NAVITAS Study subject participation will be considered complete:

- If they exit the NAVITAS early; or
- when De Novo Cohort NAVITAS study subjects complete their 12-Month Post neurostimulation trial procedure visit and decide not to continue with optional follow-up; or
- when Existing Trial Cohort NAVITAS Study subjects complete their 12-Month Post Enrollment visit and decide not to continue with optional follow-up; or
- when subjects complete their 36-Months Post Neurostimulation Trial Procedure Visit.

[redacted]

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Key Inclusion Criteria	Subjects must meet all inclusion criteria, as outlined below: IC1. Study candidate is scheduled to be trialed, on-label, with a commercially approved Boston Scientific neurostimulation system for pain, per local directions for use (DFU) IC2. Provides signed, dated, and documented NAVITAS study informed consent on an Institutional Review Board (IRB) - approved informed consent form IC3. Is willing and able to comply with completing protocol required assessments and evaluations [redacted]
Key Exclusion Criteria	Subjects must be excluded from the study if they meet any of the following exclusion criteria: [redacted]

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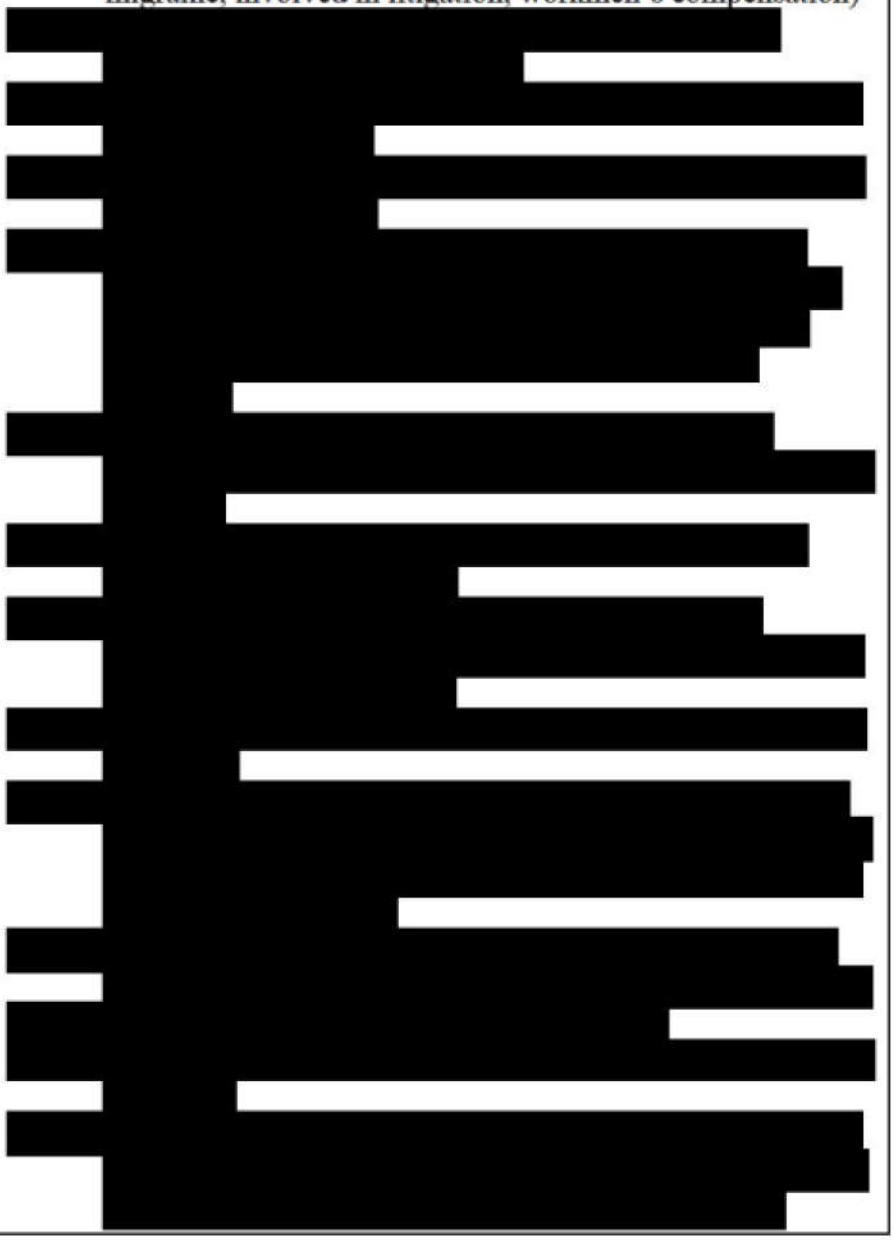
EC2. Has any pain-related diagnosis, medical/psychological condition or external factors that, in the investigator's medical judgment, might confound reporting of study outcomes (e.g. history of pelvic pain, anginal pain, chronic migraine, involved in litigation, workmen's compensation)



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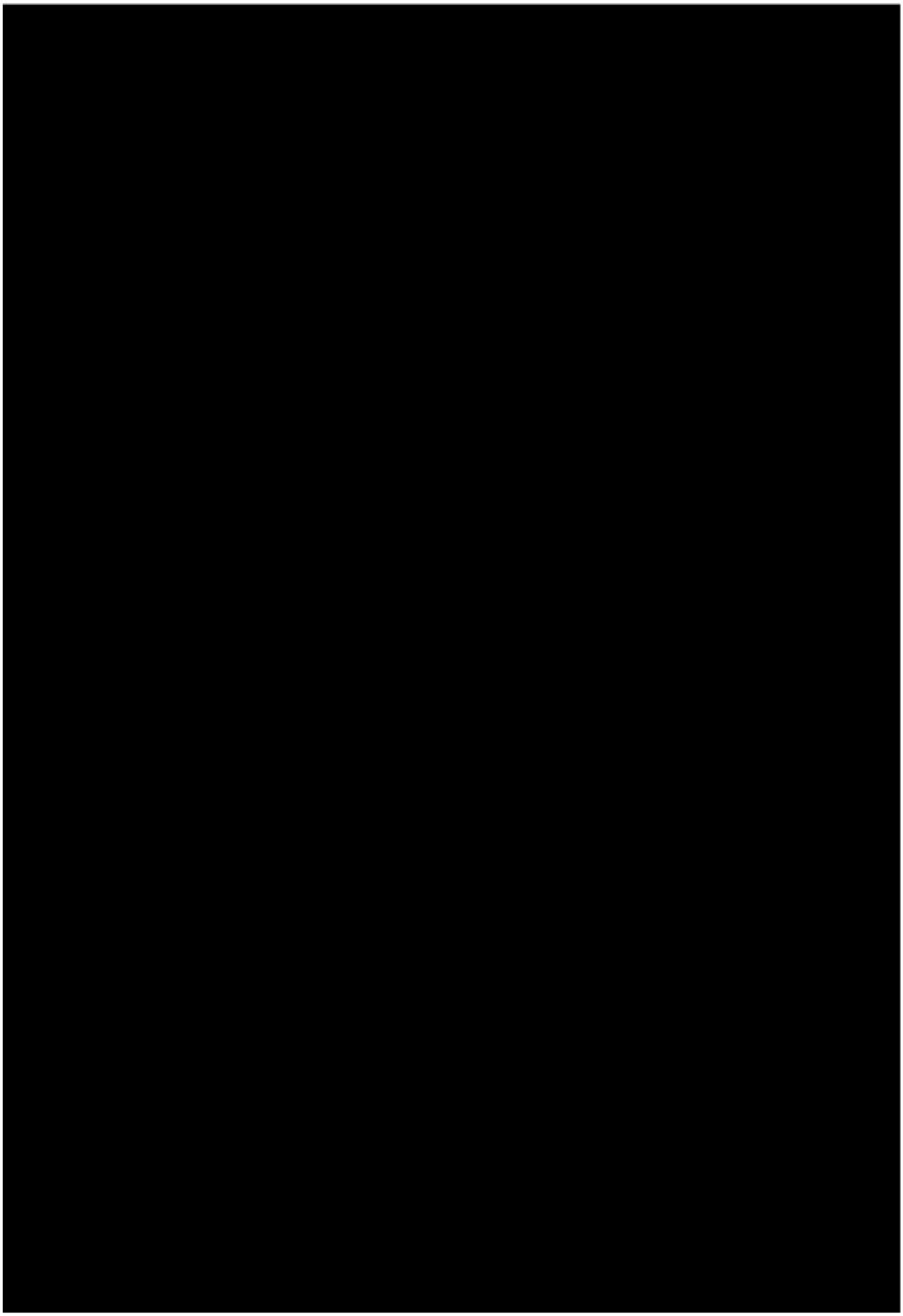
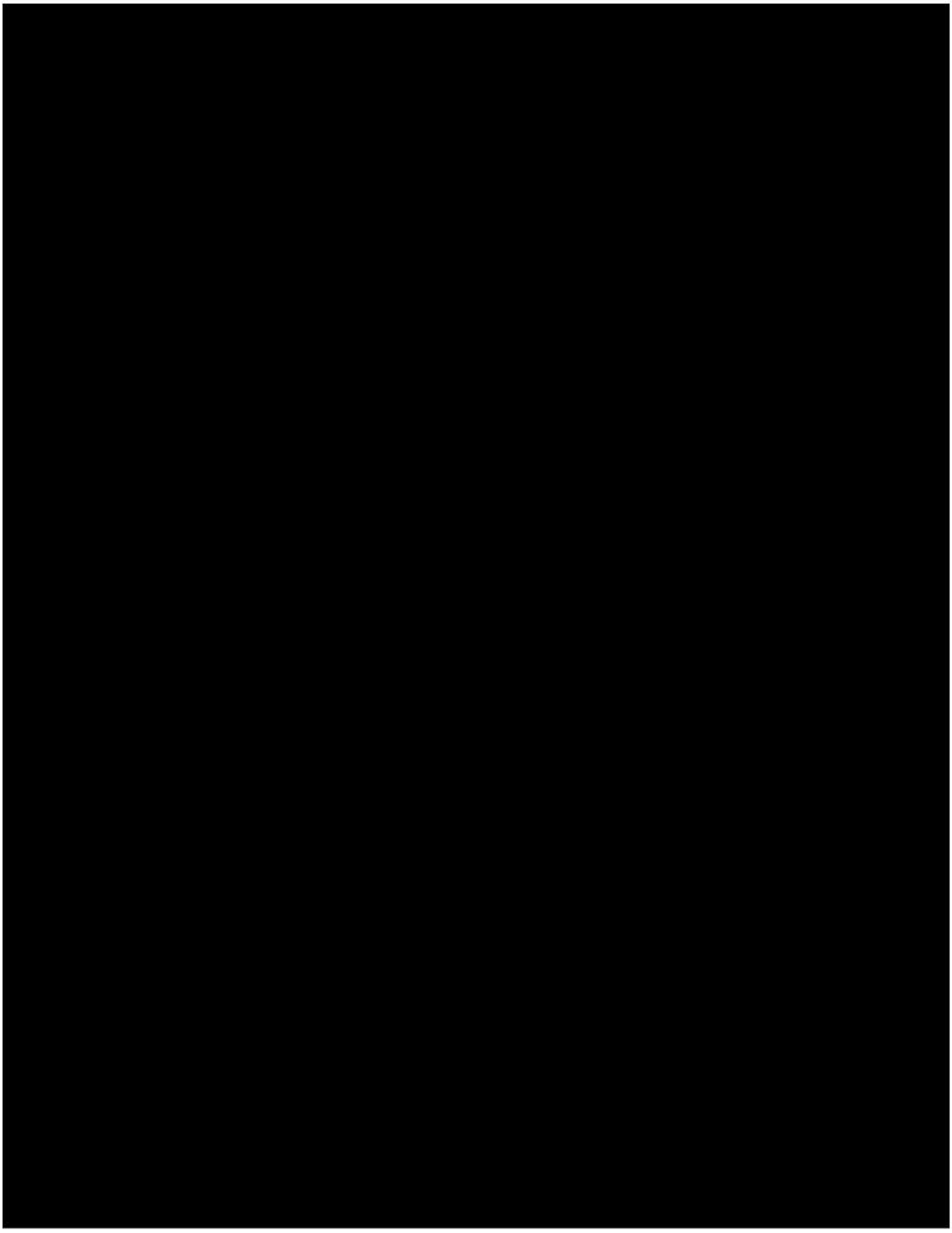
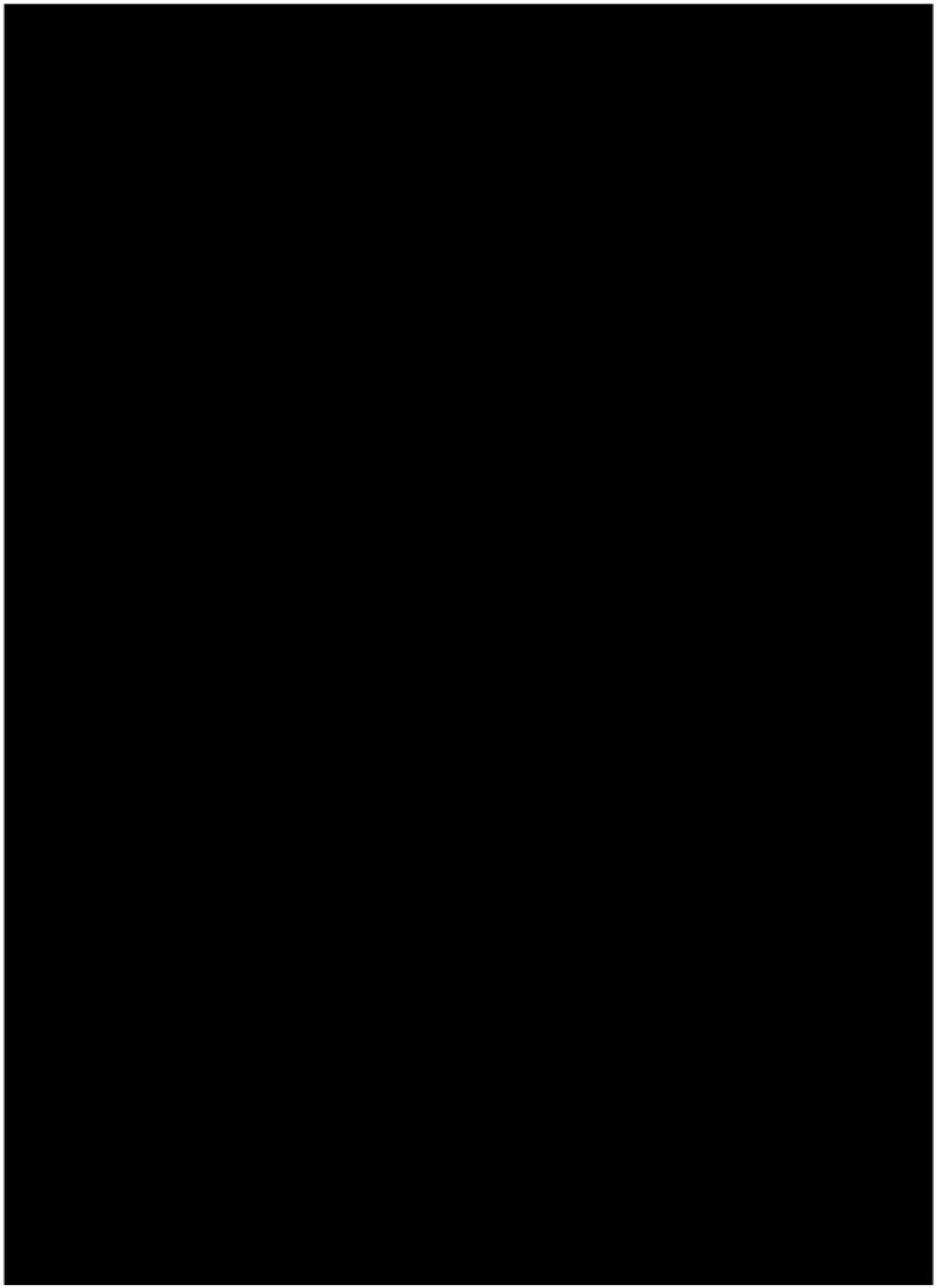
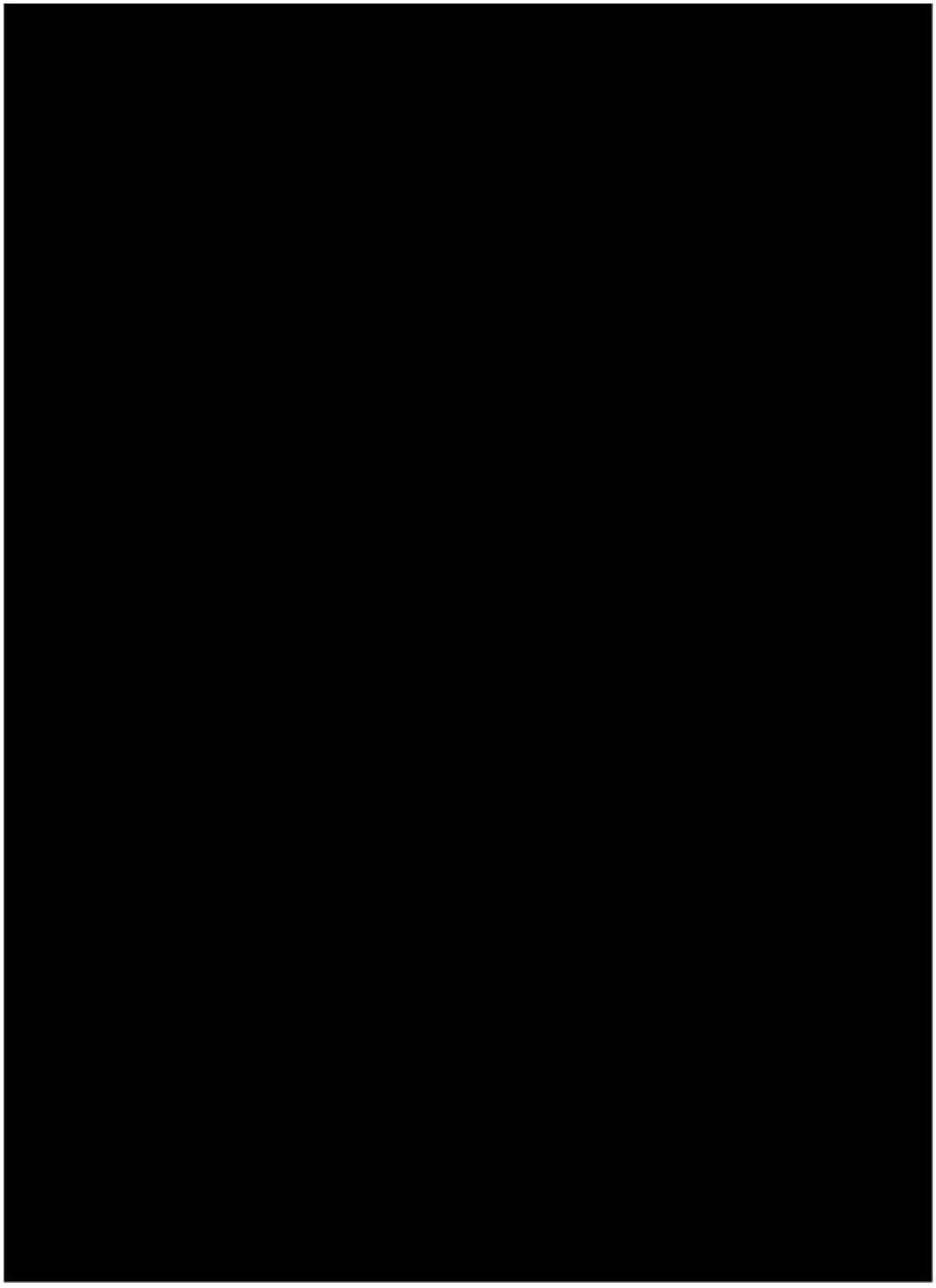
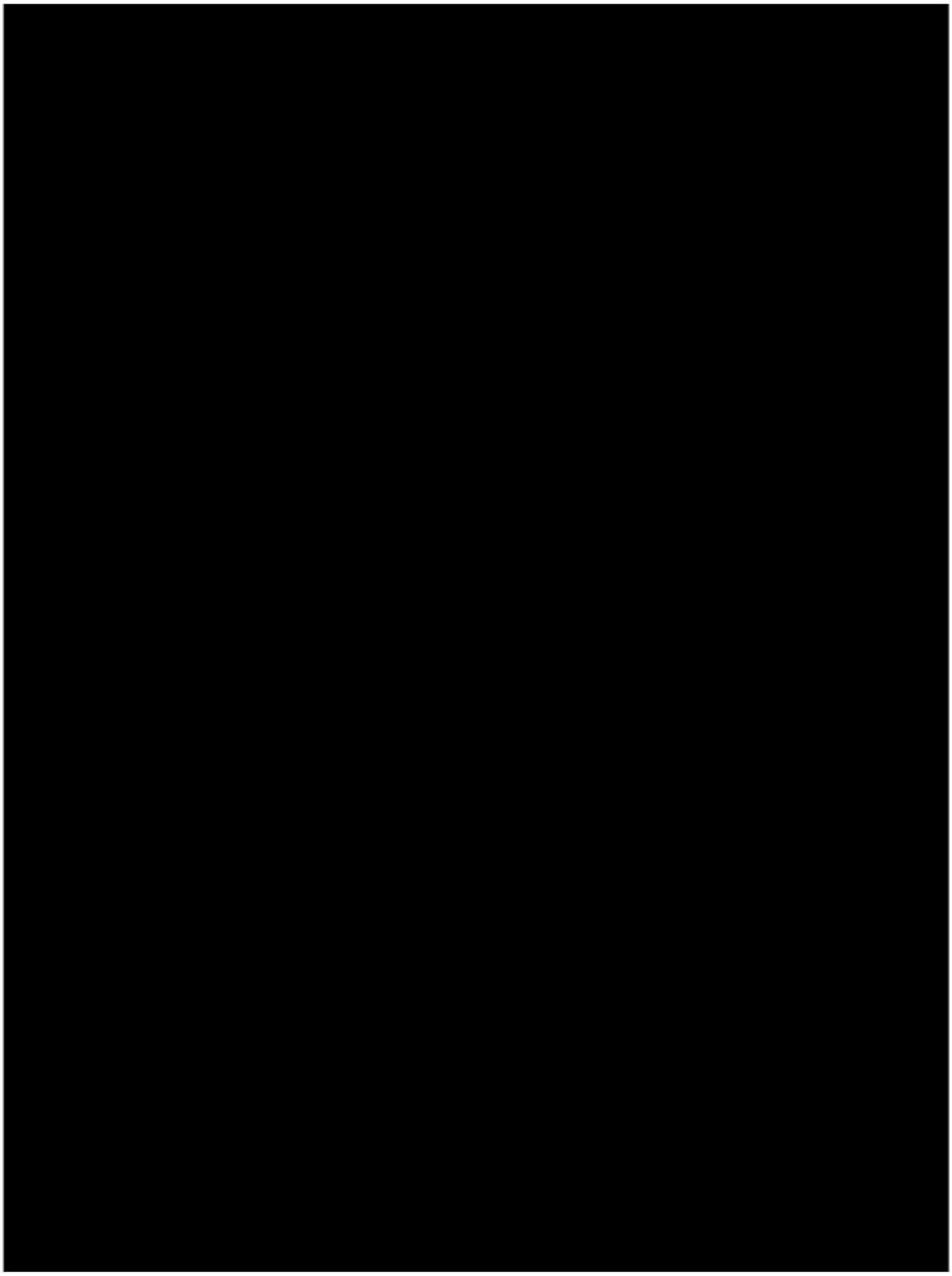
Statistical Methods	
Exploratory Statistical Methods	Univariate and multivariable models will be used to determine correlations in neurostimulation treatment effects on clinical outcomes
Sample Size Parameters	Sample size calculations for this exploratory study were calculated using an empirical analysis of current RELIEF data based an estimate of the number of subjects required to obtain a saturated level of model performance in prediction of pain scores in a subgroup given a set of covariate parameters. [redacted]

