

**Official Title of the study:** Vectors Post Market: A study to assess pain relief using spinal cord stimulation with high dose stimulation parameters

**NCT number:** NCT03345472

**Date of document:** 08MAY2018

**Document Type:** Study Protocol



<b>Medtronic</b> Clinical Investigation Plan	
<b>Clinical Investigation Plan Title</b>	Vectors Post Market: A study to assess pain relief using spinal cord stimulation (SCS) with high dose (HD) stimulation parameters
<b>Clinical Investigation Plan Identifier</b>	MDT17053
<b>Product Name</b>	Medtronic RestoreSensor® SureScan® MRI and Intellis™ AdaptiveStim® Neurostimulation System
<b>Global Sponsor</b>	Medtronic, Inc Medtronic Neuromodulation 7000 Central Ave NE Minneapolis, MN, 55432 U.S.A. +1-763-514-4000
<b>Document Version</b>	V 4.0 08 MAY 2018
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## 1. Investigator Statement

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Participating investigators will be provided with a separate Investigator Agreement to document their obligations and commitment with respect to study conduct.



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## 2. Glossary

Abbreviation	Term
ADE	Adverse Device Effect
AE	Adverse Event
AEAC	Adverse Events Advisory Committee
AGA	Activity Goal Assessment
AP	Anteroposterior Position
ASADE	Anticipated Serious Adverse Device Effect
CIP	Clinical Investigation Plan
CRF	Case Report Form
CRPS	Complex Regional Pain Syndrome
DD	Device Deficiency
DDD	Degenerative Disk Disease
DMC	Data Monitoring Committee
EC	Ethics Committee
eCRF	Electronic Case Report Form
ENS	External Neurostimulator
EQ-5D-5L	EuroQol Five Dimensions Questionnaire
FBS	Failed Back Syndrome
HD	High Dose
IC	Informed Consent
ICF	Informed Consent Form
ICH	International Conference on Harmonization
INS	Implantable Neurostimulator
IRB	Institutional Review Board
LTFU	Lost to Follow-up
MLTC	Multi-Lead Trialing Cable
NPU	Neuro Programmer Upload
ODI	Oswestry Disability Index
OUS	Outside US
PGIC	Patient Global Impression of Change
PMA	Pre-Market Application
RCT	Randomized Controlled Trial
RDC	Remote Data Capture
RSD	Reflex Sympathetic Dystrophy
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event



Abbreviation	Term
SAP	Statistical Analysis Plan
SCS	Spinal Cord Stimulation
SSA	Subject Satisfaction Assessment
US	United States
USADE	Unanticipated Serious Adverse Device Effect
VAS	Visual Analog Scale

Terms	Definitions
High Dose (HD) Stimulation	For the purposes of the Vectors Post Market study, HD stimulation is stimulation delivered at a pulse width of 90 – 200 µsec and 1000 Hz at a comfortable amplitude or intensity
Overall pain	The combination of low back and leg pain. For the purposes of this study, the HD stimulation responder rate, using the VAS for overall pain, will be compared against the performance goal
Painful Paresthesia	Uncomfortable or unexpected stimulation (e.g. jolting or shocking sensation experienced by the patient) due to excessive SCS therapy
Paresthesia	Tingling sensation typically generated by SCS therapy
Paresthesia Mapping	Test stimulation used to determine if area of stimulation overlaps with a subject's areas of pain
Perception threshold	The stimulation intensity at which the subject first perceives paresthesia
Visual Analog Scale	For the purposes of the Vectors Post Market study, the visual analog scale (VAS) will always be a single day score.

### 3. Synopsis

<b>Title</b>	Vectors Post Market: A study to assess pain relief using spinal cord stimulation (SCS) with high dose (HD) stimulation parameters
<b>Clinical Study Type</b>	Post-Market study
<b>Product Name</b>	Medtronic RestoreSensor® SureScan® MRI and Intellis™ AdaptiveStim® Neurostimulation System
<b>Global Sponsor</b>	Medtronic, Inc. Medtronic Neuromodulation 7000 Central Ave NE Minneapolis, MN, 55432 U.S.A. +1-763-514-4000