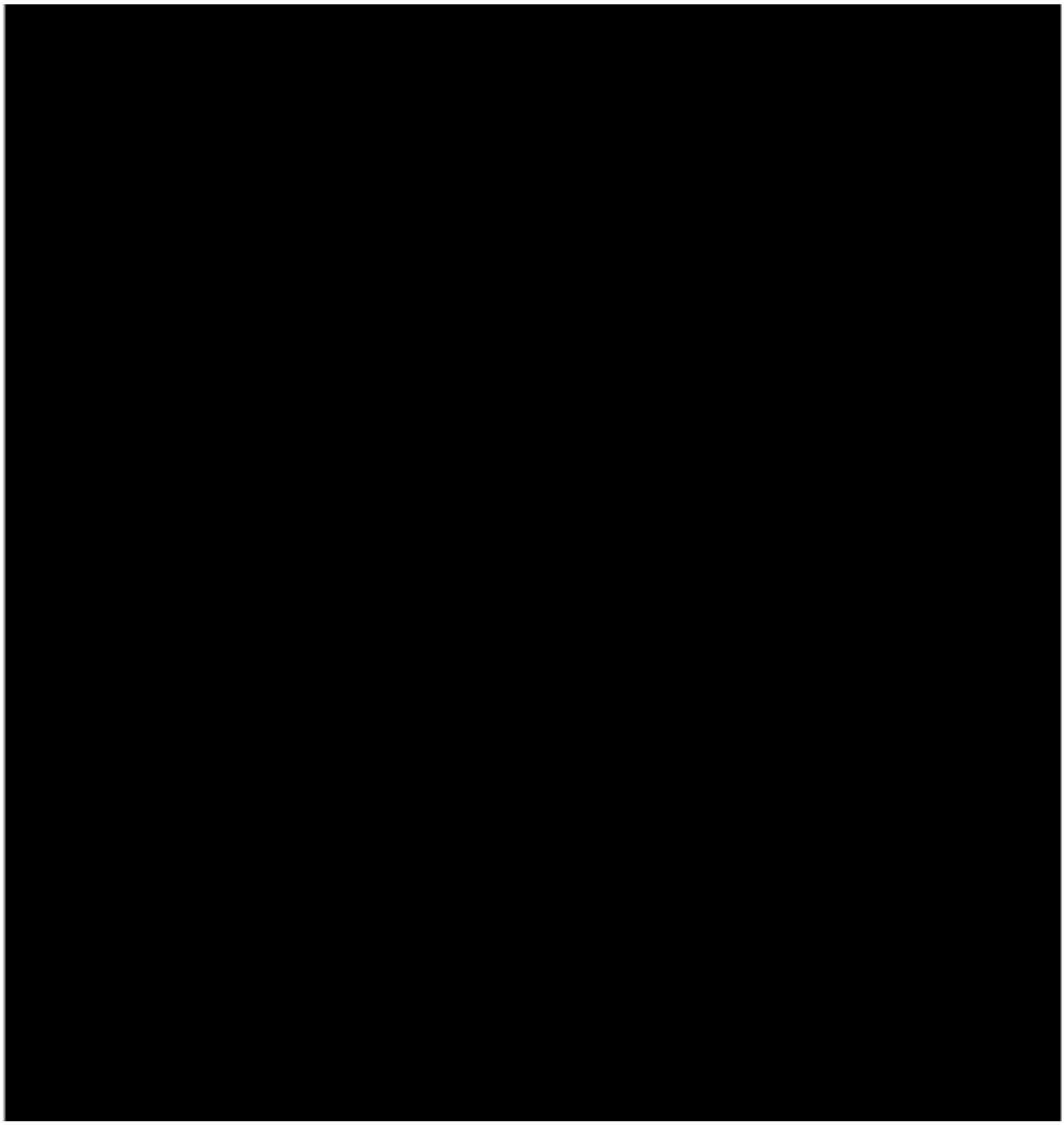












4. Introduction

NAVITAS Sub-study is being conducted under the RELIEF Study however subjects enrolled in NAVITAS will follow protocol requirements within this document only. Subjects enrolled in the NAVITAS protocol will not be enrolled in the RELIEF study and should be withdrawn from RELIEF if they are already enrolled.

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 radiofrequency (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 [1], [2], complex regional pain syndrome [3], and low back pain and leg pain [4]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 [5]. 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 [5].

In SCS pain relief is realized when the nerves that innervate the painful region(s) are electrically stimulated [6]. 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 [7]. However, recent studies indicate that effective pain relief may be obtained by employing stimulation without paresthesia ([8], [9], [10]).

4.3. *Biosensors*

Researchers have explored the idea that pain results in an imbalance of the autonomic nervous system. Thus detecting changes in autonomic tone through the use of biosensors may allow better prediction of pain status [11, 12, 13, 14, 15, 16, 17, 18, 19]. For example, heart rate variability could serve as a measure of stress and changes in perception of pain over time in patients diagnosed with chronic pain. Additional variables such as respiratory rate and activity, including motion, orientation, and sleep could also provide insight into changes in pain status.

5. Device Description

The study includes all commercially approved Boston Scientific neurostimulation systems indicated for the treatment of chronic pain, with the exception of Precision™ and Precision™ Plus, and commercially approved VitalConnect™ Sensor, indicated for continuous collection of physiological data in home and healthcare settings which is used with the physIQ VitaLink Solution.

5.1. *Boston Scientific Neurostimulator Systems (Commercial Device part of Standard of Care)*

Refer to the Directions for Use for detailed device description.

5.2. *PhysIQ VitaLink Solution*

The physIQ VitaLink Solution ("Platform") is a commercially available wireless remote monitoring system intended for use by healthcare professionals for continuous collection of physiological data in home and healthcare settings. The Platform consists of a VitalConnect Sensor ("chest-worn biosensor patch"), mobile application for data transmission, cloud-based IT infrastructure, and physiology analytics engine. The VitalConnect Sensor is a battery-operated adhesive patch with integrated sensors and a wireless transceiver. It is worn on the torso and measures and records physiological variables that can include, but are not limited to, electrocardiography (ECG) and activity. Data are transmitted wirelessly from the VitalConnect Sensor for storage and analysis. Subjects are provided the following commercial products with the VitalConnect Sensor:

- WEBCOL/Curity Alcohol Prep Pads,
- UNI-SOLVE Adhesive Remover Wipes
- Smartphone and charger

6. Study Objectives

The objective of the NAVITAS study is to characterize the relationship between select objective metrics and clinical outcomes in chronic pain patients treated with Boston Scientific commercially approved neurostimulation systems.

7. Study Endpoints

This study does not have any pre-defined endpoints but may include ad-hoc exploratory endpoint(s) to explore the relationship between metrics and clinical outcomes Exploratory endpoint(s) will be intended to generate hypotheses for future studies.

Consequently, no correction for multiple testing will be performed for exploratory endpoint(s). Any exploratory endpoint(s) will be clearly identified as such in study reports, as applicable.

7.1. *Safety Parameters*

The rate of neurostimulator device and procedure-related adverse events (AEs), Serious Adverse Events (SAEs), from informed consent through study exit will be reported.

8. Study Design

The NAVITAS Study is a prospective, post-market, non-randomized, multi-center, study.

[redacted]

8.2. *Treatment Assignment*

Consecutive eligible patients who consent to participation and have met all of the inclusion and none of the exclusion criteria will be enrolled.

8.2.1. Treatment

The study treatment will consist of neurostimulation trial therapy with any commercially approved Boston Scientific neurostimulator for pain. Subjects with a successful trial outcome may progress to permanent implant of a neurostimulation system. Neurostimulation therapy will be determined according to investigator discretion and site routine care, and in accordance with inclusion and exclusion criteria. [redacted]

9. Subject Selection

9.1. *Study Population and Eligibility*

Subjects enrolled in the NAVITAS study will be established patients in a medical practice (e.g. pain management, surgical, physical medicine and/or rehabilitation) who are eligible to receive neurostimulation therapy to treat their pain condition utilizing a commercially-approved Boston Scientific (BSC) neurostimulation system with the exception of Precision™ and Precision™ Plus. Inclusion and exclusion criteria are included, respectively, in Section 9.2 and 9.3, below.

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 8.3) is met.

Table 9.2-1: Inclusion Criteria

Clinical Inclusion Criteria	IC1. Study candidate is scheduled to be trialed, on-label, with a commercially approved Boston Scientific neurostimulation system for pain, per local directions for use (DFU) IC2. Provides signed, dated, and documented NAVITAS study informed consent on an Institutional Review Board (IRB) - approved informed consent form IC3. Is willing and able to comply with completing protocol required assessments and evaluations [redacted] IC10. 18 years of age or older when written informed consent is obtained [redacted]

Abbreviations: IRB : Institutional Review Board

9.3. *Exclusion Criteria*

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

Table 9.3-1: Exclusion Criteria

Clinical Exclusion Criteria	[redacted] EC2. Has any pain-related diagnosis, medical/psychological condition or external factors that, in the investigator's medical judgment, might confound reporting of study outcomes (e.g. history of pelvic pain, anginal pain, chronic migraine, involved in litigation, workmen's compensation) [redacted]

Abbreviations: BSC : Boston Scientific

10. Subject Accountability

10.1. *Point of Enrollment*

The point of enrollment in the NAVITAS Study is the time at which a subject signs and dates the valid, IRB/EC-approved NAVITAS informed consent form. No NAVITAS study-related procedures or assessments can take place until the NAVITAS informed consent form is signed.

10.2. *Withdrawal*

All subjects enrolled in the NAVITAS 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 NAVITAS clinical investigation, the reason(s) shall be reported. If such withdrawal is due to problems related to device safety or performance, the investigator shall ask for the subject's permission to follow his/her status/condition outside of the NAVITAS clinical study per standard of care.

Reasons for withdrawal include:

- physician discretion,
- subject choice to withdraw consent,
- subject's failure to meet inclusion or exclusion criteria after enrollment,
- failure to receive adequate pain relief during the Neurostimulation Trial,
- implant of a non-BSC neurostimulation system,
- lost to follow-up, or
- death.

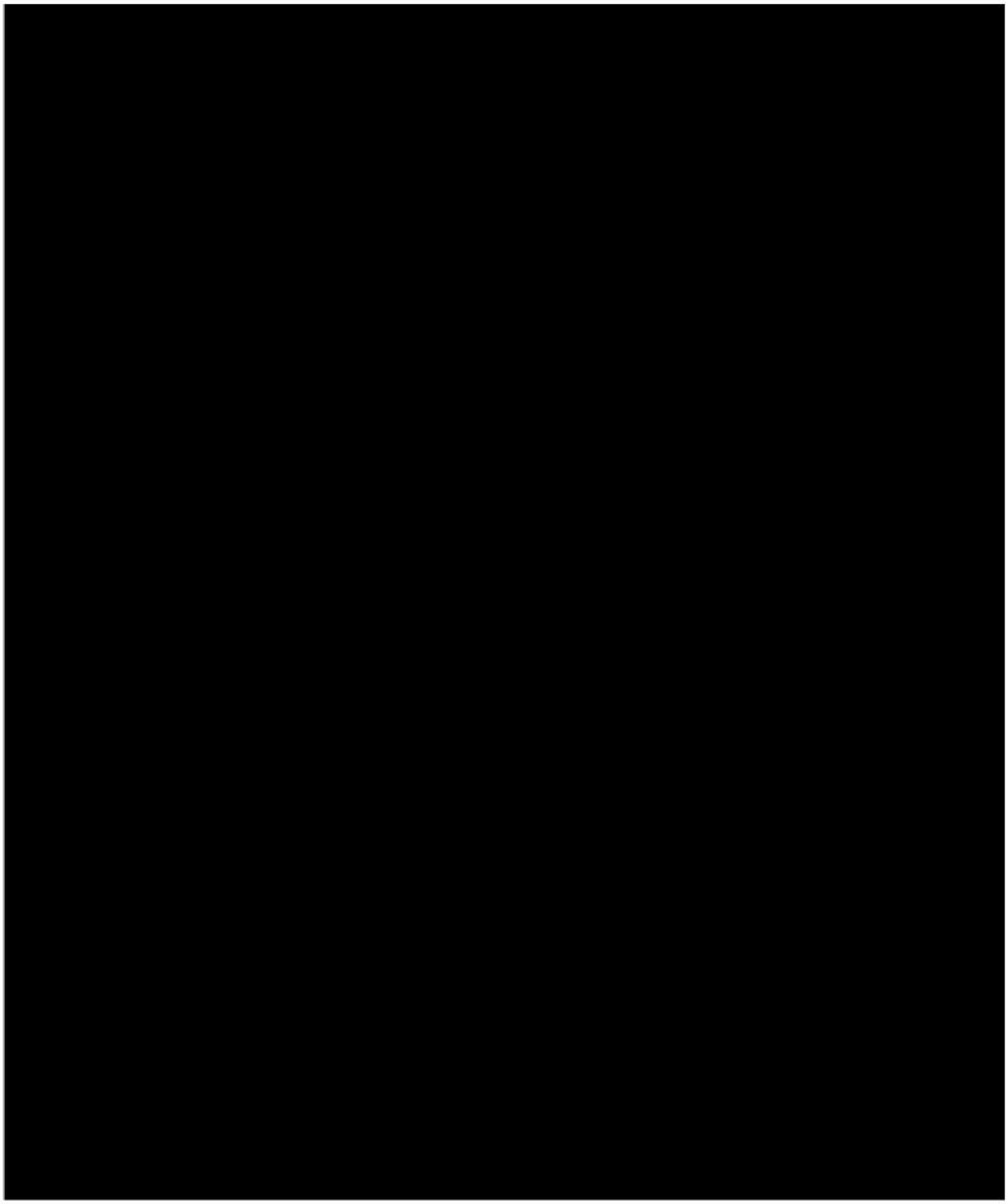
While study withdrawal is discouraged, subjects may withdraw from the study at any time, with or without reason, and without prejudice to further treatment. In all cases of withdrawal or discontinuation, the Investigator should make reasonable efforts to determine the reason for the subject's withdrawal.

Withdrawn subjects will be followed per the End of Study Action Plan as described in Section 10.5.

All applicable case report forms (CRFs) up to the point of subject withdrawal and an "End of Study" form must be completed. Any subject deemed "lost to follow-up" should have a minimum of three documented attempts to contact him/her prior to completion of the "End of Study" form.

Additional data may no longer be collected after the point at which a subject has been withdrawn from the study or withdraws consent, for whatever reason. All open adverse events should be closed or documented as unresolved. Data collected up to the point of subject withdrawal may be used and analyzed.

Withdrawn subjects will not be replaced.



10.4. *Enrollment Controls*

Enrollment will continue until one of the following events occurs:

- Up to 1,400 subjects are enrolled.
- Up to 960 enrolled subjects receive a permanent neurostimulator implant.
- The study is terminated at any time, at the study sponsor's discretion.

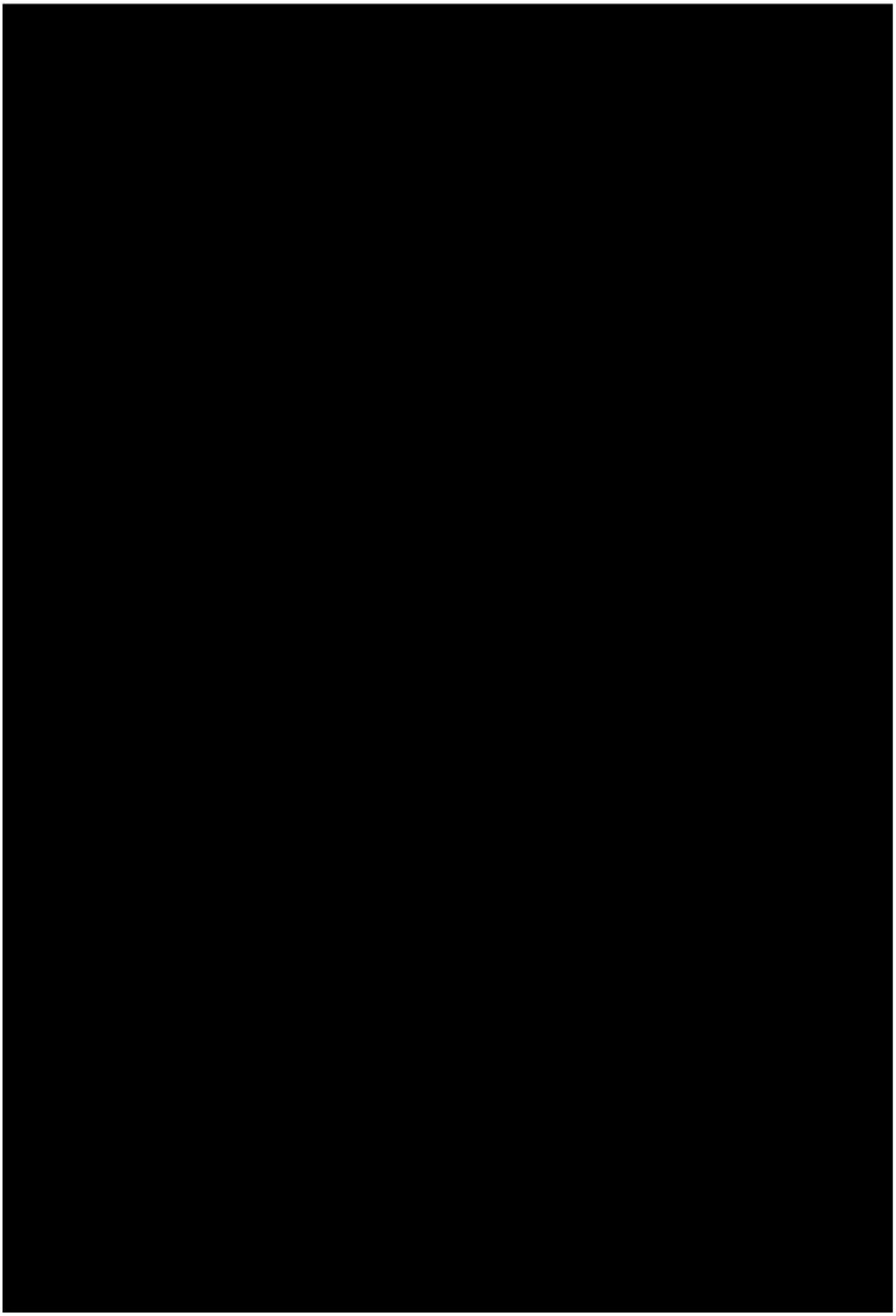
Enrollment controls will be implemented and communicated per the NAVITAS study Enrollment Communication Plan.

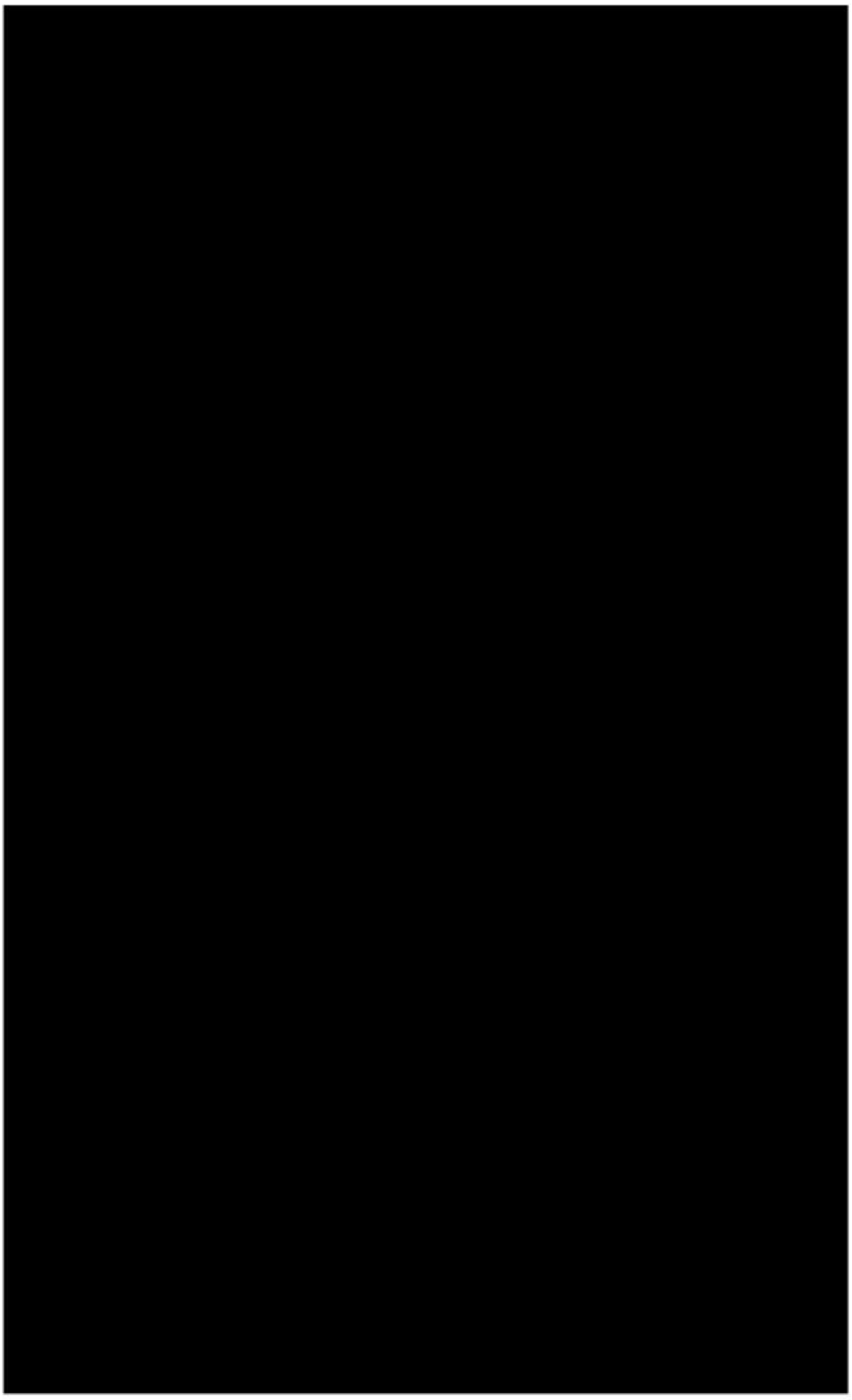
10.5. *End-of-Study Action Plan*

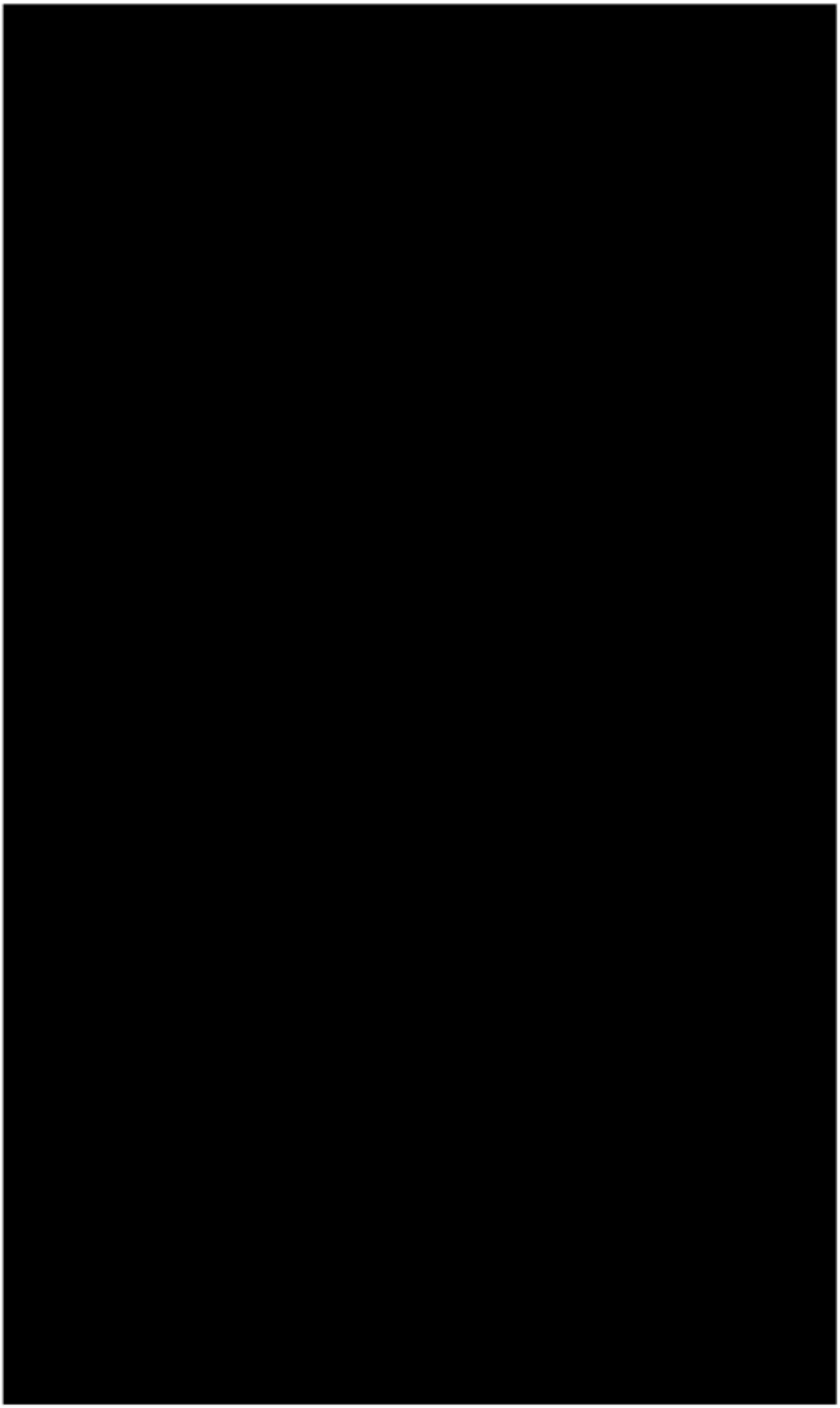
When each enrolled subject completes the NAVITAS Study, or withdraws, the subject exits the NAVITAS Study. If the subject is implanted, the subject may continue to use the neurostimulator system per the applicable Directions for Use and should be followed according to standard, routine medical care. The chest-worn biosensor, wrist-worn biosensor, study smartphone, and accessories should be returned by subjects who complete or withdraw from the NAVITAS Study to the site.

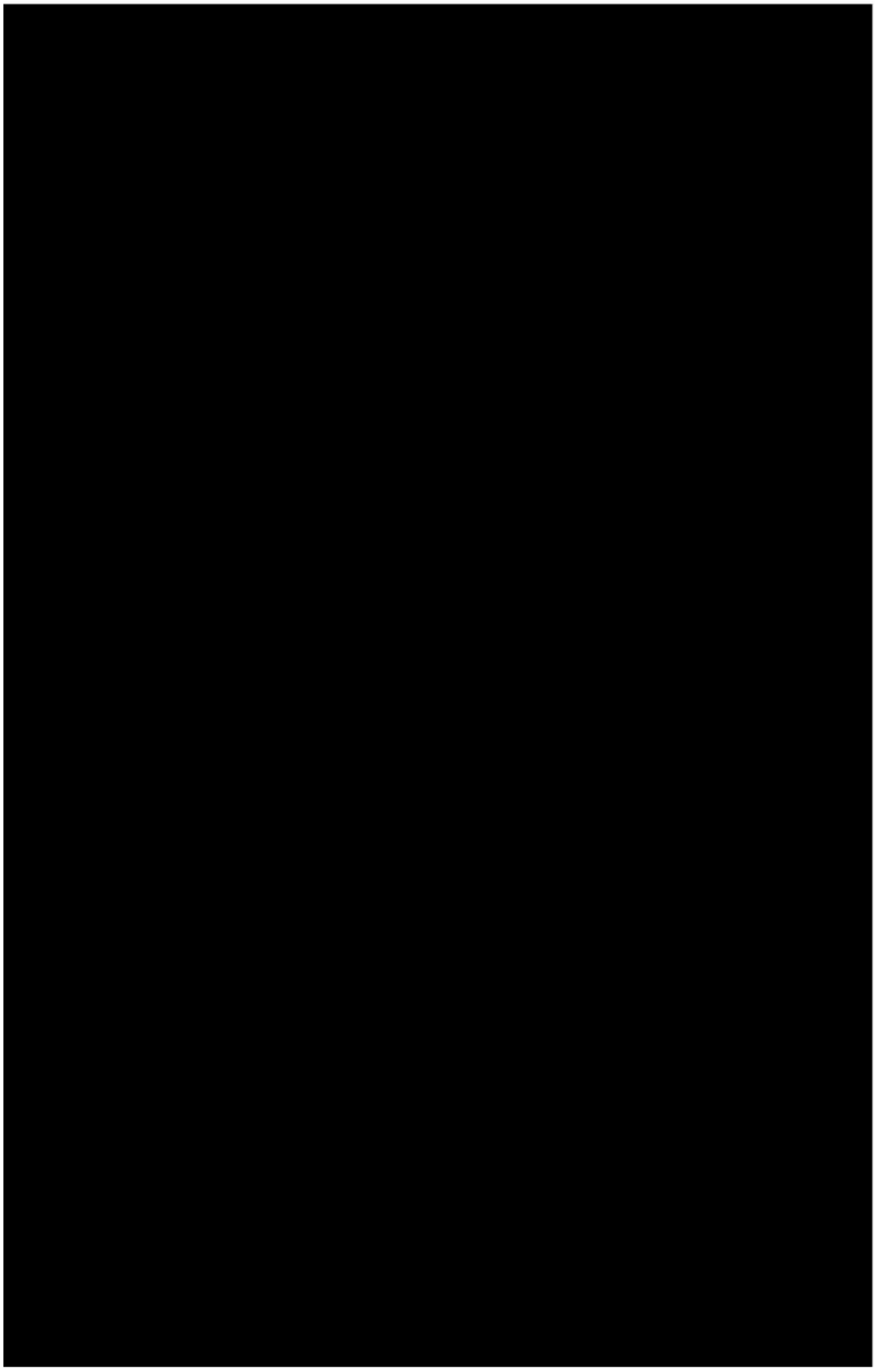
11. Study Methods

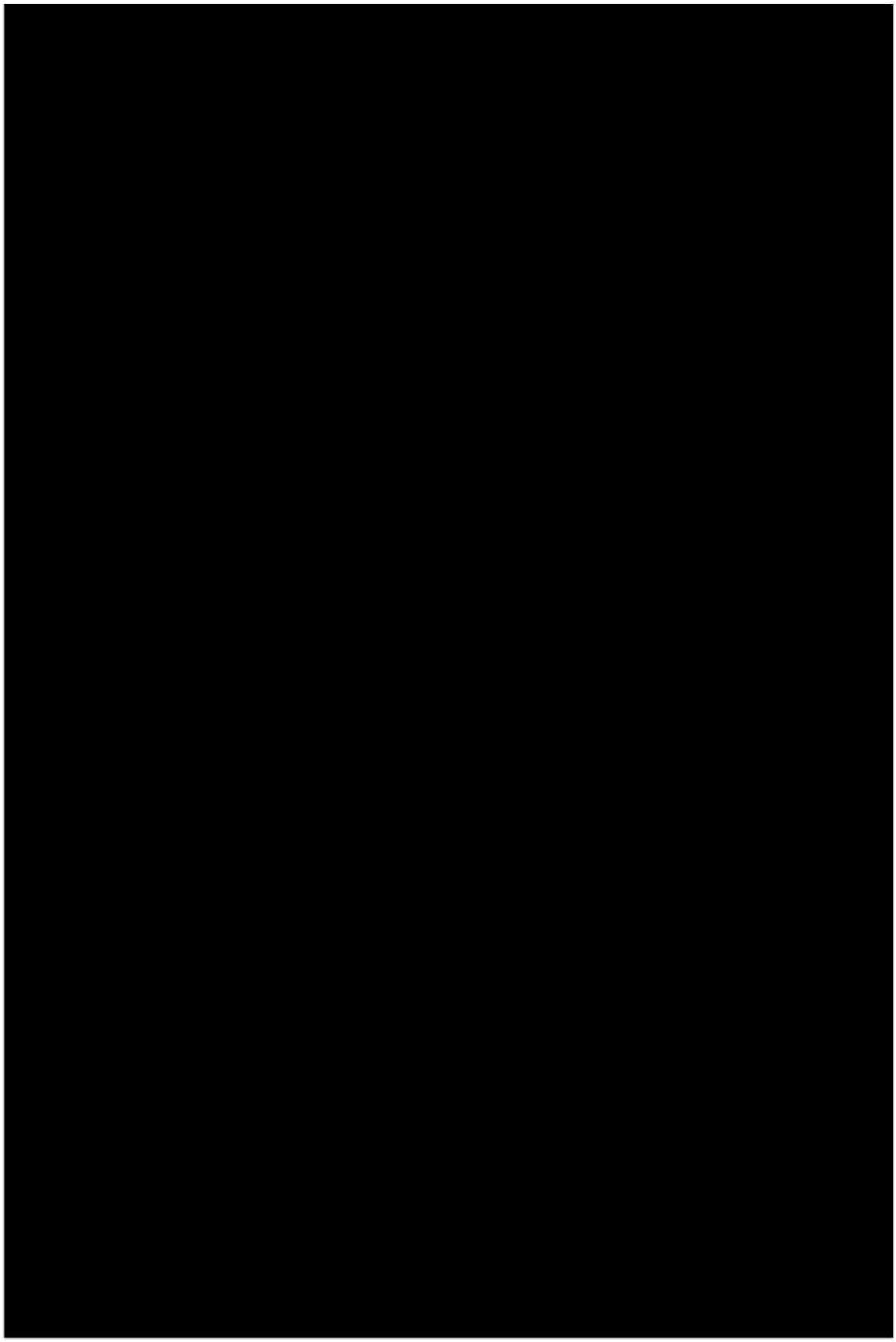
[redacted]

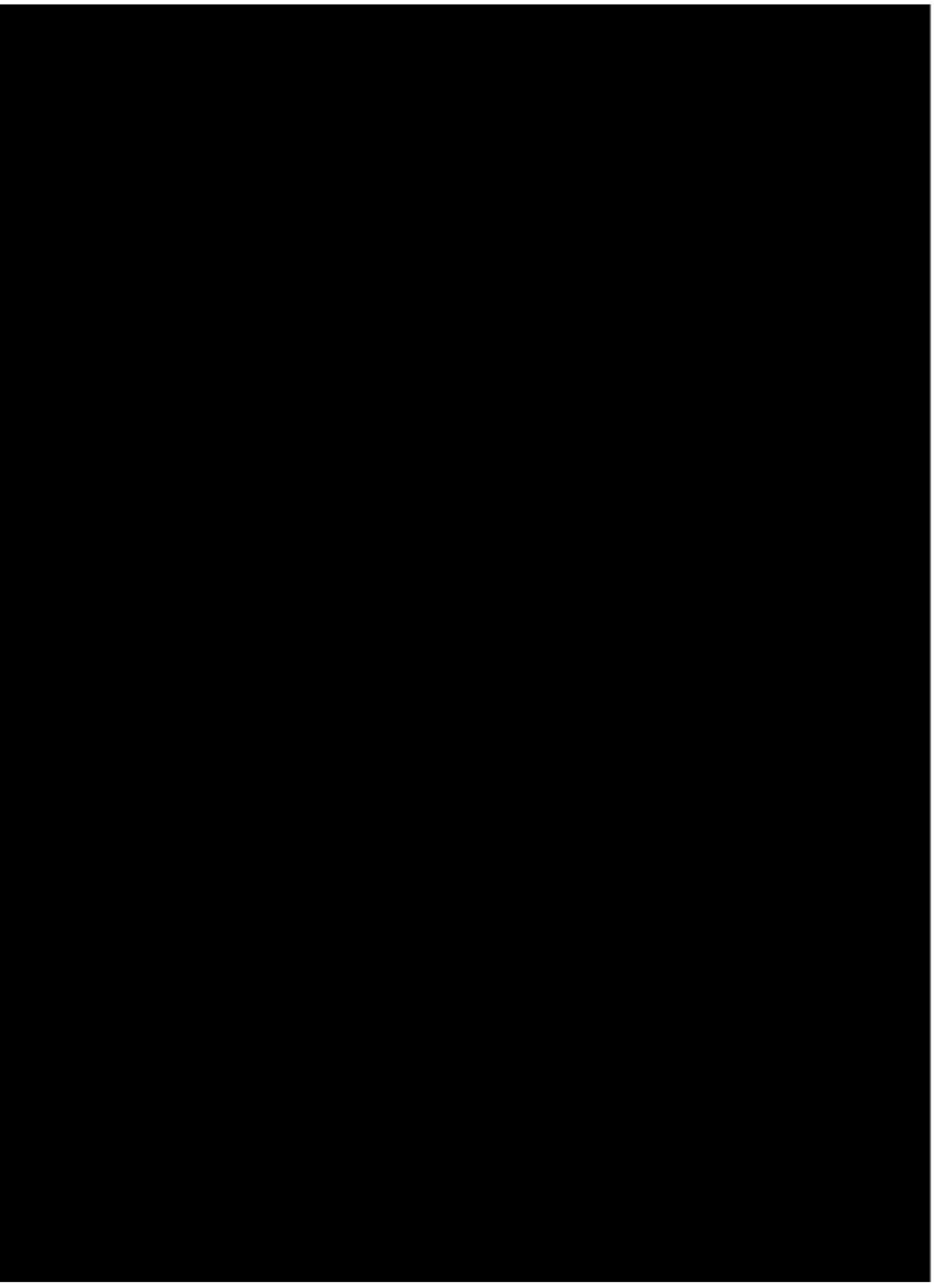












11.2. *Study Candidate Screening*

To determine eligibility for enrollment into the NAVITAS Study, the inclusion and exclusion criteria must be assessed. Screening is a process that includes criteria being assessed from the time of informed consent through the Baseline Visit. Subjects who have provided informed consent and who have been determined to not meet all eligibility requirements will be withdrawn. Those inclusion and exclusion criteria that are part of routine care for neurostimulation do not require informed consent. Patients who meet all inclusion criteria (as described in Section 9.2) and do not meet any exclusion criterion (as described in Section 9.3), may be offered participation in the NAVITAS study.

Subjects taking prescription opioids for primary chronic pain complaint (low back and/or leg pain) whose opioid medications are not stable for 30 days following informed consent will be withdrawn however may be reconsented and rescreened once 30 days have passed.

11.3. *Informed Consent*

After a patient has been identified as a potential NAVITAS study candidate, written Informed Consent must be obtained prior to any NAVITAS study related assessments.

- The context of the NAVITAS 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.

11.4. *Baseline Visit (In-office)*

The NAVITAS study subject Baseline Visit:.

- The NAVITAS visit must occur $\geq 8 - 14$ days prior to Stimulation Trial Procedure for De Novo Cohort subjects.
- This is Day 0 for Existing RELIEF cohort.
- Refer to Table 11.1-1: Data Collection Schedule for visit window and study assessments.

Subjects will be trained on the use of at home devices: a wrist-worn biosensor, a chest-worn biosensor, a pain log and a smart phone/ eDiary Application. Subjects will be instructed to wear

the wrist-worn biosensor, complete the eDiary application and Pain Log daily at home until the 12-Month Visit. Subjects will be asked to bring all devices with them to all follow-up visits.

11.5. *Baseline Period (At Home)*

- Refer to Table 11.1-1: Data Collection Schedule for visit window and study assessments.

11.6. *Neurostimulation Trial Procedure Visit (In-office, Day 0 for De Novo Cohort)*

- De Novo Cohort only
- Refer to Table 11.1-1: Data Collection Schedule for visit window and study assessments.

11.7. *Trial Period (At Home)*

- De Novo Cohort only
- Chest-worn biosensor patch Wrist-worn biosensor, Pain Log, and eDiary application daily during trial period

11.8. *End of Neurostimulation Trial Period Visit (In-office)*

- De Novo Cohort only
- Refer to Table 11.1-1: Data Collection Schedule for visit window and study assessments.

11.9. *IPG Implantation and Activation Visit (In-office)*

- Up to 12 Month Post Neurostimulation Trial Procedure Visit
- Refer to Table 11.1-1: Data Collection Schedule for visit window and study assessments.

11.10. *Month 1, 2, 3 Post Neurostimulation Trial Procedure Visit (De Novo Cohort)/Post Enrollment (Existing Cohort) Period (At Homes)*

- Refer to Table 11.1-1: Data Collection Schedule for visit window and study assessments.

11.11. *3-Month Post Neurostimulation Trial Procedure Visit*[4] *(De Novo Cohort only) Post Enrollment (Existing Cohort) Visit (In-office, 90 days ± 10 days)*

- Refer to Table 11.1-1: Data Collection Schedule for visit window and study assessments.

11.12. *Month 4, 5, 6 Post Neurostimulation Trial Procedure Visit (De Novo Cohort)/Post Enrollment (Existing Cohort) Period (At Home)*

- Refer to Table 11.1-1: Data Collection Schedule for visit window and study assessments.