	<p>[REDACTED]</p>
<b>Study Design</b>	<p>This is a global, prospective, single-arm, multi-center, non-randomized study evaluating the efficacy of SCS therapy for pain relief using HD stimulation parameters while targeting a specific anatomical location. The study will be conducted at up to 30 centers in the globally.</p>
<b>Sample Size</b>	<p>Up to 215 subjects will be enrolled globally.</p>
<b>Inclusion/Exclusion Criteria</b>	<p><u>Inclusion Criteria</u></p> <ol style="list-style-type: none"> <li>1. Willing and able to provide a signed and dated informed consent</li> <li>2. At least 18 years old at the time of enrollment</li> <li>3. Candidate per labeling for an SCS system (trial and implant) as an aid in the management of chronic, intractable pain of the trunk and limbs (low back and leg pain)</li> <li>4. Baseline VAS is <math>\geq 50</math> mm for low back pain</li> <li>5. Baseline VAS is <math>\geq 50</math> mm for leg pain</li> <li>6. ODI score of 21 to 80 out of 100</li> <li>7. On stable (no change in dose, route, or frequency) pain medications (prescribed and over-the-counter) being used for back and leg pain, as determined by the investigator, for at least 28 days prior to enrolling in the study</li> <li>8. Willing and able to attend visits and comply with the study protocol</li> <li>9. Willing and able to not increase their pain medications (prescribed and over-the-counter) being used specifically for back or leg pain through the 3-Month Visit</li> </ol> <p><u>Additional Inclusion Criterion (evaluated at Device Trial - Implant)</u></p> <ol style="list-style-type: none"> <li>1. After paresthesia mapping to confirm proper location at Device Trial, final lead placement spans the T9/T10 disc space</li> <li>2. After paresthesia mapping to confirm proper location at permanent implant, final lead placement spans the T9/T10 disc space</li> </ol> <p><u>Exclusion Criteria</u></p>



	<ol style="list-style-type: none"> <li>1. Previously trialed or implanted with spinal cord stimulator, peripheral nerve stimulator, or an implantable intrathecal drug delivery system</li> <li>2. Expected to be inaccessible for follow-up</li> <li>3. Subject is currently participating, or plans to participate, in another investigational study unless written approval is provided by the Medtronic study team</li> <li>4. Current diagnosis of moderate to severe central lumbar spinal stenosis with neurogenic claudication, as determined by the investigator</li> <li>5. Major psychiatric comorbidity or other progressive diseases that may confound study results, as determined by the investigator</li> <li>6. Serious drug-related behavioral issues (e.g. alcohol dependency, illegal substance abuse), as determined by the investigator</li> <li>7. Pregnant or planning on becoming pregnant (if female and sexually active, subject must be using a reliable form of birth control, be surgically sterile, or be at least 2 years post-menopausal)</li> <li>8. Unable to achieve supine position</li> </ol>
<p><b>Study Procedures and Assessments</b></p>	<p>Specific data and procedure requirements per visit are summarized in Table 4.</p> <p><b>Study Visits</b></p> <ul style="list-style-type: none"> <li>• Baseline Visit</li> <li>• Device Trial Day 0 – Lead Placement and initial programming</li> <li>• Device Trial Day 2</li> <li>• Device Trial Day 4 (if necessary)</li> <li>• Device Trial Day 6 (if necessary)</li> <li>• Implant</li> <li>• Device Activation Visit</li> <li>• 2-Week Visit</li> <li>• 4-Week Visit</li> <li>• 6-Week Visit</li> <li>• 3-Month Visit</li> <li>• 6-Month Visit</li> <li>• 12-Month/Final Visit</li> </ul> <p><b>Baseline Visit:</b>                  Subjects are considered enrolled at the time the study-specific informed consent/HIPAA form (or other data protection authorization as required by local regulations) is signed. Subjects in compliance with inclusion/exclusion criteria will be eligible to participate. A VAS score for overall (low back and leg), back, and leg will be collected. Subjects that do not have a VAS <math>\geq</math> 50 mm for low back pain and VAS <math>\geq</math> 50 mm for leg pain will be exited from the study. Subjects that meet the pain inclusion criteria will be asked about their back and leg pain/surgical history, be scheduled for a device trial, and complete the required assessments (e.g., EQ-5D-5L, ODI, and activity goal).</p>



	<p><b>Device Trial: Day 0 (≤ 14 days post Baseline Visit)</b>                  At Day 0, subjects will be implanted with two percutaneous leads per labeling. Subjects who have leads spanning the T9/T10 disc space will continue in the study. In the recovery room, subjects who have electrodes over the T9/T10 disc space will be programmed with 1 HD programming configuration.</p> <p><b>Device Trial Day 2: (2 – 4 days after Device Trial Day 0)</b>                  The effectiveness of the stimulation parameters programmed at Day 0 will be assessed for 2 days. If a subject has ≥ 50% reduction in pain, they will have their trial leads explanted and proceed to implant. If a subject does not have ≥ 50% pain relief, they will be reprogrammed to the second HD group and return for a Day 4 Visit.</p> <p><b>Device Trial Day 4, if necessary: (2 – 4 days after Day 2 Visit)</b>                  The effectiveness of the stimulation parameters programmed at Day 2 will be assessed for 2 days. If a subject has ≥ 50% reduction in pain, they will have their trial leads explanted and proceed to implant. If a subject does not have ≥ 50% pain relief, they will be reprogrammed using any on-label parameters (physician preference) and return for a Day 6 Visit</p> <p><b>Device Trial Day 6, if necessary: (2 – 4 days after Day 4 Visit; no later than Day 10)</b>                  Subjects will return to the clinic a minimum of two days later to assess the effectiveness of the physician preference stimulation parameters programmed at Day 4 and have their trial leads explanted. These subjects will then be exited from the study.</p> <p><b>Implant (≤ 30 days post end of device trial)</b>                  Subjects who were HD responders during the device trial and who met all eligibility criteria will be implanted with a RestoreSensor SureScan MRI or Intellis AdaptiveStim neurostimulation system. Subjects will be implanted with two compact percutaneous leads per labeling. Subjects who have leads spanning the T9/T10 disc space will continue in the study. The stimulator will be “OFF” when the subject leaves this visit.</p> <p><b>Device Activation Visit (9 – 16 days post implant)</b> The Device Activation Visit will take place 9 – 16 days after implant, pending wound healing. The stimulator will be turned “ON” at this visit and the programming that was successful for the trial will be programmed for that subject.</p> <p><b>Follow-up Visits (2 weeks, 4 weeks, 6 weeks ± 3 days and 3, 6, and 12 Months ± 15 days post Device Activation)</b>                  Visits will occur at weeks 2, 4 and 6 and months 3, 6 and 12 post device activation. EQ-5D-5L, ODI, PGIC, and SSA will be assessed at 3-, 6- and 12-Months. The VAS</p>
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	<p>will be administered at all follow-up visits and scored by site personnel. The Paresthesia Assessment and Recharging Questionnaire will be collected at the 3- and 12-Month Visits. The Activity Goal will be completed through the 3-Month Visit. Data for the primary endpoint will be collected at the 3-Month Visit.</p> <p><b>Telephone Calls (Daily during Device Trial, Monthly post Device Activation)</b> Subjects will be called 1, 3, 5, 7, 8, 9, 10 and 11 weeks post-device activation to assess their pain relief status and then monthly following the 3-Month Visit. If the subject reports inadequate pain relief, they will come in for an unscheduled visit.</p>
<p><b>Statistics</b></p>	<p>Only subjects who are implanted and have their devices activated will be included in the evaluation of the primary and secondary endpoints. The study sample size is based on the desired precision for the characterization of the secondary objectives. A sample size of 100 subjects provides a 95% confidence interval within 9.6% of the responder rate estimate, if the observed responder rate is 50%. For the primary objective, a sample size of 100 subjects ensures over 99% power to test a significant change from 0 under the following assumptions: two-sided alpha = 0.05, assumed mean reduction = 20 with a standard deviation = 30. Globally up to 215 subjects will be enrolled to ensure at least 100 subjects are implanted, have their devices activated, and are followed through the 3-Month Visit.</p> <p>The primary objective analysis will test the average change in overall pain from Baseline to the 3-Month Visit against no change, using a two-sided, one sample t-test with alpha = 0.05.</p> <p>The secondary objectives are not alpha-controlled; they will be characterized but not evaluated with statistical testing.</p>

## 4. Introduction

### 4.1. Background

Spinal Cord Stimulation (SCS) was first tested for the management of chronic intractable pain of the trunk and/or limbs in 1967.<sup>1</sup> The device system used today consists of one or more epidural leads and a subcutaneously implanted neurostimulator. The energy delivered from the electrodes on the epidural lead modulates pain signals in the nervous system. The neurostimulator generates electrical pulses that are delivered to the dorsal columns of the spinal cord based on lead location and can be controlled by adjusting the programming parameters of amplitude, frequency, and pulse width. Because the tactile sensory neurons in the dorsal columns are stimulated with SCS, paresthesias or a tingling feeling from the treatment can be felt during stimulation.