[4] Only for De Novo cohort subjects who have undergone IPG Implantation prior to this visit

11.13. *6-Month Post Neurostimulation Trial Procedure Visit* (De Novo Cohort Existing Cohort, as applicable)

- Refer to Table 11.1-1: Data Collection Schedule for visit window and study assessments.

11.14. *Month 7, 8, 9 Post Neurostimulation Trial Procedure Visit (De Novo Cohort)/ Post Enrollment (Existing Cohort) Period (At Home)*

- Refer to Table 11.1-1: Data Collection Schedule for visit window and study assessments.

11.15. *9-Months Post Neurostimulation Trial Procedure Visit[4] (De Novo Cohort only, In-office, 270 days ± 30 days)*

- Refer to Table 11.1-1: Data Collection Schedule for visit window and study assessments.

11.16. *Month 10, 11, 12 Post Neurostimulation Trial Procedure Visit (De Novo Cohort)/ Post Enrollment (Existing Cohort) Period (At Home)*

- Refer to Table 11.1-1: Data Collection Schedule for visit window and study assessments.

11.17. *12-months Post Neurostimulation Trial Procedure (De Novo and Existing, as applicable) (In-office, 365 ± 60 days Post Neurostimulation Trial Procedure Visit)/Post Enrollment (Existing) Visit (In-office, 365 ± 60 days)*

- Refer to Table 11.1-1: Data Collection Schedule for visit window and study assessments.
- NAVITAS (De Novo and Existing) Subjects may end study participation after this visit or elect to continue with Navitas optional visits and at home activities.

11.18. *Months 13-24 Post Neurostimulation Trial Procedure Visit Period (Optional De Novo and Optional Existing Cohort[5]) Period (At Home)*

- Refer to Table 11.1-1: Data Collection Schedule for visit window and study assessments.

11.19. *Optional 24-months Post Neurostimulation Trial Procedure Visit[5] (In-office, 720 ± 60 days Post Neurostimulation Trial Procedure Visit)*

- Refer to Table 11.1-1: Data Collection Schedule for visit window and study assessments.

11.20. *Months 25-36 Post Neurostimulation Trial Procedure Visit Period (Optional De Novo and Optional Existing Cohort[6]) Period (At Home)*

- Refer to Table 11.1-1: Data Collection Schedule for visit window and study assessments.

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[5] NAVITAS assessments optional only for Subjects that have not ended study participation and opted to continue NAVITAS Study follow up for > 12 months

11.21. *Optional 36-months Post Neurostimulation Trial Procedure Visit[5](In-office, 1095 ± 60 days Post Neurostimulation Trial Procedure Visit)*

- Refer to Table 11.1-1: Data Collection Schedule for visit window and study assessments.

11.22. *Unscheduled Study Visits*

Subjects may have unscheduled study visits as needed for device related visits (e.g., reprogramming, replacement, revision) or evaluation of adverse events. Refer to Table 11.1-1: Data Collection Schedule for visit window and study assessments.

11.23. *Study Completion*

An enrolled subject may complete participation in the NAVITAS Study in one of several ways:

- De Novo subjects experiencing a negative trial complete the study at the End of the Neurostimulation Trial Period visit; or in case of Permanent trials, after the trial lead(s) explant surgery.
- De Novo subjects who experienced a successful trial but do not receive a permanent implant within 12 months complete the study at the 12-months Post Neuromodulation Trial Visit.
- Existing Subjects that complete the study at the 12-months Post Enrollment Visit and decide not to continue with optional follow-up.
- De Novo Subjects that complete the study at the 12-months Post Neurostimulation Trial Visit and decide not to continue with optional follow-up.
- Subjects who withdraw, die, or become lost to follow up are considered to have exited the NAVITAS Study. Withdrawn subjects will not be replaced.
- Subjects who complete their 36-Months Post Neurostimulation Trial Procedure Visit.

After each subject completes the NAVITAS Study, medical care will continue per local treatment protocols.

11.24. *Source Documents*

See below Source Documentation Requirements for NAVITAS study source documentation requirements

Table 11.24-1: Source Documentation Requirements

Requirement	Disposition
Informed Consent Form and Consent Process Documentation	Retained at study site
Inclusion and Exclusion Criteria Documentation	Retained at study site
Saliva related collection and transmission	Retained at study site or analysis vendor

Table 11.24-1: Source Documentation Requirements

Requirement	Disposition
Imaging (MRI/CT/Fluoroscopy)	Retained at study site
Medical Records	Retained at study site
SCS Data	Electronic data collection platform/EDC
NAVITAS Study Questionnaires (in-office)	Retained at study site and/or electronic data collection platform / EDC
Technical Source Forms or other source documentation worksheets	Retained at study site
Chest-worn biosensor data	Retained in secure data server
Wrist-worn biosensor data	Retained in secure data server
Pain Log	Retained in secure data server
eDiary application Questionnaires data	Retained in secure data server
eDiary application Voice Recordings	Retained in secure data server

12. Statistical Considerations

12.1. *Endpoints*

12.1.1. Exploratory Endpoints

This study does not have any pre-defined endpoints but may include ad-hoc exploratory endpoint(s) to explore the relationship between metrics and clinical outcomes

Exploratory endpoint(s) will be intended to generate hypotheses for future studies. Consequently, no correction for multiple testing will be performed for exploratory endpoint(s). Any exploratory endpoint(s) will be clearly identified as such in study reports, as applicable.

12.1.1.1. Hypotheses

There are no formal hypotheses for this study.

12.1.1.2. Sample Size

Sample size calculations for this exploratory study were calculated based an estimate of the number of subjects required to obtain a saturated level of model performance in prediction of pain scores in a subgroup given a set of covariate parameters.

[redacted]

[redacted]

12.1.1.3. Statistical Methods

Univariate and multivariable models will be used to determine correlations between neurostimulation treatment parameters on clinical outcomes.

Data from all eligible patients will be used for analysis. Subgroup/cohort analyses will be defined by demographics, pain diagnosis, treatment parameters, treatment efficacy and medication use.

Missing data from biosensors will not be imputed. A sensitivity analysis using LOCF imputation of clinical outcomes will be completed. [redacted]

12.2. *General Statistical Methods*

[redacted]

[redacted]

12.2.2. Control of Systematic Error/Bias

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

A chest-worn biosensor patch, a wrist-worn biosensor and eDiary Application will be provided to all patients enrolled in the study. Patients are reminded to complete questionnaires on a schedule and monitored during the study duration.

12.3. *Data Analyses*

All consented subjects will be included in analyses. Subjects who wear a chest-worn biosensor patch, and/or a wrist-worn biosensor will be included in safety analyses.

[redacted]

[redacted]

[redacted]

12.3.6. Changes to Planned Analyses

Any changes to the planned statistical analyses will be documented. Rationale for changes to planned analyses as noted in this protocol will be included in the final study report and other reports, as applicable.

13. Data Management

13.1. *Data Collection, Processing, and Review*

Subject study data will be recorded in a limited access secure electronic data capture (EDC) system. The chest-worn biosensor patch and/or wrist-worn biosensor data and smartphone data will be transferred via encrypted processes and will be stored in a secure server.

The clinical database will reside on a production server hosted by Medidata. All changes made to the clinical data will be captured in an electronic audit trail and available for review by Boston Scientific Corporation (BSC) 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. Study data collected, reported, maintained and stored by the study vendor will be maintained by the study vendor on a secure server, with access allowed only by authorized individuals.

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 on an electronic data collection platform at the clinical site (e.g. iPad). After completion by the subject/clinician, data from the electronic questionnaires will be transmitted directly into the EDC system.

[redacted]

13.2. *Study Assessments*

13.2.1. Chest-worn Biosensor Patch

The chest-worn biosensor patch (VitalConnect Sensor) is a commercially available battery-operated adhesive patch with integrated sensors and a wireless transceiver. It is worn on the torso and measures and records physiological variables that can include electrocardiography (ECG), skin temperature, activity and posture (body position relative to gravity). Data are transmitted wirelessly from the VitalConnect Sensor for storage and analysis.

Chest-worn biosensor patch wear requirements reflect total days. Subjects are encouraged to wear the patch for consecutive days however one day breaks are allowed in between patch changes. Breaks do not count towards the total.

13.2.2. Wrist-worn Biosensor

Subjects will also be asked to wear a commercially available wrist-worn biosensor, similar to a watch or wrist-worn fitness band. The wrist-worn biosensor will also collect biosensor data, such as heart rate and may be used to collect the pain log and respond to questions and/or questionnaires. Responses may be provided via voice responses.

The information collected from both the biosensors will be streamed to a secured data server. The wrist-worn biosensor may have other functionality removed.

13.2.3. Pain Log:

The NAVITAS study will utilize an off-the shelf, commercially available, customized smartphone or wrist-worn biosensor with the study-specific Pain Log loaded onto the device, as a data collection device. The subject will use the Pain Log to record changes in pain-level. The information collected will be streamed to a secured data server. The study-specific smartphone may have other functionality removed.

13.2.4. eDiary Application with Voice recording

The NAVITAS study will utilize an off-the shelf, commercially available, customized smartphone with the study-specific eDiary Application loaded onto the smartphone, as a data collection device. The subject will use the eDiary Application to respond to questions and/or questionnaires. Subject will also use voice recording in the eDiary Application to provide a brief (approximately two to five minutes) voice recording. Subjects will not be asked to record protected health information. Cell signal capability will be used to retrieve and report data to a secure data server. The study-specific smartphone will have other functionality restricted.

13.2.5. Fear Avoidance Beliefs Questionnaire (FABQ)

The Fear Avoidance Beliefs Questionnaire (FABQ) was developed by Waddell to investigate fear-avoidance beliefs among low back pain subjects in the clinical setting [20]. This survey is designed to assist in predicting which subjects may have a high pain avoidance behavior. This questionnaire consists of 16 items, with each item scored from 0-6. Higher scores on the FABQ are indicative of greater fear and avoidance beliefs.

The FABQ consists of 2 subscales. The first subscale (items 1-5) is the Physical Activity subscale (FABQPA), and the second subscale (items 6-16) is the Work subscale (FABQW). It is expected to take about three to five (3-5) minutes to complete.

13.2.6. Pain Catastrophizing Scale (PCS)

The Pain Catastrophizing Scale measures cognitive responses to chronic pain, specifically a subject's rumination, magnification and feelings of helplessness relative to their pain. It consists of thirteen (13) questions and is expected to take about three to five (3-5) minutes to complete.

13.2.7. Optional Magnetic Resonance Imaging

A thoracolumbar MRI may optionally be performed for the De Novo cohort to confirm spine anatomy and planned neurostimulator lead position. MRI of subject's spine and planned electrode location will be collected during Baseline period prior to Trial Procedure for the de novo cohort. If an MRI was performed up to 6 months prior to consent as per standard of care, it does not need to be repeated for study purposes.

13.2.8. Optional Computerized Axial Tomography (CT)

A CT scan of subject's spine and lead electrode location may optionally be collected after receiving the permanent neurostimulator implantable pulse generator implant, to confirm subject spine anatomy and placement of permanent neurostimulator Implantable Pulse Generator (IPG) lead position.

13.2.9. Fluoroscopy

Standard of care thoracic and lumbar imaging will be collected at the Neurostimulator Trial Stimulation Procedure and permanent neurostimulator IPG Implantation. Images should reflect

final lead spinal placement from these procedures and be marked to denote vertebral level. An optional thoracic and lumbar image may be taken to show the location of the leads in the spine at the End of Trial Procedure Visit for subjects who sign optional NAVITAS informed consent addendum

[redacted]

13.2.11. 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 study procedure and/or device, action taken and outcome. All device-related and procedure-related adverse events, all serious adverse events and serious adverse device effects will be reported from the time of enrollment until the end of study participation.

13.2.12. 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).

13.2.13. 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.

13.2.14. Concomitant Medications

All prescribed 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, start and stop dates, indication or purpose, dose, frequency, and route of administration.

13.2.15. Demography

Demographic information will include birth year, birth day and month (if allowed by local regulations), gender, and race/ethnicity.

13.2.16. Ease-of-Use Questionnaire

The Ease-of-Use Questionnaire asks questions about the subject's ease in using the various device components. The questionnaire asks the subject to rate how strongly they agree or disagree with statements on how easy it is to use their stimulation device system. This questionnaire utilizes a 7-point scale ranging from 'completely agree' to 'completely disagree'. The ease-of-use questionnaire is a direct global measure of the patient's experience with the device.

13.2.17. End of Trial Period Evaluation

The End of Trial Period Evaluation is the clinician's professional assessment of whether the subject is a candidate for permanent implantation of a neurostimulation system based on the outcome of the subject's device trial.

13.2.18. End of Study

End of Study form will collect the date the subject completed participation in the study and the reason (i.e. completed study, withdrawal, etc.).

13.2.19. 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 "thermometer" is a visual analog scale used to record the subject's self-rated health on a scale from 0 'the worst health you can imagine' to 100 'the best health you can imagine'.

13.2.20. Maintenance of Pain Coverage (MPC)

MPC consists of two items assessing new areas of pain that the subject has developed since first receiving neurostimulation treatment, as assessed by the treating clinician. Item one assesses whether the subject has developed any new areas of pain, and the second item assesses the extent of coverage by paresthesia in these areas.

13.2.21. Medical History

Medical history will include medical and procedural history relating to pain management, onset of chronic pain, and all pain-related diagnoses.

13.2.22. Oswestry Disability Index version 2.1a (ODI v2.1a)

Oswestry Disability Index questionnaire is to be used when the targeted pain area involves the back or legs.

ODI v2.1a assesses the degree of patient 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.

13.2.23. Pain Intensity

Pain Intensity is a questionnaire assessing the intensity of the subject's different areas of pain. 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".

13.2.24. Paresthesia Coverage

Paresthesia Coverage assesses how much of the subject's painful areas are covered by neurostimulation-induced paresthesia. Paresthesia coverage is expressed as a percentage from 0 – 100%.

13.2.25. 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 enrollment in the study. Subjects will rate themselves as: very much improved; much improved; minimally improved; no change; minimally worse; much worse; or very much worse.

13.2.26. Percent Pain Relief (PPR)

PPR is a three-item questionnaire assessing how much of the subject's different areas of pain from before the pre-study neurostimulation trial has been relieved by the current neurostimulation treatment. Pain relief is expressed as a percentage from 0 – 100%.

Targeted pain is defined as areas of pain, indicated at Baseline that the clinician will attempt to address with the neurostimulation system.

13.2.27. Physical Exam

A complete physical exam will be performed by the clinician.

13.2.28. Procedure Information

General information will be collected regarding all neurostimulation procedures performed during the study, including all neurostimulation trial procedures and IPG implantation procedures.

13.2.29. 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

13.2.30. Satisfaction with Stimulation Treatment (SST)

SST assesses the subject's satisfaction with stimulation treatment across three domains: comfort, coverage, and global satisfaction.

13.2.31. Short Form McGill Pain Questionnaire (SF-MPQ-2)

SF-MPQ-2 provides a comprehensive measure of pain symptoms for both neuropathic and non-neuropathic pain conditions. It is a self-administered questionnaire comprised of 22 11-point NRS items. SF-MPQ-2 includes four subscales: Continuous Pain descriptor score, Intermittent Pain descriptor score, Predominantly Neuropathic Pain descriptor score, and Affective descriptor score. The scores from the four subscales are averaged to compute the overall SF-MPQ-2 score.

13.2.32. Work Productivity and Activity Impairment Questionnaire: Specific Health Problem Version 2.0 (WPAI:SHP)

The WPAI:SHP is a patient-reported quantitative assessment 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 consists of six questions addressing the subject's employment status, true work status, productivity while working, and ability to carry out regular daily activities.

13.2.33. Fitness Assessments

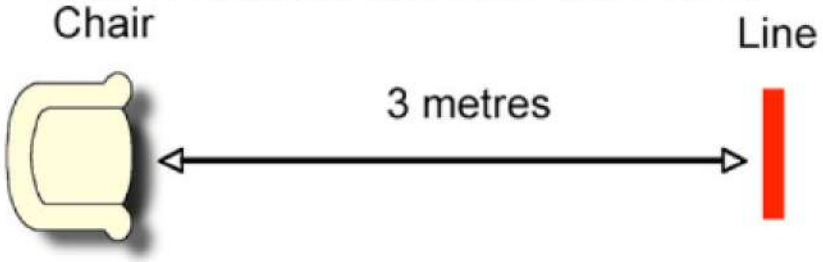
During fitness assessments subjects will wear the chest-worn biosensor patch and wrist-worn biosensor.

13.2.33.1. Timed Up-and-Go Test

The Timed Up-and-Go Test is administered to assess mobility and dynamic balance [21]. Timed-up-and-go performance and low-back pain are both predictors of quality of life [22].

Subjects will begin with being seated on a chair, then asked to stand and walk to a line that is 3 meters (9.8 feet) away, turn around at the line, walk back to the chair, and sit down (see Figure 1 below). The test is timed, in seconds, with a stopwatch and begins as the subject stands from the chair and ends when the subject's buttocks return to the seat. Self-reported pain will be assessed at two separate times during the timed up-and-go test: 1.) sitting in the chair immediately before beginning the test, and 2.) sitting in the chair immediately at the conclusion of the test.

Figure 1: Illustration of the Timed Up-and-Go Test



13.2.33.2. 6 Minute Walk Test (6MWT)

Subjects will complete the 6MWT to obtain an estimate of functional capacity, cardiorespiratory fitness (maximal oxygen consumption or VO2 max) and pain during walking activity. The 6MWT is the most well-studied and established walk test in the cardiorespiratory domain [23] [24] [25].

Subjects will be asked to walk back and forth down a 100 feet (30.48 meters) hallway with cones on either end (i.e., turnaround points) and marks every 10 feet (3.05 meters). They will be instructed to walk as briskly as comfortable down this hallway for six consecutive minutes, pivoting at each cone and returning in the opposite direction. The number of 100 feet (30.48 meters) laps completed will be recorded and the additional distance, in feet, covered during the final partial lap will be added to the total distance traveled from the completed laps.

Self-reported pain will be assessed seven separate times during the 6MWT: immediately before beginning the test and then each minute (1, 2, 3, 4, 5, and 6min) thereafter until the test is completed. Additional questions related to the test may be asked of subjects, as per the test design.

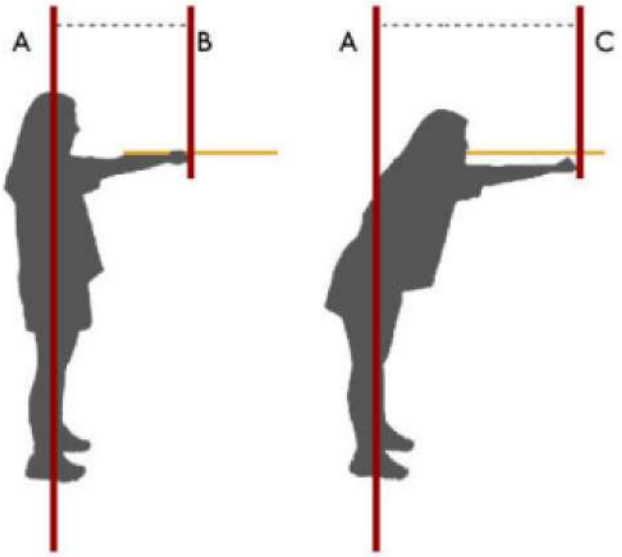
Subjects who require physical assistance to walk will be exempt from completing this test.

13.2.33.3. Functional Reach Test

The Functional Reach Test is designed to assess subject's stability. Subjects will stand near, without making contact with, a wall and extend the arm with a clenched fist nearest to the wall to 90^0 from their body. Research personnel will record the initial location of their hand on the wall at the third metacarpal (i.e., knuckle of middle finger). Subjects are then instructed to "reach as far forward as you can without taking a step." Assuming the participant does not move their feet, research personnel will again record the location of their hand on the wall in this final

position. The distance from the initial (point B on Figure 2) to the final (point C on Figure 2) location the subject can reach is then measured in inches (see figure 1 below). Three trials are performed and the final two attempts are averaged as the measure of functional reach. Self-reported pain will be assessed during the final position of each trial and the average of the final two trials will be recorded as the measure of pain during the functional reach test.

Figure 2: Illustration of the Functional Reach Test



[redacted]

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/EC/FDA/CA) 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.

NAVITAS subject non-compliance with wearing chest-worn biosensor patch or wrist-worn biosensors, reporting pain on the pain log, completing eDiary Application, and/or completing in-office fitness tests or questionnaires will not be reported as deviations, as there are no powered endpoints, nor is there any risk to subjects not completing these assessments as part of study participation. All other 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. General statistics regarding assessment completion will be included in the study progress report(s) 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 IRB notification, site re-training, or site discontinuation/termination) will be put into place by the sponsor.

16. Device/Equipment Accountability

Because this study is a post-market study using commercially available devices, device accountability will not be required.

17. Compliance

17.1. *Statement of Compliance*

This study will be conducted in accordance with the spirit of ICH/GCP, ISO 14155: Clinical Investigation of Medical Devices for Human Subjects – Good Clinical Practice, the relevant parts of the ICH Guidelines for Good Clinical Practices, ethical principles that have their origins in the Declaration of Helsinki, and applicable individual country laws and regulations. The study shall not begin until the required approval/favorable opinion from the IRB/EC and/or regulatory authority has been obtained, if appropriate. Also, the study shall not begin prior to issuance of the site Authorization to Enroll, as provided by the sponsor. Any additional requirements imposed by the IRB/EC or regulatory authority shall be followed, if appropriate.