Two branded types of stimulation, HF10™ and BurstDR™, have recently come on the SCS market. HF10 therapy delivers SCS therapy at a frequency of 10 kHz, which is significantly higher than other



commercial SCS devices with rates between 2 and 1200 Hz. Due to the high frequency used, the HF10 pulse width is typically around 30  $\mu$ sec. In contrast, BurstDR is delivered in a series of five pulses at 500 Hz, delivered at a 40-Hz rate. Pulse width is typically set at 1000  $\mu$ sec. Both of these programming algorithms deliver a higher dose of energy than conventional stimulation by increasing the parameters of frequency and/or pulse width.<sup>2</sup> A “dose” of therapy can be calculated and presented as charge per second in micro-Coulombs ( $\mu$ C/s).<sup>2</sup> In fact, the idea of higher energy delivery and energy/sec was reported as a possible explanation for the effects of BurstDR.<sup>3</sup> Other programming parameters may also result in “high dose” (HD) stimulation. High dose contrasts with low dose (LD) therapy, which typically uses lower energy and frequencies between 30-100 Hz. Table 1 describes an example of parameters of HD stimulation.

**Table 1 SCS Dose**

Parameter	Medtronic Device Range	Description	Conventional	High Dose
<b>Dose</b>	Variable, based on settings	A product of pulse width, frequency, and current.  Reported in micro Coulombs per second ( $\mu$ C/sec), also referred to as Charge per second.	50 Hz, 400 $\mu$ sec, 4 mA = 80 $\mu$ C/sec	1000 Hz, 90 $\mu$ sec, 4 mA = 360 $\mu$ C/sec

SCS therapy relies on the delivery of energy to a specified stimulation spinal cord target. Conventional stimulation has targeted any area of the dorsal columns that result in a comfortable paresthesia perception over the painful area. HF10 therapy simplified SCS therapy by staggering two epidural leads along the midline from T8 to T11. The typical starting target for HF10 therapy is a bipole at the T9-T10 disc space.<sup>4</sup> This is in accord with a study by Barolat et al. (1993), who determined that targeting the T9-T10 implanted “strictly midline” was the “best location” for SCS to treat low back pain without stimulation of the chest or abdominal wall.<sup>5</sup> Barolat (2001) used conventional stimulation parameters at T9-T10 in which 68.8% of patients reported fair to excellent pain relief after 1 year of stimulation.<sup>6</sup> In a recent study of HF10, the investigators placed two leads over the T9-T10 intervertebral space and reported that 84.5% of HF10 subjects were back pain responders, reporting greater than 50% pain relief.<sup>4</sup>



While the patient outcomes with these stimulation parameters and location is promising, additional clinical research is needed to understand the amount of energy and the specific stimulation target that will result in the best patient outcomes.

## 4.2. Purpose

The purpose of this study is to evaluate the efficacy of spinal cord stimulation (SCS) therapy using HD stimulation parameters while targeting a specific anatomical location.

## 4.3. Regulatory Study Classification

This on-label, post-market clinical study using the RestoreSensor SureScan MRI and Intellis AdaptiveStim Neurostimulation Systems, FDA-approved, CE-marked, or licensed/market released devices, will be conducted in up to 30 sites and approximately 215 subjects with chronic, intractable pain of the back and legs may be enrolled globally. The study will be conducted in accordance with this protocol, the ethical principles that have their origin in the Declaration of Helsinki, all applicable regulatory requirements (In the US: 21 Code of Federal Regulations [CFR] §50 Protection of Human Subjects, and 21CFR§56 Institutional Review Board [IRB], 21CFR§803 Medical Device Reporting), and International Conference on Harmonization (ICH GCP E6). Regulatory requirements applicable to individual countries outside the US will be included in geography-specific addenda. This study will be posted on ClinicalTrials.gov as part of Medtronic's commitment to full disclosure for ongoing studies that meet the requirements for public posting.

Documentation for this study will be produced and maintained to ensure that a complete history of the study exists. Documents created for this study, including all versions of original documents, will be identifiable and appropriately stored to assure control and traceability of data related to this study.

## 5. Objectives and Endpoints

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### 5.1. Objectives

#### 5.1.1. Primary Objective(s)

To demonstrate a significant improvement in overall (low back and leg) pain intensity using HD stimulation starting at 90 - 200  $\mu$ sec and 1000 Hz with lead placement spanning the T9/T10 disc space, as measured by the Visual Analog Scale (VAS), from Baseline to the 3-Month Visit.