17.2. *Investigator Responsibilities*

The Principal Investigator of an investigational center is responsible for ensuring that the study is conducted in accordance with the Clinical Study Agreement, the clinical investigation plan, the spirit of ISO 14155, ethical principles that have their origins in the Declaration of Helsinki, any conditions of approval imposed by the reviewing IRB/EC, 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.
- 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 clinical investigation.
- Create and maintain source documents throughout the clinical study and ensure their availability with direct access during monitoring visits or audits; ensure that all clinical-investigation-related records are retained per requirements.
- Ensure the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor in the CRFs and in all required reports.
- Record, report, and assess (seriousness and relationship to the device/procedure) every adverse event as applicable per the protocol and observed device deficiency.
- Report to sponsor, per the protocol requirements, all 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 applicable laws or regulations or this protocol or by the IRB, and supply BSC with any additional requested information related to the safety reporting of a particular event.
- 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 when it is used/operated by the subject.
- Inform the subject of any new significant findings occurring during the clinical investigation, including the need for additional medical care that may be required.
- Provide the subject with well-defined procedures for possible emergency situations related to the clinical study, and make the necessary arrangements for emergency treatment, including decoding procedures for blinded/masked clinical investigations, as needed.
- Ensure that clinical medical records are clearly marked to indicate that the subject is enrolled in this clinical study.
- Inform, with the subject's approval or when required by national regulations, the subject's personal physician about the subject's participation in the clinical investigation.
- Make all reasonable efforts to ascertain the reason(s) for a subject's premature withdrawal from clinical investigation while fully respecting the subject's rights.
- Ensure that an adequate investigation site team and facilities exist and are maintained and documented during the clinical investigation.
- .

17.2.1. Delegation of Responsibility

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

17.3. *Institutional Review Board/ Ethics Committee*

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

A copy of the written IRB/EC 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.

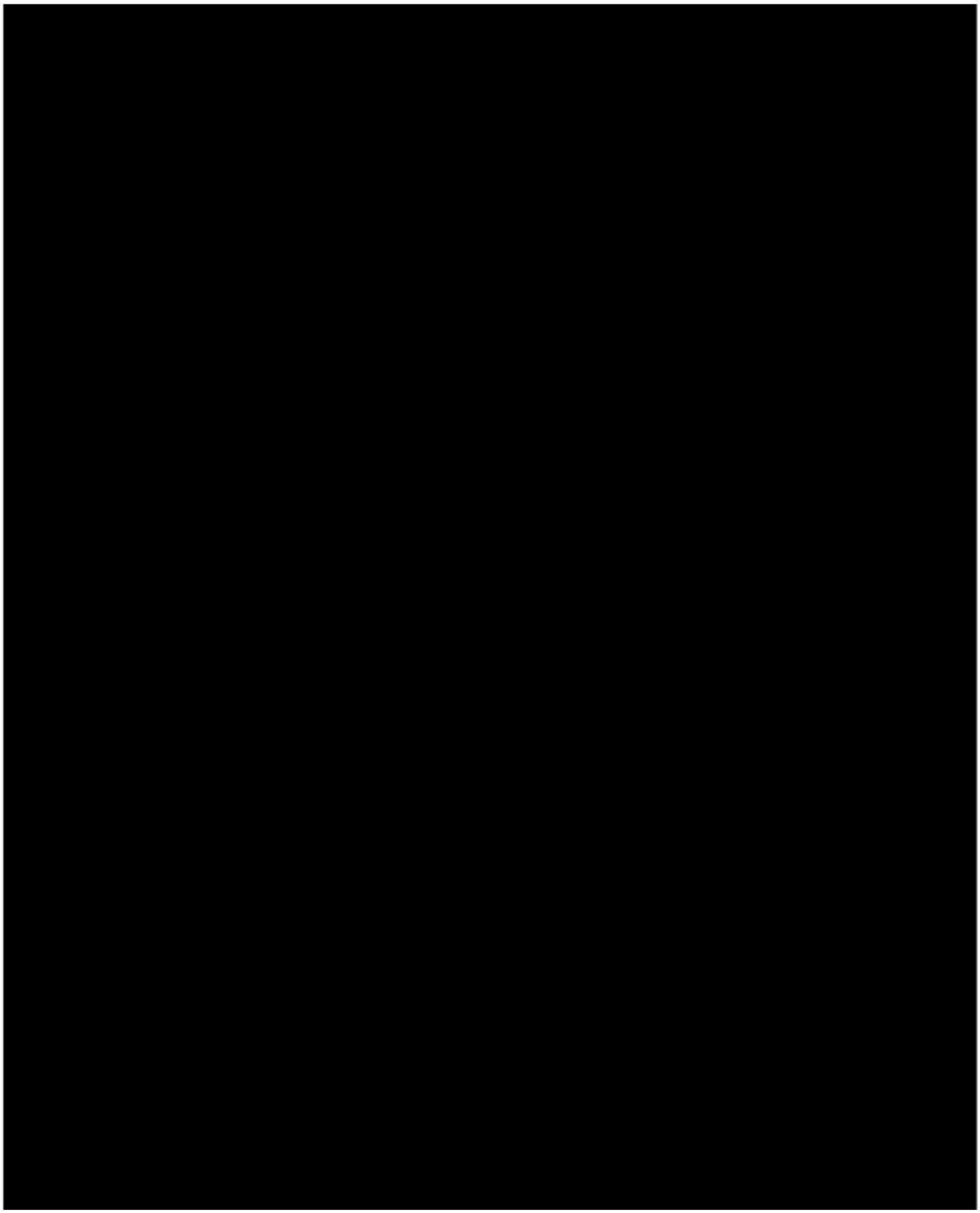
Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. All changes to the ICF will be IRB approved; a determination will be made regarding whether a new ICF needs to be obtained from participants who provided consent, using a previously approved ICF.

Annual IRB/EC approval and renewals will be obtained throughout the duration of the study as required by local/country or IRB/EC requirements. Copies of the Investigator's reports and the IRB/EC 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 and will be kept confidential in accordance with all applicable laws and regulations. Only authorized BSC personnel and/or a BSC representative including, but not limited to Contract Research Organization (CRO), will have access to this information. Authorized regulatory personnel have the right to inspect and copy all records pertinent to this study. Study data collected during this study may be used by BSC for the purposes of this study, publication, and to support future research and/or other business purposes, such as overseeing and improving the performance of its device, new medical research and proposals for developing new medical products and procedures. All data used in the analysis and reporting of this study or shared with a third-party researcher will be without identifiable reference to specific subjects.

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



18. Monitoring

Monitoring will be performed during the study to assess continued compliance with the protocol and applicable regulations. In addition, the 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 Investigator continues to have sufficient staff and facilities to conduct the study safely and effectively. The Investigator/institution guarantees direct access to original source documents by BSC personnel, their designees, 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 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. *Directions for Use*

Please refer to the Directions for Use for an overview of anticipated adverse (device) effects, and risks associated to the commercial device(s).

19.2. *Risks Associated with the chest-worn biosensor patch:*

- Adverse skin reactions, discomfort and itchiness are possible with use of the chest-worn biosensor patch. If these symptoms become more than mildly tolerable, the chest-worn biosensor patch should be removed immediately.
- It is possible to experience mild soreness and/or redness after removal of a chest-worn biosensor patch. If these symptoms occur with the chest-worn biosensor patch removal the subject should not place the next patch in the same area.
- *The chest-worn biosensor patch should be applied and used per commercial Directions for Use (DFU) to ensure proper function. The chest-worn biosensor patch should not be worn while undergoing any medical imaging procedures such as magnetic resonance imaging (MRI), computerized tomography (CT), positron emission tomography (PET), etc.*

Accessories provided with the biosensor patch include alcohol prep pads and adhesive remover wipes. These may be used as needed to assist with use of the biosensor patch and should be applied according to their instructions. Adverse skin reactions could occur in sensitive individuals. Otherwise, when used as directed, these items should present no significant risks.

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

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

If the subject's pain had improved during therapy, there is a risk that some or all of this improvement may be lost when the therapy is stopped.

Magnetic Resonance Imaging (MRI) Risk

There are no known or foreseeable side effects associated with MRI when performed according to standard guidelines. Subjects, especially those who are claustrophobic or anxious, may become uncomfortable with the enclosed space or knocking sounds made by the MRI.

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

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

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

MRI in Subjects with implanted Neurostimulator Systems:

Subjects who have an MRI-conditional neurostimulator system may have an MRI performed according to the Directions for Use (DFU) of that neurostimulator system. The DFU lists the potential risks of MRI, which include heating and undesired sensations. These risks are minimized by following all instructions in the DFU regarding the MRI conditions. If an MRI scan is performed in a condition other than advised in the DFU, it may result in more serious risks such as tissue damage or severe subject injury, including death.

Subjects should not wear the chest-worn or wrist-worn biosensor while undergoing an MRI.

Computerized Tomography (CT) Risk

CT exposes subjects to small amounts of radiation. A CT of the spine will use a typical radiation dose of approximately 6 millisievert, which is comparable to naturally-occurring "background" radiation experienced by the average person in the U.S. over 2 years. There is no conclusive evidence that radiation delivered by a single CT scan significantly increases the risk of cancer. Large population studies have shown a slight increase in cancer from much larger amounts of radiation, such as from radiation therapy. Thus, there is always concern that this risk may also apply to the lower amounts of radiation delivered by a CT exam.

Women should always inform their physician and CT scan technologist if there is any possibility that they are pregnant, as it is not recommended for pregnant women unless

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

Subjects should not wear the chest-worn or wrist-worn biosensor while undergoing a CT.

Fluoroscopy

An X-ray of the spine will expose subjects to small amounts of radiation. A single X-ray of the spine will typically use a radiation dose of approximately 1.5 millisievert, which is comparable to naturally-occurring "background" radiation experienced by the average U.S. person over 6 months. Large population studies have shown an increase in cancer risk with much larger amounts of radiation, but there is always a potential concern that this risk may apply to the lower amounts delivered by an X-ray.

Women should always inform their physician and X-ray technologist if there is any possibility that they are pregnant, as it is not recommended for pregnant women unless medically necessary. It is possible that the X-ray will show an unexpected abnormal finding, which could cause subject anxiety as well as the need for additional procedures.

Subjects should not wear the chest-worn biosensor while undergoing the X-ray of the spine.

Saliva Sample

There is no known or foreseeable risk in collecting a saliva sample.

Study Assessments

Subjects may find any of the various study assessments repetitive or inconvenient. They may feel uncomfortable answering questions or performing some of the activities. The fitness assessments may feel strenuous or tiring. Although unlikely, it is possible these assessments could worsen the subjects' pain temporarily or, more rarely, could create new pain or lasting exacerbation.

Wrist-worn Biosensor

There is no known or foreseeable risk in wearing a wrist-worn biosensor.

19.4. *Possible Interactions with Concomitant Medical Treatments*

There are no concomitant medical treatments required outside of standard of care treatment.

19.5. *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.

19.6. *Anticipated Benefits*

The reported benefit of SCS is to reduce chronic pain of the trunk and/or limbs. Refer to the Directions for Use for more information. There are no anticipated benefits to the subject for wearing the chest-worn and wrist-worn biosensor and reporting answers to questions on the study-specific smartphone.

19.7. *Risk to Benefit Rationale*

The risk evaluation for BSC neurostimulation systems determined that all hazards attributed to BSC neurostimulation systems and overall remaining residual risks after implementations of the required mitigations have been evaluated. Based on the risk evaluation results, the benefit provided by BSC neurostimulation systems to treat chronic intractable pain of the trunk and limbs outweighs the remaining residual risk. As the overall residual risk meets BSC's criteria, BSC neurostimulation systems are acceptable for use in a clinical setting.

The risk to benefit rationale for study participation is reasonable.

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 Device Deficiencies
- Unanticipated Adverse Device Effects
- New findings/updates in relation to already reported events
- All Device Related Adverse Events (Device Hardware and Stimulation Related)
- All Procedure Related Adverse Events

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

If it is unclear whether 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 after the procedure, must be recorded in the eCRF.

Underlying diseases are not reported as AEs unless there is an increase in severity or frequency during 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 Directions for Use for the known risks associated with the commercial device(s).

20.2. *Definitions and Classification*

Adverse event definitions are provided in Table 20.2-1. Administrative edits were made on the safety definitions 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* *Ref: MEDDEV 2.7/3*	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 study medical device. **NOTE 1**: This includes events related to the study medical device or comparator. **NOTE 2**: This definition includes events related to the procedures involved. **NOTE 3**: For users or other persons, this definition is restricted to events related to the study medical device.
Adverse Device Effect (ADE) *Ref: ISO 14155* *Ref: MEDDEV 2.7/3*	Adverse event related to the use of the study 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 study medical device. **NOTE 2**: This definition includes any event resulting from use error or intentional abnormal use of the study 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.

Table 20.2-1: Safety Definitions

Term	Definition
	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.
Unanticipated Serious Adverse Device Effect (USADE) *Ref: ISO 14155* *Ref: MEDDEV 2.7/3*	Serious adverse device effect which by its nature, incidence, severity, or outcome has not been identified in the current version of the risk analysis report. **NOTE 1**: Anticipated serious adverse device effect (ASADE) is an effect which by its nature, incidence, severity or outcome has been identified in the risk analysis report.
Device Deficiency *Ref: ISO 14155* *Ref: MEDDEV 2.7/3*	An inadequacy of the study 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.

Underlying diseases are not reported as AEs unless there is an increase in severity, location, or frequency, beyond the expected course or progression of the disease, during the investigation. Death should not be recorded as an AE, but should only be reflected as an outcome of a specific SAE.

Hospitalization is defined as any in-patient admission regardless of duration of stay. Emergency room admissions and outpatient visits are not considered hospitalizations.

Any adverse event or complaint occurring in subjects who withdraw participation in the study and opt to remain implanted with the device should be reported to the Complaints Call Center as detailed in the "Directions for Use (DFU)".

In accordance with FDA regulations 21 CFR 820.3, a complaint is any written, electronic or verbal communication that alleges deficiencies related to the identity, design, quality, durability, reliability, safety, effectiveness or performance of a product after it is released for distribution.

Pregnancy will not be considered an adverse event. If a subject becomes pregnant, she may withdraw from the study or remain in the study at her discretion with concurrence of her physician.

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, 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 will be reported as AEs.
6. Lack of efficacy/decreased therapeutic response will not be collected as AEs. Also, return of the patient's pain symptoms to their pre-SCS level does not meet the criteria for an AE.
7. Clinically significant worsening of symptoms, beyond the pre-SCS symptoms or the expected course or progression of the disease, should be reported as an AE.
8. Device/lead migration will not be collected as an AE. However, if the device/lead migration precipitated an AE, the AE should be reported in the *Adverse Event* eCRF. Device/lead migration should be documented in the *Device Deficiency* eCRF.
9. Device deficiencies, failures, malfunctions, and product nonconformities should not be reported as adverse events. However, if an adverse event resulted from a device failure or malfunction, that specific event would be recorded on the *Adverse Event* eCRF. Device deficiencies, failures, malfunctions, and product non-conformities should be documented in the *Device Deficiency* eCRF.

20.3. *Relationship to Device(s)*

The Investigator must assess the relationship of the reportable AE to the 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
Unrelated	The adverse event is determined to be due to a concurrent illness or effect of another device/drug and is not related to the investigational product.
Related	d) The adverse event is determined to be potentially related to the investigational product, and an alternative etiology is equally or less likely compared to the potential relationship to investigational product, or

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

Classification	Description
	e) There is a strong relationship to investigational product, or recurs on re-challenge, and another etiology is unlikely, or There is no other reasonable medical explanation for the event.

The Investigator should assess the potential relationship of the adverse event to the **study device.** All **study device** related adverse events will be assessed according to their relationship to one of the following sub-categories:

a) Device hardware-related AEs will be those that reasonably can be attributed to mere presence of the device or to a malfunction of the device or a deficiency of the device (such as, allergy to device materials). The following criteria are used to determine device hardware-relatedness:

b) The adverse event is determined to be potentially related to the investigational product, and an alternative etiology is equally or less likely compared to the potential relationship to investigational product, or

c) There is a strong relationship to investigational product, or recurs on re-challenge, and another etiology is unlikely, or

d) There is no other reasonable medical explanation for the event.

e) Stimulation-related AEs, will be those that show a relationship to stimulation on and off (such as, undesired sensations). It will also include those that are thought to be stimulation-related, but that relationship cannot be demonstrated with stimulation on/off.

The Investigator should also assess the potential relationship of the adverse event to the **study procedure.**

20.4. *Investigator Reporting Requirements*

The communication requirements for reporting to BSC are as shown below.

Event Classification	Communication Method	Communication Timeline
Serious Adverse Event including 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

Event Classification	Communication Method	Communication Timeline
	Provide all relevant source documentation (unidentified) for reported event	• When documentation is available
Adverse Event	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 after becoming aware of the information • Reporting required through end of study participation • Only device-related and procedure-related adverse events
Device Deficiencies (including but not limited to failures, malfunctions, and product nonconformities) Note: Any 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 CRF 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
	Complete Device Deficiency eCRF with all available new and updated information	• For 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 reporting required within 2 business days of first becoming aware of the event and as per local/regional regulations • Reporting required through the end of the study

The investigator must report Device and Procedure Related Adverse Events, Adverse Device Effects, Serious Adverse Events (regardless of relationship to device hardware, stimulation and/or procedure), Unanticipated Adverse Device Effects, and Device Deficiencies for each subject from the time of Information Consent through the end of study participation. AEs and Device Deficiencies may be reported via phone, fax or email if the electronic data capture (EDC) system is unavailable. The paper AE Notification Form or Device Deficiency Notification Form should be used to report AEs and/or device deficiencies during this time.

The Investigator must assess the potential relationship of all adverse events to the study device and/or to study procedures.

- Adverse events must be assessed according to their relationship to one of the following categories:
    - **Device Hardware-Related AEs:** AEs that can reasonably (i.e. Unlikely, Possibly, Probably and Causally Related) 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 (i.e. Unlikely, Possibly, Probably and Causally Related) 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.
- **Procedure Related AEs:** AEs that can reasonably (i.e. Unlikely, Possibly, Probably and Causally Related) be attributed to a study protocol required procedure.

20.5. *Boston Scientific Device Deficiencies*

Device deficiencies for Boston Scientific devices will be documented and reported to BSC. If possible, the device(s) should be returned to BSC for analysis. Instructions for returning the device(s) will be provided from the study sponsor. Device deficiencies should also be documented in the subject's source records.

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

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

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

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

20.7. *Chest-worn biosensor patch and accessories*

All chest-worn biosensor patch and accessory (WEBCOL/Curity Alcohol Prep Pads and UNI-SOLVE Adhesive Remover Wipes) complaints (including but not limited to failures, malfunctions, use errors, product nonconformities, and inadequacy in the information supplied by the manufacturer) are to be reported by submitting of an issue ticket to physIQ's help portal. The authorized distributor of the patches and accessories will be responsible for ensuring safety reporting related to product complaints, deficiencies and malfunctions, as applicable.

Device related adverse events, failures and malfunctions should also be documented in the subject's medical record. Site investigators and their designees will be responsible for reporting to their IRBs, as required and applicable.

Boston Scientific, vendors, site investigator and/or their designee will not monitor biosensor data for adverse events and/or medical care.

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

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

Boston Scientific will provide a study-specific template of the ICF to investigators participating in this study. The ICF template may be modified to meet the requirements of the investigative site's IRB. Any modification requires acceptance from BSC prior to use of the form. The ICF must be in a language understandable to the subject. 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 or his/her legal representative,
- 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 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 person signing the form.

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

If new information becomes available that can significantly affect a subject's future health and medical care, that information shall be provided to the affected subject(s) in written form via a revised ICF or, in some situations, enrolled subjects may be requested to sign and date an

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

22. Committees

22.1. *Safety Monitoring Process*

The BSC Medical Safety group reviews unmonitored data as soon as the event is reported, on a continuous basis. During scheduled monitoring activities, clinical research monitors will support this continuous review through their review of source document and other data information. The BSC Medical Safety group includes a board-certified physician with expertise in neurology and neuromodulation and with the necessary therapeutic and subject matter expertise to evaluate and classify the events into the categories outlined above.

23. Suspension or Termination

23.1. *Premature Termination of the Study*

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

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/marketing of the device.

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

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

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/ECs/REBs, 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 devices, if supplied by 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 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 for a period beyond 6 months after site initiation, 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 devices and testing equipment, as applicable, will be returned to BSC unless this action would jeopardize the rights, safety or well-being of the subjects. The IRB and regulatory authorities, as applicable, will be notified. Study participants will be contacted, as applicable, and be informed of changes to study visit schedule.

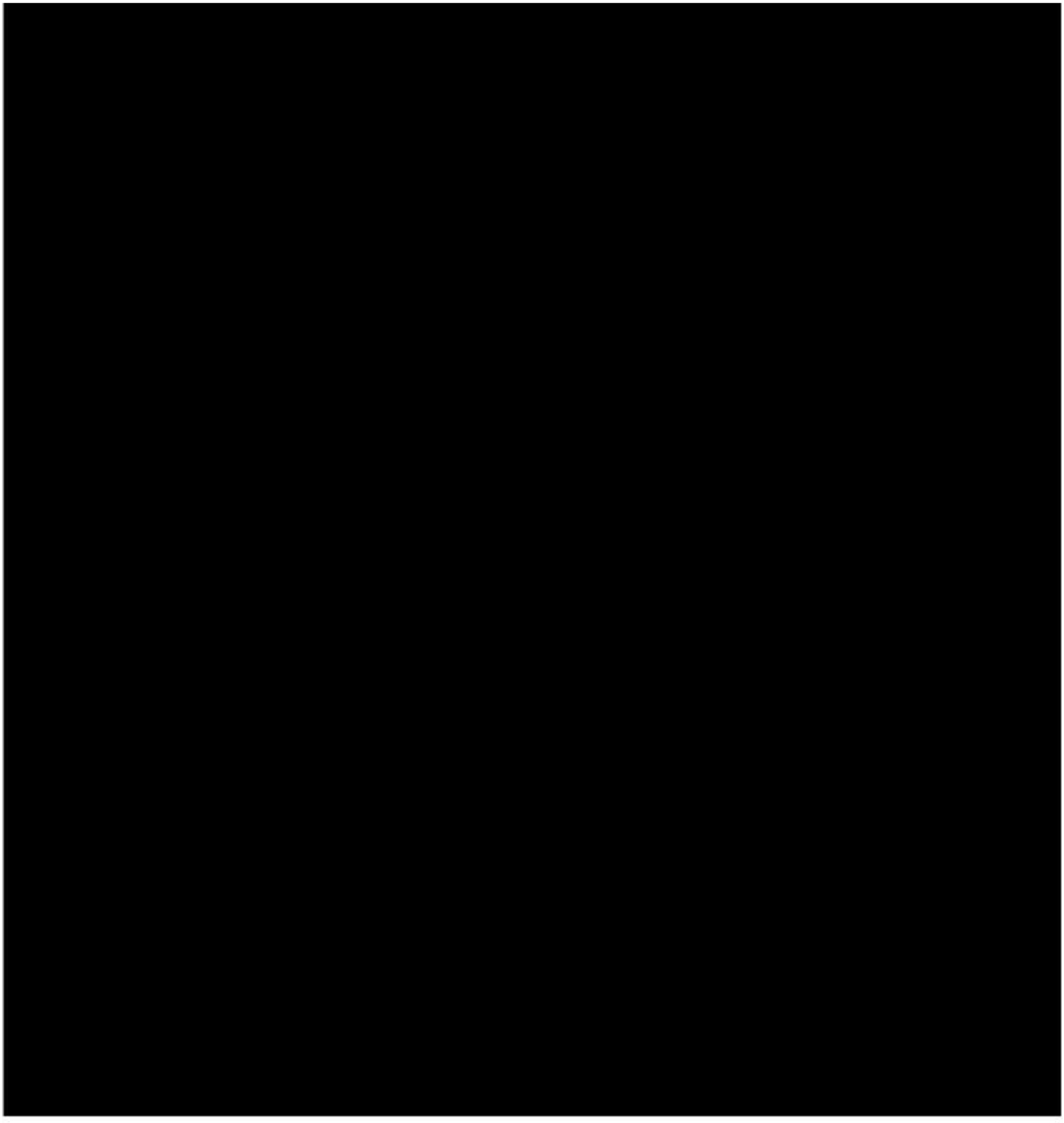
24. Publication Policy

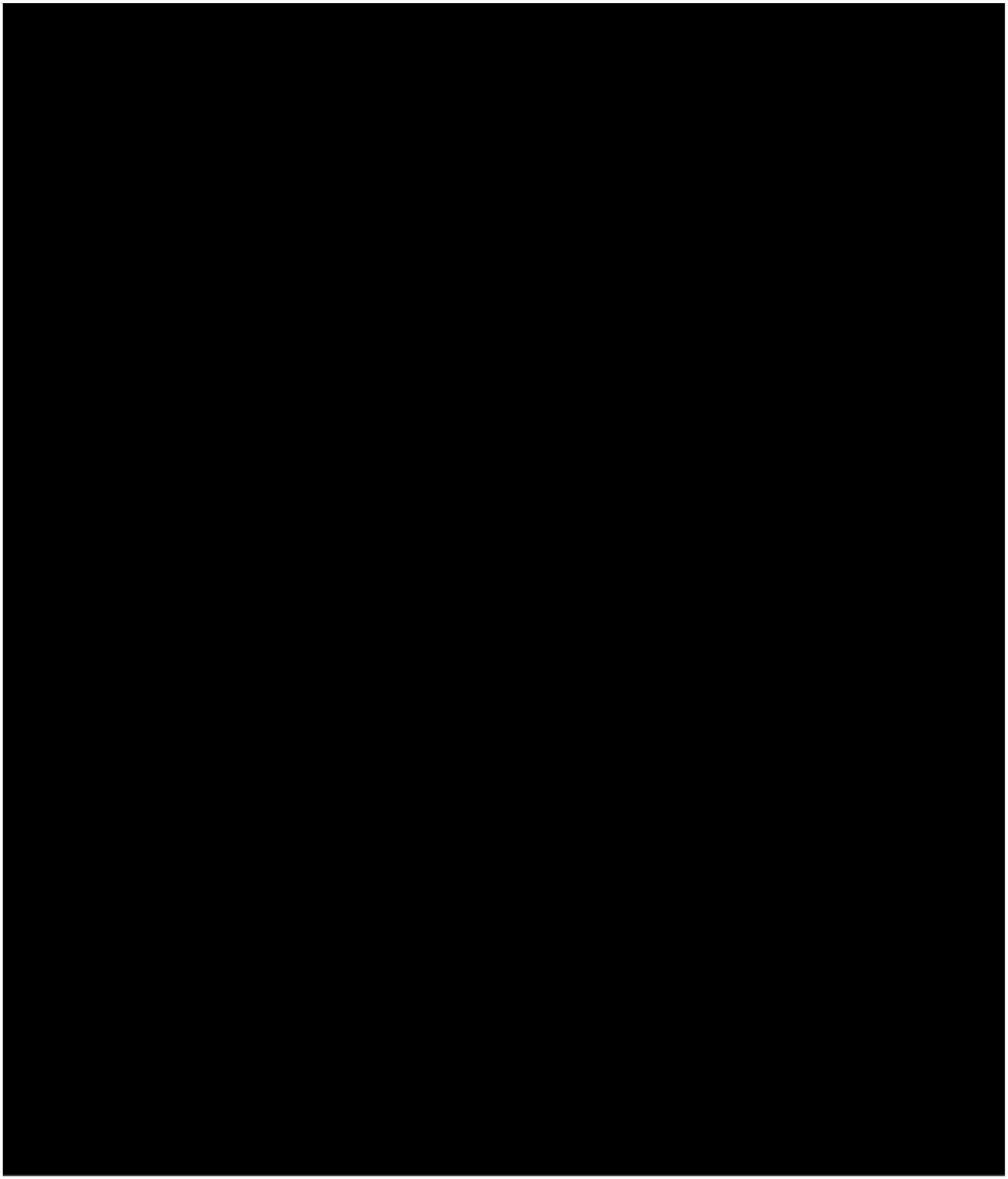
BSC requires disclosure of its involvement as a sponsor or financial supporter in any publication or presentation relating to a BSC study or its results. BSC will submit study results for publication (regardless of study outcome) following the conclusion or termination of the study. Boston Scientific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

- All authorship and contributorship requirements as described above must be followed.
- BSC involvement in the publication preparation and the BSC Publication Policy should be discussed with the Coordinating Principal Investigator(s) and/or Executive/Steering Committee at the onset of the project.

- The First and Senior authors are the primary drivers of decisions regarding publication content, review, approval, and submission.

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





[redacted]

26. Abbreviations and Definitions

26.1. *Abbreviations*

Table 26.1-1: Abbreviations

Abbreviation/Acronym	Term
6MWT	6 Minute Walk Test
ADE	Adverse device event
AE	Adverse event
BDI-II	Beck depression inventory
BSC	Boston Scientific Corporation
CGI-C: Sub	Clinical global impression of change: subject
CFR	Code of Federal Regulations
CMM	Conventional medical management
DFU	Directions for use
EC	Exclusion criteria
EC	Ethics committee
eCRF	Electronic case report form
EDC	Electronic data capture
EQ-5D-5L	EuroQol Group, 5 dimensions, 5 level
ETS	External Trial Stimulator
FBSS	Failed Back Surgery Syndrome
FABQ	Fear Avoidance Beliefs Questionnaire
FCC	Federal communications commission
FDA	Food and Drug Administration
GAD-7	Generalized anxiety disorder
GCP	Good clinical practice
HCP	Health care personnel
HRQOL	Health-related quality of life
IC	Inclusion criteria
ICF	Informed consent form
ICH	International conference on harmonisation
INS	International Neuromodulation Society
IPG	Implantable pulse generator
IRB	Institutional review board
ISO	International Organization for Standardization
MEDDEV	Medical device directives
MPC	Maintenance of pain
MRI	Magnetic resonance imaging

Table 26.1-1: Abbreviations

Abbreviation/Acronym	Term
Mg	Milligram
NRS	Numerical rating scale
ODI	Oswestry Disability Index
PCS	Pain Catastrophizing Scale
PGI-C	Patient global impression of change
PPR	Percent pain relief
PRO	Patient-reported outcome
PSWT	Patient satisfaction with treatment
QOL	Quality of life
RCT	Randomized controlled trial
RUI	Resource utilization inventory
SADE	Serious adverse device effect
SAE	Serious adverse event
SCS	Spinal cord stimulation
SF-MPQ-2	Short form McGill pain questionnaire
SF-36v2	Short Form 36 Health Survey ver 2
SST	Treatment satisfaction questionnaire
VRS	Verbal rating scale
VAS	Visual analog scale
WPAI:SHP	Work Productivity and Activity Impairment: Specific Health Problem

26.2. *Definitions*

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

RELIEF Study - ENVISION Cohort

APPENDIX

TO THE RELIEF STUDY PROTOCOL

A7007

CLINICAL INVESTIGATION PLAN

National Clinical Trial (NCT) Identified Number: NCT03240588

Sponsored By

Boston Scientific Corporation
Neuromodulation
25155 Rye Canyon Loop
Valencia, CA 91355
United States of America

[redacted]

Original Release: April 3, 2019

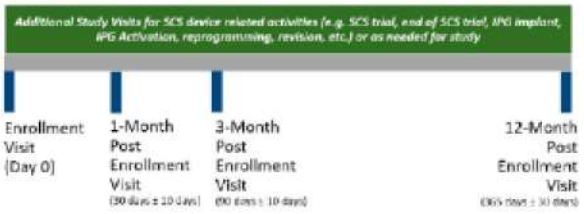
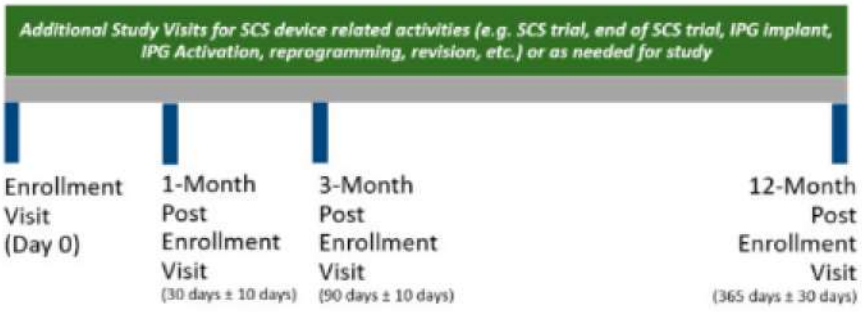
Current Version: June 20, 2022

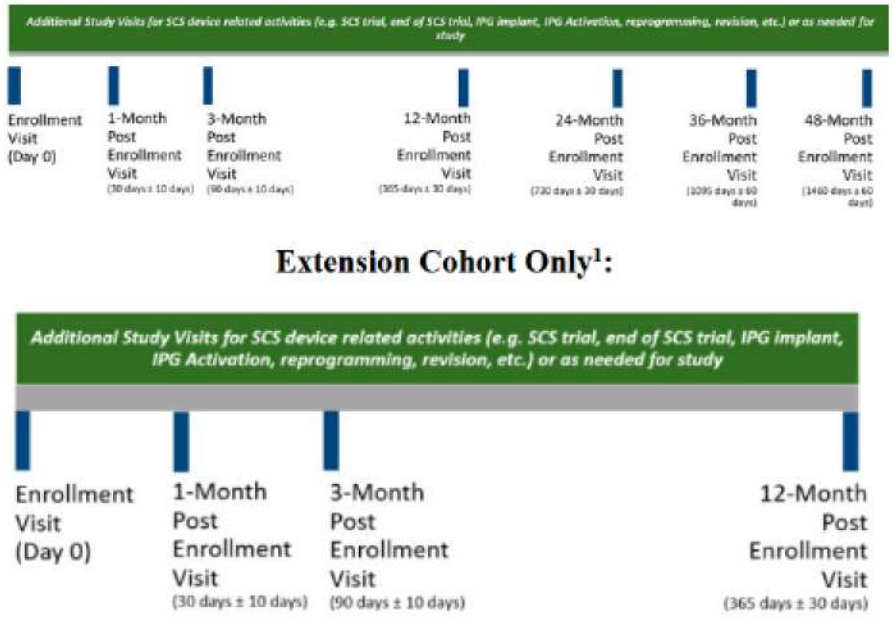
[redacted]

[redacted]

[redacted]

2. Protocol Synopsis

RELIEF Study - ENVISION Cohort	
The ENVISION Cohort is being conducted under the RELIEF Study however subjects enrolled in ENVISION will follow protocol requirements within this document only. Subjects enrolled in the ENVISION protocol will not and cannot be enrolled in the RELIEF study.	
Study Objective	The objective of the study is to characterize the relationship between select objective metrics and clinical outcomes in chronic pain patients treated with Boston Scientific commercially approved neurostimulation systems and may use observed relationships to make recommendations.
Commercial Device/System applied as Standard of Care	All commercially approved Boston Scientific neurostimulation systems indicated for the treatment of chronic pain, except for Precision™ and Precision™ Plus.
Study Design	Prospective, post-market, multi-center study   **Figure 7.1-1: ENVISION Study Design**



Extension Cohort Only[1]:

Figure 7.1-12: ENVISION Study Design for Extension Cohort Only

[redacted]

Planned Number of Sites / Countries	The study will be conducted at up to 30 sites in the United States
Safety Parameters	The rate of neurostimulator device and procedure-related adverse events (AEs), Serious Adverse Events (SAEs) from informed consent through study exit will be reported.
Exploratory Endpoints	This study does not have any pre-defined endpoints but may include ad-hoc exploratory endpoint(s) to explore the relationship between metrics and clinical outcomes and/or to evaluate the effects of any recommendations made on outcomes.

[1] Extension Cohort: up to 300 enrolled subjects that consent to extend ENVISION study participation to approximately 48 months

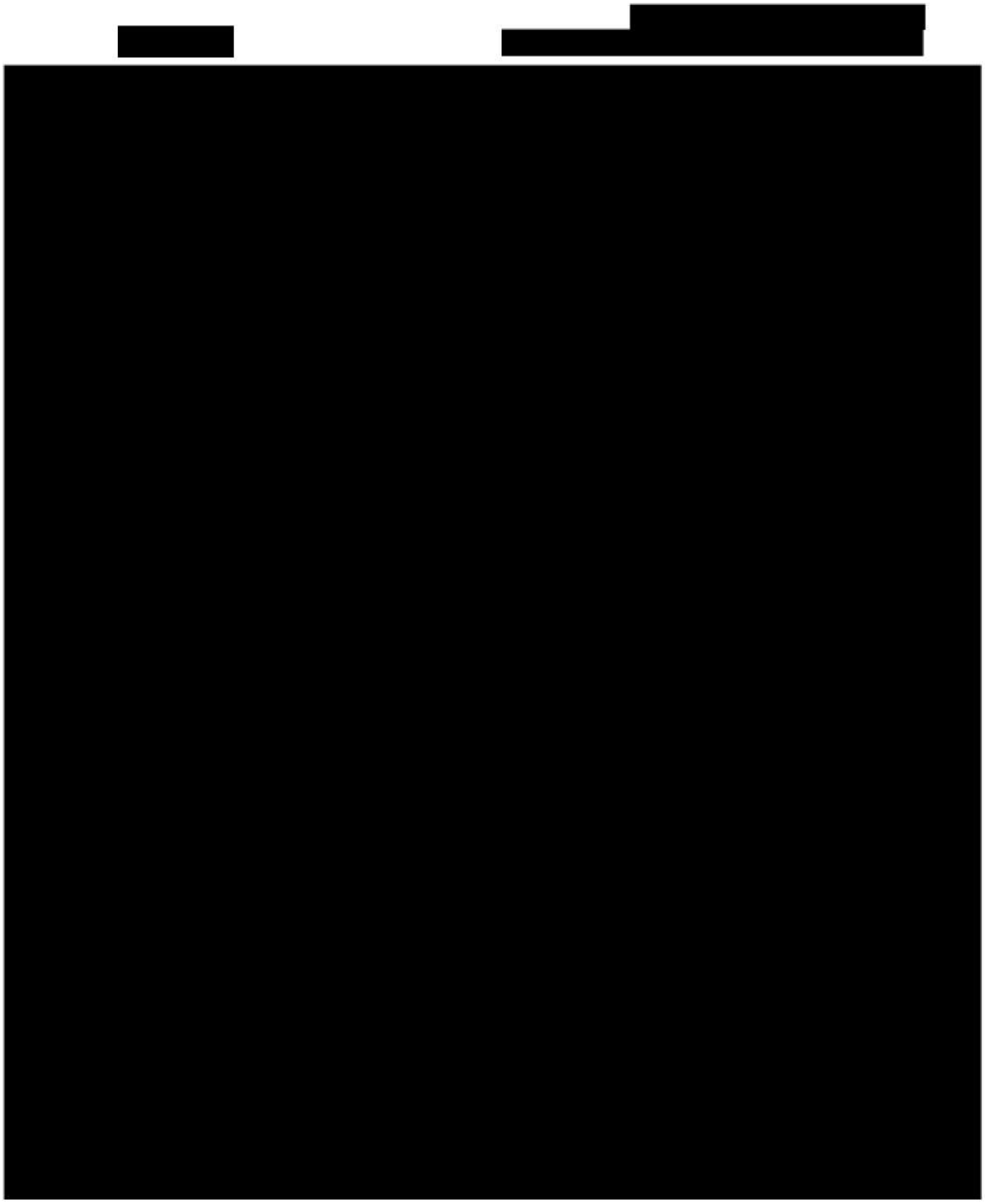
	Exploratory endpoint(s) will be intended to generate hypotheses for future studies. Consequently, no correction for multiple testing will be performed for exploratory endpoint(s). Any exploratory endpoint(s) will be clearly identified as such in study reports, as applicable.
Follow-up Schedule	Study assessments will be required, as appropriate, at the following time points: • Enrollment Visit (Day 0) • 1-Month Post-Enrollment Visit (30 days ± 10 days) • 3-Month Post-Enrollment Visit (90 days ± 10 days) • 12-Month Post-Enrollment Visit (365 days ± 30 days) • Extension Cohort only: 24-Month Post-Enrollment Visit (730 days ± 30 days)[1] • Additional Study Visit for SCS device related activities (e.g. SCS trial, end of SCS trial, IPG implant, IPG Activation, reprogramming, revision, etc.) or as needed for study. ○ Extension Cohort only: Additional Study Visits at 36 months (1095 days ± 60 days) and 48 months (1460 days ± 60 days) post enrollment
[redacted]	[redacted]
Participant Duration	The study duration for up to 300 enrolled subjects in the Extension Cohort[1] is expected to be approximately 48 months. The study duration for the remaining subjects is expected to be 12 months.
Inclusion Criteria	Subjects must meet all inclusion criteria, as outlined below: IC1. Study candidate is planning to receive or has received a commercially approved Boston Scientific neurostimulation system for pain, per local directions for use (DFU) IC2. Subject signed a valid, ENVISION IRB-approved informed consent form in English IC3. 18 years of age or older when written informed consent is obtained IC4. Is willing and able to comply with completing protocol required assessments and evaluations [redacted] [redacted]

	[redacted]
Exclusion Criteria	Subjects must be excluded from the study if they meet any of the following exclusion criteria: [redacted] [redacted] a history of visceral pain referred to the low back and/or legs EC4. Has any pain-related diagnosis, medical/psychological condition or external factors that, in the investigator's medical judgment, might confound reporting of study outcomes (e.g. history of pelvic pain, anginal pain, chronic migraine, involved in litigation, workmen's compensation) [redacted]
Statistical Methods	

[redacted]	[redacted]

[redacted]

[redacted]



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 radiofrequency (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 [1], [2], complex regional pain syndrome [3], and low back pain and leg pain [4]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 [5]. 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 [5].

In SCS pain relief is realized when the nerves that innervate the painful region(s) are electrically stimulated [6]. 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 [7]. However, recent studies indicate that effective pain relief may be obtained by employing stimulation without paresthesia ([8], [9], [10]).

4.3. *Study Rationale*

Traditional SCS therapy optimization requires face to face interaction with healthcare professionals. Wearable devices, digital solutions, and other recent technology advances that allow for more frequent, comprehensive monitoring of and interaction with patients present an opportunity to optimize therapy remotely. Additionally, a more patient tailored optimization is possible. Automation of therapy optimization, in theory, could reduce the number of in person interactions required while improving outcomes (and overall costs). The results from this study are anticipated to provide initial data in developing such a system and to generate hypotheses for future studies.

5. Commercial Device Description (part of Standard of Care)

5.1. *Commercial Device*

This study includes all commercially approved Boston Scientific neurostimulation systems indicated for the treatment of chronic pain, except for Precision™ and Precision™ Plus. Refer to the Directions for Use for detailed device description.

6. Study Objectives and Endpoints

The objective of the study is to characterize the relationship between select objective metrics and clinical outcomes in chronic pain patients treated with Boston Scientific commercially approved neurostimulation systems and may use observed relationships to make recommendations.

6.1. *Exploratory Endpoints*

This study does not have any pre-defined endpoints but may include ad-hoc exploratory endpoint(s) to explore the relationship between metrics and clinical outcomes and/or to evaluate the effects of any recommendations made on outcomes.

Exploratory endpoint(s) will be intended to generate hypotheses for future studies. Consequently, no correction for multiple testing will be performed for exploratory endpoint(s). Any exploratory endpoint(s) will be clearly identified as such in study reports, as applicable.