#### 5.1.2. Safety Assessment

This study will characterize all device-, therapy-, or procedure-related adverse events and device deficiencies from enrollment to study exit.



### 5.1.3. Secondary Objective(s)

1. To characterize the overall (low back and leg) pain efficacy responder rate, as measured by the VAS, from Baseline to the 3-Month Visit, with a confidence interval within  $\pm 10\%$
2. To characterize the low back pain efficacy responder rate, as measured by the VAS, from Baseline to the 3-Month Visit, with a confidence interval within  $\pm 10\%$
3. To characterize the leg pain efficacy responder rate, as measured by the VAS, from Baseline to the 3-Month Visit, with a confidence interval within  $\pm 10\%$

### 5.1.4. Additional Measures

[Redacted text block]

## 6. Study Design

This is a prospective, single-arm, multi-center, non-randomized study evaluating the efficacy of SCS therapy for pain relief using HD stimulation parameters while targeting a specific anatomical location. The study will be conducted at up to 30 centers globally.



Approximately 215 subjects are expected to be enrolled in the study to allow for at least 100 subjects to complete the 3-Month Visit. All implanted subjects with devices activated at the Device Activation Visit will be followed through the 12-Month Visit. The study sample size accounts for expected attrition; therefore, subjects who discontinue after implant will not be replaced.

To ensure a widespread distribution of data and minimize center bias in study results, the maximum number of subjects that may be implanted at a single site is 25 subjects. .

There is no minimum enrollment requirement for any study site; however, each site will be encouraged to enroll at least 8 subjects. If a site does not enroll any subjects within three months of activation, they may forfeit their participation in the clinical study to another site to ensure timely enrollment.

Selection of subjects, treatment of subjects, and evaluation of study data are potential sources of bias. Potential sources of bias that may be encountered in this study have been considered and minimized by careful study design. Methods incorporated in the study design to minimize potential bias include (but are not limited to) the following:

- Subjects will be screened to confirm eligibility for enrollment with defined inclusion/exclusion criteria
- Subject demographics will be collected at baseline to assess possible characteristics that may influence endpoints
- To ensure widespread distribution and data among centers, the maximum number of implanted subjects per center will be no more than 25. Additionally, centers will be encouraged to enroll at least 8 subjects.
- A statistical analysis plan will be developed prior to analyzing data which will document pre-specified analysis and analysis methods
- All study site personnel and Medtronic personnel will be trained on their respective aspects of the study using standardized training materials
- All study site personnel will be trained on and required to follow the Clinical Investigation Plan





## 6.1. Duration

The start of the study for each subject is defined as the date the subject first signs the informed consent/HIPAA form or other data protection form as required by local regulations. Enrolled subjects will have up to 13 scheduled visits. The expected study commitment for each subject is up to 15 months. The overall study duration, from first subject enrollment to last subject visit, is expected to last approximately 3 - 4 years.

## 6.2. Rationale

Spinal cord stimulation is a well-established therapy for the treatment of chronic intractable pain, with Level I and Level II evidence for the efficacy of the therapy as a treatment of persistent post-lumbar surgery pain.<sup>7</sup> The efficacy of conventional spinal cord stimulation in the treatment of back pain has lagged leg pain relief associated with SCS.<sup>8</sup> There is evidence that the T9/T10 intervertebral disc space has been a common location to target stimulation for chronic low back pain and leg pain using conventional parameters for over 20 years.<sup>5,9-11</sup> However, to date, there have been no large clinical trials evaluating outcomes of HD stimulation at frequencies below 10,000 Hz at the T9/T10 intervertebral disc space.

## 7. Product Description

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### 7.1. General

The Medtronic RestoreSensor SureScan MRI and Intellis AdaptiveStim neurostimulation system will be used in this study. All study devices shall be used in accordance with their product labeling and will only be used in the geographies in which they are commercially available. See OUS geography-specific addenda for further information as applicable. For Section 9 (Study Procedures) RestoreSensor SureScan MRI will be referred to as RestoreSensor and Intellis AdaptiveStim will be referred to as Intellis. The implanted components of the SCS neurostimulation system include the following:

- Model 97714 RestoreSensor SureScan MRI neurostimulator (INS)
- Model 97715 Intellis AdaptiveStim neurostimulation system
- Model 977D260 Vectris™ 1x8 Compact Trial Screening Lead Kit
- Models 977A260, 977A275, and 977A290 Vectris™ SureScan® MRI 1x8 Compact Lead Kits
- Models 97791 and 97792 Injex™ Anchor Accessory Kits