7. Study Design

The study is a prospective, post-market, multi-center study for chronic pain.

7.1. [redacted]

[redacted]

[redacted]

Please see below study design.

Figure 7.1-1: ENVISION Study Design

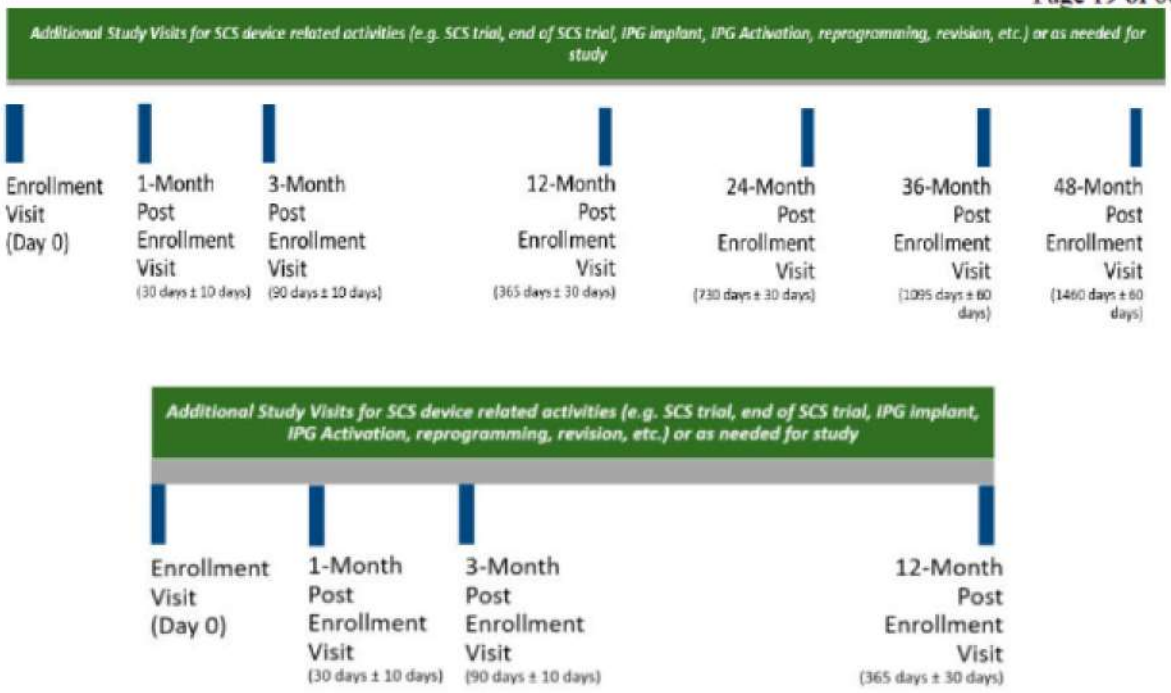


Figure 7.1-1: ENVISION Study Design for Extension Cohort

7.2. *Treatment Assignment*

Consecutive eligible patients who consent to participation and have met all the inclusion and none of the exclusion criteria will be enrolled.

7.2.1. Treatment

The study treatment will consist of neurostimulation trial therapy with any commercially approved Boston Scientific neurostimulator for pain. Individualization of neurostimulation therapy for pain will be determined according to investigator discretion and site routine care, and in accordance with inclusion and exclusion criteria.

7.3. *Justification for the Study Design*

All devices used in this study are approved for commercial release.

This study is designed to gather data which will be analyzed to characterize the relationship between select objective metrics and clinical outcomes in chronic pain patients treated with Boston Scientific commercially approved neurostimulation systems.

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.

8. Subject Selection

8.1. *Study Population and Eligibility*

Subjects enrolled in this study will be established patients in a medical practice (e.g. pain management, surgical, physical medicine and/or rehabilitation) who are planning to receive or have received a commercially approved Boston Scientific neurostimulation system are eligible to receive neurostimulation therapy to treat their pain condition.

8.2. *Inclusion Criteria*

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

Table 8.2-1: Inclusion Criteria

Inclusion Criteria	IC1.	Study candidate is planning to receive or has received a commercially approved Boston Scientific neurostimulation system for pain, per local directions for use (DFU)
	IC2.	Subject signed a valid, ENVISION IRB-approved informed consent form in English
	IC3.	18 years of age or older when written informed consent is obtained
	IC4.	Is willing and able to comply with completing protocol required assessments and evaluations
	[redacted]	[redacted]
	[redacted]	[redacted]

8.3. *Exclusion Criteria*

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

Table 8.3-1: Exclusion Criteria

Exclusion Criteria	[redacted] EC4. Has any pain-related diagnosis, medical/psychological condition or external factors that, in the investigator's medical judgment, might confound reporting of study outcomes (e.g. history of pelvic pain, anginal pain, chronic migraine, involved in litigation, workmen's compensation) [redacted]

9. Subject Accountability

9.1. *Point of Enrollment*

The point of enrollment is when subject signs and dates the valid, IRB-approved ENVISION informed consent form. No study-related activities can take place until the ENVISION informed consent form is signed.

9.2. *Withdrawal*

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

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, lost to follow-up, or until subject deletes the mobile app and/or ends data transmission by removing and returning the wrist-worn biosensor and/or sleep sensor (for subjects enrolled under protocol ver. A and B) may be used for study analysis in accordance with applicable regulations. Subjects can stop data transmission by deleting the mobile app from their phone. Subjects can end wrist-worn biosensor transmission by removing the device and returning to the study site. Subjects enrolled under protocol Ver A and B can end sleep sensor transmission by removing the device and returning to the study site.

[redacted]

9.3. [redacted]

[redacted]

- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]

9.4. [redacted]

[redacted]

[redacted]

9.5. *End-of-Study Definition & Plan*

A clinical trial is considered completed when participants are no longer being examined or the last participant's last study visit has occurred.

When each subject enrolled in the Extension Cohort reaches 36 months post-enrollment (maximum 1155 days post-enrollment) or withdraws, the subject exits the study and ends study participation. If the subject is implanted, the subject may continue to use the neurostimulator system per the applicable Directions for Use and should be followed according to standard, routine medical care.

When each enrolled subject who is not enrolled in the Extension Cohort completes the 12-Month Visit or withdraws, the subject exits the study and ends study participation. If the subject is implanted, the subject may continue to use the neurostimulator system per the applicable Directions for Use and should be followed according to standard, routine medical care.

10. Study Methods

10.1. [redacted]

[redacted]

[redacted]

10.2. *Study Candidate Screening*

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

10.3. *Informed Consent*

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

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

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

10.4. *Enrollment Visit (In-office)*

All required Enrollment Visit assessments, as outlined in the Data Collection table, should be performed after obtaining informed consent and confirming study eligibility and prior to any procedures.

Throughout the study subjects who will not receive or don't already have a commercially available Remote Control compatible with the mobile app may be provided one to allow transmission of SCS data.

Subjects will be trained on the use of at home devices (e.g. watch, mobile app, sleep sensor, etc.).

10.5. *1-Month Post Enrollment Visit (30 days ± 10 days)*

Subjects should bring their phone with mobile app and watch to this visit.

All required assessments, as outlined in the Data Collection Table, should be performed at the beginning of the visit.

10.6. *3-Month Post Enrollment Visit (90 days ± 10 days)*

Subjects should bring their phone with mobile app and watch to this visit.

All required assessments, as outlined in the Data Collection Table, should be performed at the beginning of the visit.

10.7. *12-Month Post Enrollment Visit (365 days ± 30 days)*

Subjects should bring their phone with mobile app and watch to this visit. The wrist-worn biosensor and sleep sensor, as applicable for subjects enrolled under protocol A and B, will be returned to the site and mobile app needs to be deleted for the subject's phone at the end of this visit unless they are participating in the Extension Cohort. Subjects may keep the commercially available Remote Control provided for the study however the subject needs to delete the mobile app to stop transmission of SCS data.

All required assessments, as outlined in the Data Collection Table, should be performed at the beginning of the visit.

10.8. *Extension Cohort Only: 24-Month Post Enrollment Visit (730 days ± 30 days)*

Subjects in the Extension Cohort should bring their phone with mobile app and watch to this visit.

All required assessments, as outlined in the Data Collection Table, should be performed at the beginning of the visit.

10.9. *Additional Study Visit(s)*

Subjects may have additional study visits for SCS device related activities (e.g. SCS trial, end of SCS trial, IPG implant, IPG Activation, reprogramming, revision, etc.) or as needed for study. These visits may be combined with required study visits if protocol windows allow. If they are combined required study visit requirements and additional study visits requirements must be completed however duplicate information should not be collected.

Please refer to Data Collection Table for additional data collection and/or assessments. If a subject has an SCS Trial and/or IPG Implant while participating in the study additional data collection forms will be completed at the Start of the SCS Trial, End of SCS Trial, IPG Implant and/or IPG Activation visits.

Subjects should bring their phone with mobile app and watch to these visit(s) and may be asked to respond to questions and/or questionnaires, submit voice recording/responses, log information such as pain, complete body map drawings, complete fitness assessments, and/or review notifications and/or recommendations on the mobile app during these visit(s). Assessments should be performed at the beginning of the visit.

10.9.1 *Extension Cohort Only: Additional Study Visits at 36 and 48 months post enrollment*

For Extension Cohort subjects only, additional study visit may be completed 36 and 48 Months post enrollment to allow the subject to complete study participation.

Subjects in the Extension Cohort should bring their phone with mobile app and watch to these optional visits. The wrist-worn biosensor and sleep sensor, as applicable for subjects enrolled under protocol A and B, will be returned to the site and mobile app needs to be deleted for the subject's phone at the end of this visit. Subjects may keep the commercially available Remote Control provided for the study however the subject needs to delete the mobile app to stop transmission of SCS data.

All required assessments, as outlined in the Data Collection Table, should be performed at the beginning of the visit.

10.10. *Study Completion*

An enrolled subject may complete participation in one of several ways:

- Subjects not in the Extension Cohort who complete the 12-Month Post Enrollment Visit.
- Subjects in the Extension Cohort who
  - Complete an Additional Study Visit Day 1095 ± 60 days post enrollment
  - Complete an Additional Study Visit Day 1460 ± 60 days post enrollment
  - Reach maximum 1520 days post enrollment.
- Subjects who withdraw, die, or become lost to follow up. Withdrawn subjects will not be replaced.
- Subjects who have a negative trial will not proceed to permanent implant, will complete the study 7-30 days post negative trial completion.
- Subjects who have a positive trial but do not proceed to permanent implant will be withdrawn.

Upon study completion subjects will be asked to return the wrist-worn biosensor and sleep sensor, as applicable for subjects enrolled under protocol A and B, to the site and deactivate the mobile app. Subjects may keep the commercially available Remote Control provided to allow data upload by connecting to their SCS device for the study.

10.11. *Source Documents*

It is preferable that original source documents are maintained, when available. In lieu of original source documents, certified copies are required to be maintained. A certified copy is a copy (irrespective of the type of media used) of the original record that has been verified (i.e., by a dated signature or by generation through a validated process) to have the same information, including data that describe the context, content, and structure, as the original. Source documentation includes but is not limited to those items noted in Table 10.11-1.

Data collected on Mobile app wrist-worn biosensor, sleep sensor is collected directly so will be the source.

Table 10.11-1: 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 study site
Assessments and questionnaires	Retained at study site and/or electronic data collection platform/EDC
Imaging (Fluoroscopy)	Retained at study site
Medical Records	Retained at study site
SCS data	Electronic data collection platform/EDC

11. Statistical Considerations

11.1. *Endpoints*

11.1.1. Exploratory Endpoints

Ad-hoc exploratory endpoint(s) may be included to explore the relationship between metrics and clinical outcomes and/or to evaluate the effects of any recommendations made on outcomes.

Exploratory endpoints will be intended to generate hypotheses for future studies. Consequently, no correction for multiple testing will be performed for exploratory endpoint(s). Any exploratory endpoint(s) will be clearly identified as such in study reports, as applicable.

11.1.1.1. Hypotheses

There are no formal hypotheses for this study.

[redacted]

[redacted]

11.1.1.3. Statistical Methods

Univariate and multivariable models will be used to determine correlations between neurostimulation treatment parameters on clinical outcomes.

Data from all eligible patients will be used for analysis. Subgroup/cohort analyses will be defined by demographics, pain diagnosis, treatment parameters, treatment efficacy and medication use.

Missing data from biosensors will not be imputed. A sensitivity analysis using LOCF imputation of clinical outcomes will be completed. Further details of statistical analysis will be provided in the study reports, as applicable.

11.2. *General Statistical Methods*

[redacted]

[redacted]

- [redacted]
- [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

11.3. ***Data Analyses***

All consented subjects will be included in analyses.

[redacted]

Subject demographics and medical history will be summarized using descriptive statistics (e.g., mean, standard deviation, N, minimum, maximum) for continuous variables and frequency tables for discrete variables.

[redacted]

11.3.6. Changes to Planned Analyses

Any changes to the planned statistical analyses will be documented. Rationale for analyses and changes to analyses will be included in the final study report and other reports, as applicable.

12. Data Management

12.1. *Data Collection, Processing, and Review*

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

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

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

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

[redacted]

12.2. *Electronic Questionnaires*

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

12.3. [redacted]

[redacted]

12.4. ***Study Assessments***

12.4.1. Adverse Events

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

12.4.2. 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.).

12.4.3. Concomitant Medications

All opioid pain-related medications will be collected throughout the study 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.

12.4.4. Demography

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

12.4.5. Device Deficiency Evaluation

Device Deficiency evaluation will be conducted to identify deficiencies occurring during the study and device type and action taken. Safety events will be reported as specified in the Safety Reporting Section.

12.4.6. End of Trial Period Evaluation

The End of Trial Period Evaluation is the clinician's professional assessment of whether the subject is a candidate for permanent implantation of a neurostimulation system based on the outcome of the subject's device trial.

12.4.7. End of Study

End of Study form will collect the date the subject completed participation in the study and the reason (i.e. completed study, withdrawal, etc.).

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

EQ-5D-5L is a standardized measure of health status developed by the EuroQol Group 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'.

12.4.9. Fear Avoidance Beliefs Questionnaire (FABQ)

The Fear Avoidance Beliefs Questionnaire (FABQ) was developed by Waddell to investigate fear-avoidance beliefs among low back pain subjects in the clinical setting [11]. This survey is designed to assist in predicting which subjects may have a high pain avoidance behavior. This questionnaire consists of 16 items, with each item scored from 0-6. Higher scores on the FABQ are indicative of greater fear and avoidance beliefs.

The FABQ consists of 2 subscales. The first subscale (items 1-5) is the Physical Activity subscale (FABQPA), and the second subscale (items 6-16) is the Work subscale (FABQW). It is expected to take about three to five (3-5) minutes to complete

12.4.10. Fitness Assessments

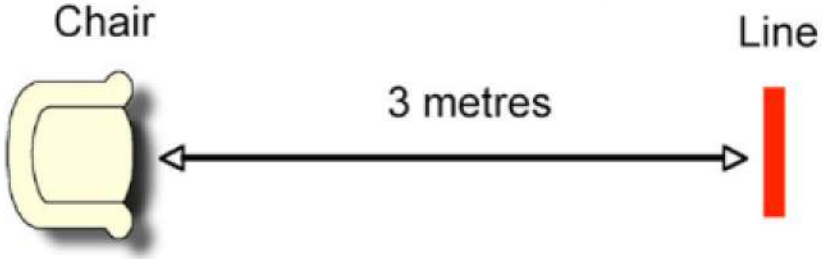
During fitness assessments subjects will wear wrist-worn biosensor.

12.4.10.1. Timed Up-and-Go Test

The Timed Up-and-Go Test is administered to assess mobility and dynamic balance [12]. Timed-up-and-go performance and low-back pain are both predictors of quality of life [13].

Subjects will begin with being seated on a chair, then asked to stand and walk to a line that is 3 meters (9.8 feet) away, turn around at the line, walk back to the chair, and sit down (see Figure 1 below). The test is timed, in seconds, with a stopwatch and begins as the subject stands from the chair and ends when the subject's buttocks return to the seat. Self-reported pain will be assessed at two separate times during the timed up-and-go test: 1.) sitting in the chair immediately before beginning the test, and 2.) sitting in the chair immediately at the conclusion of the test.

Figure 12.4-1: Illustration of the Timed Up-and-Go Test



12.4.10.2. 6 Minute Walk Test (6MWT)

Subjects will complete the 6MWT to obtain an estimate of functional capacity, cardiorespiratory fitness (maximal oxygen consumption or VO2 max) and pain during walking activity. The 6MWT is the most well-studied and established walk test in the cardiorespiratory domain [14] [15] [16].

Subjects will be asked to walk back and forth down 100 feet (30.48 meters) hallway with cones on either end (i.e., turnaround points) and marks every 10 feet (3.05 meters). They will be instructed to walk as briskly as comfortable down this hallway for six consecutive minutes, pivoting at each cone and returning in the opposite direction. The number of 100 feet (30.48 meters) laps completed will be recorded and the additional distance, in feet, covered during the final partial lap will be added to the total distance traveled from the completed laps.

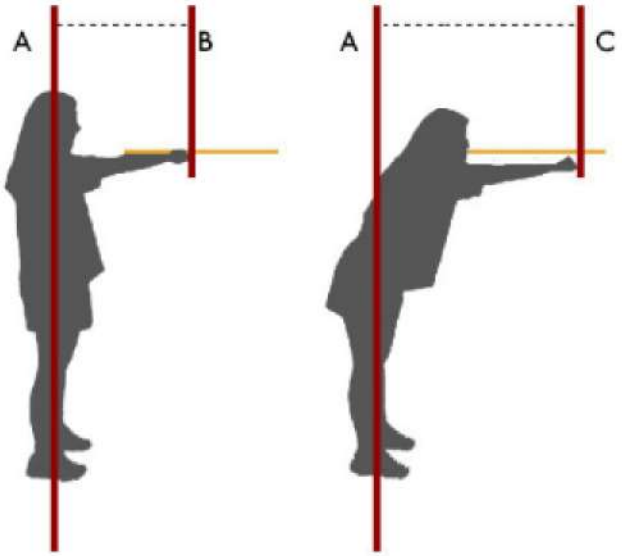
Self-reported pain will be assessed seven separate times during the 6MWT: immediately before beginning the test and then each minute (1, 2, 3, 4, 5, and 6 min) thereafter until the test is completed. Additional questions related to the test may be asked of subjects, as per the test design.

Subjects who require physical assistance to walk will be exempt from completing this test.

12.4.10.3. Functional Reach Test

The Functional Reach Test is designed to assess subject's stability. Subjects will stand near, without contacting, a wall and extend the arm with a clenched fist nearest to the wall to 90^0 from their body. Research personnel will record the initial location of their hand on the wall at the third metacarpal (i.e., knuckle of middle finger). Subjects are then instructed to "reach as far forward as you can without taking a step." Assuming the participant does not move their feet, research personnel will again record the location of their hand on the wall in this final position. The distance from the initial (point B on Figure 2) to the final (point C on Figure 2) location the subject can reach is then measured in inches (see figure 1 below). Three trials are performed, and the final two attempts are averaged as the measure of functional reach. Self-reported pain will be assessed during the final position of each trial and the average of the final two trials will be recorded as the measure of pain during the functional reach test.

Figure 12.4-2: Illustration of the Functional Reach Test



12.4.11. Fluoroscopy

Thoracic and lumbar imaging taken as part of standard of care may be collected at the Neurostimulator Trial Stimulation Procedure, permanent neurostimulator IPG Implantation and/or if images captured as part of standard of care while participating in the study (e.g. lead revision, reprogramming, etc.). Images should reflect final lead spinal placement from these procedures and be marked to denote vertebral level.

12.4.12. Medical History

Medical history will include medical and procedural history relating to pain management, onset of chronic pain, etc.

12.4.13. Mobile App

The Mobile App is available to be downloaded from the app store onto the subject's smartphone. A QR code or a 9-digit study code provided by the study site to a study subject is required to access the study. The Mobile App only works when connected to the internet via cell or WIFI signal.

The subject will use the Mobile App to respond to questions and/or questionnaires, submit voice recording/responses, log information such as pain, complete body map drawings, complete fitness assessments, and review notifications and/or recommendations. Subjects may also choose to share other data collected through their phone such as steps, and activity by allowing the Mobile App to access data through a function such as AppleHealth, GoogleFit, SamsungSHealth and FitBit. Subjects with a compatible Remote Control may also connect to their SCS device to upload programming usage data.

Subjects are periodically reminded in the mobile app when they should not provide PHI/PII. Each subject will be identified via a unique identification code and these data will be related to other data sources via their clinical study subject ID which will be entered at enrollment.

12.4.14. 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.

12.4.15. Pain Catastrophizing Scale (PCS)

The Pain Catastrophizing Scale measures cognitive responses to chronic pain, specifically a subject's rumination, magnification and feelings of helplessness relative to their pain. It consists of thirteen (13) questions and is expected to take about three to five (3-5) minutes to complete.

12.4.16. 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.

12.4.17. 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.

12.4.18. 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%.

12.4.19. Procedure Information

General information will be collected regarding the SCS procedures performed during the study, including all neurostimulation trial procedures and IPG implantation procedures.

12.4.20. Programming Data Download

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

12.4.21. Sleep Sensor (Optional for subjects enrolled under Protocol Ver. A and B. Not applicable for subjects enrolled in Protocol Ver. C or later)

Subjects will have the option to use a commercially available non-contact sleep sensor. Subjects will install the sleep sensor under their primary sleep location (e.g. under a mattress) After set-up, the sleep sensor health monitor will collect biosensor data such as heart rate, respiration rate and in-bed activity and will automatically transfer the deidentified data to a secure server via a cellular network.

12.4.22. Wrist-worn Biosensor

Subjects will also be asked to wear a commercially available wrist-worn biosensor, like a watch or wrist-worn fitness band. The wrist-worn biosensor will also collect biosensor data, such as heart rate and may be used to log information such as pain and respond to questions and/or questionnaires. Responses may be provided via voice responses.

12.5. [redacted]

[redacted]

13. Deviations

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

All deviations from the investigational plan, with the reason for the deviation and the date of occurrence, must be documented and reported to the sponsor using the EDC system. Subject non-compliance for at home activities, including but not limited to, wrist-worn biosensors, sleep sensor, and mobile app and/or completing in-office fitness assessments or questionnaires will not be reported as deviations, as there are no powered endpoints, nor is there any risk to subjects not completing these assessments as part of study participation.

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

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

The sponsor will not approve protocol waivers.

14. Compliance

14.1. *Statement of Compliance*

This clinical investigation is financed by the study sponsor. Before the site can be "Authorized to Enroll," the investigational site must enter into a Clinical Study Agreement with the sponsor that details the financing of the study as well as the rights and obligations of the investigational site and the investigator. This study will be conducted in accordance with the spirit of EN ISO 14155: Clinical Investigation of Medical Devices for Human Subjects – Good Clinical Practice, the relevant parts of the ICH Guidelines for Good Clinical Practices, ethical principles that have their origins in the Declaration of Helsinki, and applicable individual country laws and regulations. The study shall not begin until the required approval/favorable opinion from the IRB and/or regulatory authority has been obtained, if appropriate. Also, the study shall not begin prior to issuance of the site Authorization to Enroll, as provided by the sponsor. Any additional requirements imposed by the IRB or regulatory authority shall be followed, if appropriate.

14.2. *Investigator Responsibilities*

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

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

- Prior to beginning the study, sign the Clinical Study Agreement and comply with the Investigator responsibilities as described in such Agreement.
- 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 clinical investigation.

- Create and maintain source documents throughout the clinical study and ensure their availability with direct access during monitoring visits or audits; ensure that all clinical-investigation-related records are retained per requirements.
- Ensure the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor in the CRFs and in all required reports.
- Record, report, and assess (seriousness and relationship to the device/procedure) every adverse event as applicable per the protocol and observed device deficiency.
- Report to sponsor, per the protocol requirements, all reportable events.
- Report to the IRB and regulatory authorities any SAEs and device deficiencies that could have led to a SADE and potential/USADE or UADE, if required by applicable laws or regulations or this protocol or by the IRB, and supply BSC with any additional requested information related to the safety reporting of a particular event.
- 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 when it is used/operated by the subject.
- Inform the subject of any new significant findings occurring during the clinical investigation, including the need for additional medical care that may be required.
- Provide the subject with well-defined procedures for possible emergency situations related to the clinical study, and make the necessary arrangements for emergency treatment, including decoding procedures for blinded/masked clinical investigations, as needed.
- Ensure that clinical medical records are clearly marked to indicate that the subject is enrolled in this clinical study.
- Inform, with the subject's approval or when required by national regulations, the subject's personal physician about the subject's participation in the clinical investigation.
- Make all reasonable efforts to ascertain the reason(s) for a subject's premature withdrawal from clinical investigation while fully respecting the subject's rights.

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

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

14.2.1. 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, are competent to perform the tasks they have been delegated and adequate supervision of those to whom tasks are delegated. Where there is a sub investigator at a site, the sub investigator should not be delegated the primary supervisory responsibility for the site. The investigator is accountable for regulatory violations resulting from failure to adequately supervise the conduct of the clinical study.

14.3. *Institutional Review Board/ Ethics Committee*

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

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

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

14.4. *Sponsor Responsibilities*

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

the analysis and reporting of this study or shared with a third-party researcher will be without identifiable reference to specific subjects.

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

[redacted]

[redacted]

15. Monitoring

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

The sponsor will put a plan in place to document the specific monitoring requirements.

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

16. Potential Risks and Benefits

16.1. *Directions for Use*

Please refer to the Directions for Use for an overview of anticipated adverse (device) effects, and risks associated to the commercial device(s).

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

The subject might find it difficult, uncomfortable, or tiresome to complete study visits.

Fluoroscopy

An X-ray of the spine will expose subjects to small amounts of radiation. A single X-ray of the spine will typically use a radiation dose of approximately 1.5 millisievert, which is comparable to naturally occurring "background" radiation experienced by the average U.S. person over 6 months. Large population studies have shown an increase in cancer risk with much larger amounts of radiation, but there is always a potential concern that this risk may apply to the lower amounts delivered by an X-ray.

Women should always inform their physician and X-ray technologist if there is any possibility that they are pregnant, as it is not recommended for pregnant women unless medically necessary. It is possible that the X-ray will show an unexpected abnormal finding, which could cause subject anxiety as well as the need for additional procedures.

Study Assessments/Mobile App

Subjects may find any of the various study assessments or Mobile App repetitive or inconvenient. They may feel uncomfortable answering questions or performing some of the activities.

The fitness assessments may feel strenuous or tiring. Although unlikely, it is possible these assessments could worsen the subjects' pain temporarily or, more rarely, could create new pain or lasting exacerbation.

Wrist-worn Biosensor

Subjects may find wearing a wrist-worn biosensor inconvenient or uncomfortable.

16.3. *Possible Interactions with Concomitant Medical Treatments, if applicable*

There are no concomitant medical treatments required outside of standard of care treatment.

16.4. ***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.

16.5. ***Anticipated Benefits***

The reported benefit of SCS is to reduce chronic pain of the trunk and/or limbs. Refer to the Directions for Use for more information.

16.6. ***Risk to Benefit Rationale, if applicable***

The risk evaluation for BSC neurostimulation systems determined that all hazards attributed to BSC neurostimulation systems and overall remaining residual risks after implementations of the required mitigations have been evaluated. Based on the risk evaluation results, the benefit provided by BSC neurostimulation systems to treat chronic intractable pain of the trunk and limbs outweighs the remaining residual risk. As the overall residual risk meets BSC's criteria, BSC neurostimulation systems are acceptable for use in a clinical setting.

17. Safety Reporting

17.1. ***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 Device Deficiencies
- New findings/updates in relation to already reported events
- All Device Related Adverse Events (Device Hardware and Stimulation Related)
- All Procedure Related Adverse Events

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

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

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

Underlying diseases and chronic conditions are not reported as AEs unless there is an increase in severity or frequency during the investigation. Death should not be recorded as an AE but should only be reflected as an outcome of one (1) specific SAE (see Table 17.2-1 for AE definitions).

Refer to Directions for Use for the known risks associated with the commercial device(s).

17.2. *Definitions and Classification*

Adverse event definitions are provided in Table 17.2-1. Administrative edits were made on the safety definitions from ISO 14155 and MEDDEV 2.7/3 for clarification purposes.

Table 17.2-1: Safety Definitions

Term	Definition
Adverse Event (AE) *Ref: ISO 14155* *Ref: MDCG 2020-10/1*	Any untoward medical occurrence, unintended disease or injury, or any untoward clinical signs (including an abnormal laboratory finding) in subjects, users or other persons, in the context of a clinical investigation and whether or not related to the study medical device and whether anticipated or unanticipated. **NOTE 1**: This includes events related to the study medical device or comparator. **NOTE 2**: This definition includes events related to the procedures involved. **NOTE 3**: For users or other persons, this definition is restricted to events related to the study medical device.
Adverse Device Effect (ADE) *Ref: ISO 14155* *Ref: MDCG 2020-10/1*	Adverse event related to the use of the study 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 study medical device. **NOTE 2**: This definition includes any event resulting from use error or intentional misuse of the study medical device. **NOTE 3**: This includes 'comparator' if the comparator is a medical device.
Serious Adverse Event (SAE) *Ref: ISO 14155* *Ref: MDCG 2020-10/1*	Adverse event that led to any of the following: a) death, b) serious deterioration in the health of the subject, users or other persons as defined by either: 1) a life-threatening illness or injury, or 2) a permanent impairment of a body structure or a body function, including chronic diseases, or 3) in-patient hospitalization or prolongation of existing hospitalization, or 4) medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function c) foetal distress, foetal death, or a congenital abnormality or birth defect including physical or mental impairment.

Table 17.2-1: Safety Definitions

Term	Definition
	NOTE 1: Planned hospitalization for a pre-existing condition, or a procedure required by the clinical investigational plan, without a serious deterioration in health, is not considered a serious adverse event.
Serious Adverse Device Effect (SADE) *Ref: ISO 14155* *Ref: MDCG 2020-10/1*	Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.
Unanticipated Adverse Device Effect (UADE) *Ref: 21 CFR Part 812*	Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.
Unanticipated Serious Adverse Device Effect (USADE) *Ref: ISO 14155* *Ref: MDCG 2020-10/1*	Serious adverse device effect which by its nature, incidence, severity, or outcome has not been identified in the current risk assessment. **NOTE 1**: Anticipated serious adverse device effect (ASADE) is an effect which by its nature, incidence, severity or outcome has been identified in the risk assessment.
Serious Health Threat *Ref: ISO 14155*	Signal from any adverse event or device deficiency that indicates an imminent risk of death or a serious deterioration in the health in subjects, users or other persons, and that requires prompt remedial action for other subjects, users or other persons. **NOTE 1**: This would include events that are of significant and unexpected nature such that they become alarming as a potential serious health hazard or possibility of multiple deaths occurring at short intervals.
Device Deficiency *Ref: ISO 14155* *Ref: MDCG 2020-10/1*	An inadequacy of the study medical device related to its identity, quality, durability, reliability, usability, safety or performance. **NOTE 1**: Device deficiencies include malfunctions, use errors, and inadequacy in the information supplied by the manufacturer including labelling. **NOTE 2**: This definition includes device deficiencies related to the device under study, or the comparator.
The following definitions will be used for defining hospitalization or prolongation of hospitalization for SAE classification purposes:	
Hospitalizations	Hospitalization does not include: • emergency room visit that does not result in in-patient admission Note: although an emergency room visit does not itself meet the definition for hospitalization, it may meet other serious criteria (e.g. medical or surgical intervention to prevent permanent impairment or damage) • elective and pre-planned treatment/surgery for a pre-existing condition that is documented in the subject's record at the time of consent/enrollment

Table 17.2-1: Safety Definitions

Term	Definition
	• admission for social reasons and/or respite care in the absence of any deterioration in the subject's general condition (e.g. subject is homeless, caregiver relief) pre-planned, protocol-specified admission related to the clinical study (e.g. procedure required by protocol)
Prolongation of hospitalization	In-patient admission to the hospital that is prolonged beyond the expected standard duration for the condition under treatment. Note: new adverse events occurring during the hospitalization are evaluated to determine if they prolonged hospitalization or meet another SAE criteria.

Underlying diseases are not reported as AEs unless there is an increase in severity, location, or frequency, beyond the expected course or progression of the disease, during the investigation. Death should not be recorded as an AE, but should only be reflected as an outcome of a specific SAE.

Hospitalization is defined as any in-patient admission regardless of duration of stay. Emergency room admissions and outpatient visits are not considered hospitalizations.

Any adverse event or complaint occurring in subjects who withdraw participation in the study and opt to remain implanted with the device should be reported to the Complaints Call Center as detailed in the "Directions for Use (DFU)".

In accordance with FDA regulations 21 CFR 820.3, a complaint is any written, electronic or verbal communication that alleges deficiencies related to the identity, design, quality, durability, reliability, safety, effectiveness or performance of a product after it is released for distribution.

Pregnancy will not be considered an adverse event. If a subject becomes pregnant, she may withdraw from the study or remain in the study at her discretion with concurrence of her physician.

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, 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 will be reported as AEs.
6. Lack of efficacy/decreased therapeutic response will not be collected as AEs. Also, return of the patient's pain symptoms to their pre-SCS level does not meet the criteria for an AE.
7. Clinically significant worsening of symptoms, beyond the pre-SCS symptoms or the expected course or progression of the disease, should be reported as an AE.
8. Device/lead migration will not be collected as an AE. However, if the device/lead migration precipitated an AE, the AE should be reported in the *Adverse Event* eCRF. Device/lead migration should be documented in the *Device Deficiency* eCRF.
9. Device deficiencies, failures, malfunctions, and product nonconformities should not be reported as adverse events. However, if an adverse event resulted from a device failure or malfunction, that specific event would be recorded on the *Adverse Event* eCRF. Device deficiencies, failures, malfunctions, and product non-conformities should be documented in the *Device Deficiency* eCRF.

17.3. ***Relationship to Study Device(s), (Device Under Study and Comparator Device, if applicable) and/or Study Procedure***

The Investigator must assess the relationship of the reportable AE to the study device(s), stimulation and/or procedure. See criteria in Table 17.3-1:

Table 17.3-1: Criteria for Assessing Relationship of Study Device(s) (Device Under Study and Comparator Device, if applicable) or Procedure to Adverse Event

Classification	Description
Not Related *Ref: MDCG 2020-10/1*	Relationship to the device, comparator or procedures can be excluded when: - the event has no temporal relationship with the use of the study device or the procedures related to the use of the study device; - the serious event does not follow a known response pattern to the medical device (if the response pattern is previously known) and is biologically implausible; - the discontinuation of medical device application or the reduction of the level of activation/exposure - when clinically feasible – and reintroduction of its use (or increase of the level of activation/exposure), do not impact on the serious event; - the event involves a body-site or an organ that cannot be affected by the device or procedure; - the serious event can be attributed to another cause (e.g. an underlying or concurrent illness/ clinical condition, an effect of another device, drug, treatment or other risk factors); - the event does not depend on a false result given by the study device used for diagnosis, when applicable; - In order to establish the non-relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the serious event.
Unlikely Related *Ref: MEDDEV 2.7/3*	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. NOTE: Causality "Unlikely Related" was added in compliance with MED DEV 2.7/3 rev 3 and will continue to be collected from the sites.
Possibly Related *Ref: MDCG 2020-10/1*	The relationship with the use of the study device or comparator, or the relationship with procedures is weak but cannot be ruled out completely. Alternative causes are also possible (e.g. an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment). Cases where relatedness cannot be assessed or no information has been obtained should also be classified as possible.
Probably Related *Ref: MDCG 2020-10/1*	The relationship with the use of the study device or comparator, or the relationship with procedures seems relevant and/or the event cannot be reasonably explained by another cause.

Table 17.3-1: Criteria for Assessing Relationship of Study Device(s) (Device Under Study and Comparator Device, if applicable) or Procedure to Adverse Event

Classification	Description
Causal Relationship *Ref: MDCG 2020-10/1*	The serious event is associated with the study device, comparator or with procedures beyond reasonable doubt when: - the event is a known side effect of the product category the device belongs to or of similar devices and procedures; - the event has a temporal relationship with the study device use/application or procedures; - the event involves a body-site or organ that -the study device or procedures are applied to; -the study 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 study 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.

17.4. *Investigator Reporting Requirements*

The communication requirements for reporting to BSC are as shown in Table 17.4-1: Investigator Reporting Requirements.

Table 17.4-1: Investigator Reporting Requirements

Event Classification	Communication Method	Communication Timeline post-market studies* (*MDCG 2020-10/1* MEDDEV 2.12/2 : GUIDELINES ON A MEDICAL DEVICE VIGILANCE SYSTEM)
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 end of study.
	Provide all relevant source documentation (de-identified/ pseudonymized)	• When documentation is available • Upon request of sponsor

Event Classification	Communication Method	Communication Timeline post-market studies* (*MDCG 2020-10/1* MEDDEV 2.12/2 : GUIDELINES ON A MEDICAL DEVICE VIGILANCE SYSTEM)
	for reported event upon request.	
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 (de-identified/ pseudonymized) for reported event.	• When documentation is available • Upon request of sponsor
Device Deficiencies (including but not limited to malfunctions, use errors, and inadequacy in information supplied by the manufacturer, including labelling) Note: Any Device Deficiency that might have led to a serious adverse event if appropriate action had not been taken, intervention had not occurred, or if circumstances had been less fortunate is considered a reportable event.	Complete Device Deficiency CRF 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
	Provide all relevant source documentation (de-identified/ pseudonymized) for reported event upon request.	• Upon request of sponsor
Adverse Event including Adverse Device Effects	Complete AE eCRF page, which contains such information as date of AE, treatment of AE resolution, assessment of seriousness and relationship to the device.	• Adverse Device Effects (or other key events of interest, e.g., Heart Failure): In a timely manner (e.g. recommend within 30 business days) after becoming aware of the information • Adverse Events: In a timely manner (e.g. recommend within 30 business days) after becoming aware of the information • Reporting required through end of study. • Reporting required for all procedure and device (stimulation and hardware) related adverse events
	Provide all relevant source documentation (de-identified/ pseudonymized) for reported event.	• Upon request of sponsor

Event Classification	Communication Method	Communication Timeline post-market studies* (*MDCG 2020-10/1* MEDDEV 2.12/2 : GUIDELINES ON A MEDICAL DEVICE VIGILANCE SYSTEM)

The investigator must report Device and Procedure Related Adverse Events, Adverse Device Effects, Serious Adverse Events (regardless of relationship to device hardware, stimulation and/or procedure), and Device Deficiencies for each subject from the time of Information Consent through the end of study participation. AEs and Device Deficiencies may be reported via phone, fax or email if the electronic data capture (EDC) system is unavailable. The paper AE Notification Form or Device Deficiency Notification Form should be used to report AEs and/or device deficiencies during this time.

The Investigator must assess the potential relationship of all adverse events to the study device and/or to study procedures.

- Adverse events must be assessed according to their relationship to one of the following categories:
    - **Device Hardware-Related AEs:** AEs that can reasonably (i.e. Unlikely, Possibly, Probably and Causally Related) 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 (i.e. Unlikely, Possibly, Probably and Causally Related) 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.
    - **Procedure Related AEs:** AEs that can reasonably (i.e. Unlikely, Possibly, Probably and Causally Related) be attributed to a study protocol required procedure.

17.5. *Boston Scientific Device Deficiencies*

Device deficiencies for Boston Scientific devices will be documented and reported to BSC. If possible, the device(s) should be returned to BSC for analysis. Instructions for returning the device(s) will be provided from the study sponsor. Device deficiencies should also be documented in the subject's source records.

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

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

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

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

18. Informed Consent

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

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

Boston Scientific will provide a study-specific template of the ICF to investigators participating in this study. The ICF template may be modified to meet the requirements of the investigative site's IRB. Any modification requires acceptance from BSC prior to use of the form. The ICF must be in a language understandable to the subject. 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 or his/her legal representative,
- 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 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 person signing the form.

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

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

19. Committees

19.1. *Safety Monitoring Process*

The BSC personnel from the BSC Medical Safety group review safety data as soon as it is reported, by the sites throughout the duration of the study. During scheduled monitoring activities, clinical research monitors further support this review through their review of source documents and other data information. The BSC Medical Safety group includes a physician with the necessary therapeutic and subject matter expertise to evaluate and classify the events into the categories outlined above.

20. Suspension or Termination

20.1. *Premature Termination of the Study*

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

20.1.1. Criteria for Premature Termination of the Study

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

- Suspicion of an unacceptable risk, including serious health threat. In this case, the sponsor shall suspend the clinical investigation while the risk is assessed. The sponsor shall terminate the clinical investigation if an unacceptable risk which cannot be controlled is confirmed.

- Instructions by the IRB or regulatory authorities to suspend or terminate the clinical investigation.
- An enrollment rate far below expectation that prejudices the conclusion of the study.
- A decision on the part of Boston Scientific to suspend or discontinue development/marketing of the device.

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

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

20.3. *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/ECs/REBs, 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 devices, if supplied by Boston Scientific, unless this action would jeopardize the rights, safety, or welfare of the subjects.

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

Boston Scientific reserves the right to stop the inclusion of subjects at a study site at any time after the study initiation visit if no subjects have been enrolled for a period beyond 6 months after site initiation, 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 devices and testing equipment, as applicable, will be returned to BSC unless this action would jeopardize the rights, safety or well-being of the subjects. The IRB and regulatory authorities, as applicable, will be notified. Study participants will be contacted, as applicable, and be informed of changes to study visit schedule.

21. Study Registration and Results

21.1. *Study Registration*

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

21.2. [redacted]

[redacted]

21.3. *Publication Policy*

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

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

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

[redacted]

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[redacted]

23. Abbreviations and Definitions

23.1. *Abbreviations*

Abbreviations are shown in Table 23.1-1.

Table 23.1-1: Abbreviations

Abbreviation/Acronym	Term
6MWT	6 Minute Walk Test
ADE	Adverse device event
AE	Adverse event
BDI-II	Beck depression inventory
BSC	Boston Scientific Corporation
CFR	Code of Federal Regulations
DFU	Directions for use
eCRF	Electronic case report form
EDC	Electronic data capture
EQ-5D-5L	EuroQol Group, 5 dimensions, 5 level
EC	Exclusion criteria
ETS	External Trial Stimulator
FBSS	Failed Back Surgery Syndrome
FABQ	Fear Avoidance Beliefs Questionnaire
FDA	Food and Drug Administration
GCP	Good clinical practice
HCP	Health care personnel
IC	Inclusion criteria
ICF	Informed consent form
ICH	International conference on harmonization
IPG	Implantable pulse generator
IRB	Institutional review board
ISO	International Organization for Standardization
Mg	Milligram
NRS	Numerical rating scale
ODI	Oswetry Disability Index
PCS	Pain Catastrophizing Scale
PPR	Percent pain relief
SADE	Serious adverse device effect
SAE	Serious adverse event
SCS	Spinal cord stimulation

Table 23.1-1: Abbreviations

SF-36v2	Short Form 36 Health Survey ver 2
UADE	Unanticipated adverse device effect
VRS	Verbal rating scale

23.2. *Definitions*

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