The non-implanted components of the RestoreSensor SureScan MRI system include the following:

- Model 37022 External Neurostimulator
- Model 355531 Multi-lead Trialing Cable (MLTC)
- Model 8840 N'Vision® Clinician Programmer
- Model 8870 N'Vision® Software Application Card
- Model 8580 N'Vision® Report Link
- Model 97740 MyStim Patient Programmer
- Model 37092 Patient Programmer Antenna



- Model 97754 Recharger Charging System (Includes Model 37751 INS Recharger, Model 37761 AC Power Supply & applicable accessories)
- Model 3550-54 Patient Waist Belt
- Other accessories used (e.g., tunneling tools, needle kits, wrenches, or screws)

The non-implanted components of the Intellis AdaptiveStim system include the following:

- Model 97725 Wireless External Neurostimulator
- Model 97745 Patient Controller
- Model 375003 Boot for Wireless External Neurostimulator
- Model 97755 Recharger
- Model 8880T2 Communicator

## 7.2. Manufacturer

The neurostimulation system is manufactured by Medtronic, Inc. with operational headquarters in Minneapolis, Minnesota 55432-5604, USA.

## 7.3. Packaging

All of the devices that will be used in this study have been approved or cleared by the FDA for spinal cord stimulation as an aid in the management of chronic, intractable pain of the trunk and/or limbs. The devices specified in Section 7.1 will be shipped in their commercially available form in each geography, which includes packaging and labeling. See geography-specific addenda for applicable OUS information.

## 7.4. Intended Population

In the United States a Medtronic implantable neurostimulation system is indicated for spinal cord stimulation (SCS) systems as an aid in the management of chronic, intractable pain of the trunk and/or limbs-including unilateral or bilateral pain associated with the following conditions:

- Failed Back Syndrome (FBS) or low back syndrome or failed back
- Radicular pain syndrome or radiculopathies resulting in pain secondary to FBS or herniated disk
- Postlaminectomy pain
- Multiple low back operations
- Unsuccessful disk surgery
- Degenerative Disk Disease (DDD)/herniated disk pain refractory to conservative and surgical interventions
- Peripheral causalgia
- Epidural fibrosis
- Arachnoiditis or lumbar adhesive arachnoiditis
- Complex Regional Pain Syndrome (CRPS), Reflex Sympathetic Dystrophy (RSD), or Causalgia

Refer to geography-specific addenda for OUS information.



## 7.5. Product Use

The Medtronic RestoreSensor SureScan MRI and Intellis AdaptiveStim Neurostimulation System and related components and accessories are commercially available for SCS in the United States and shall be used in accordance with commercial labeling in all geographies. Exposure to the study product is considered from the time the subject is first exposed to the neurostimulation system, during the device trial visit, until the product is explanted or the subject discontinues from the study, if later.

## 7.6. Product Training Requirements

Only investigators who are trained and experienced in implanting neurostimulation spinal cord stimulation systems will perform the implant procedures required for this clinical study.

## 7.7. Product Accountability

All products are considered commercially available and Medtronic will not be providing devices for this study. Therefore, device accountability and traceability is not required for this study.

## 7.8. Product Return

All explanted devices should also be returned to Medtronic for analysis when permissible by local laws and regulations. Furthermore, Medtronic requests the return of explanted product from non-clinical sources such as funeral homes and will assume responsibility for storage and disposal of the product once received. Please contact your local Medtronic representative for instructions on returning products to Medtronic or to receive a Returned Product Mailer Kit.

## 8. Selection of Subjects

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### 8.1. Study Population

The intended study population is patients with chronic intractable low back and leg pain.

### 8.2. Subject Enrollment

Each subject must be in compliance with all of the inclusion/exclusion criteria to be eligible to participate in this study. A subject who does not meet inclusion/exclusion criteria or who discontinues prior to implant for any other reason (e.g. fails device trial, cannot be implanted due to hardware, etc.) will be considered a screen fail. Once subjects have completed device activation, subjects will continue to be followed in the study unless they are an early withdrawal.

### 8.3. Inclusion Criteria

1. Willing and able to provide a signed and dated informed consent
2. At least 18 years old at the time of enrollment
3. Candidate per labeling for an SCS system (trial and implant) as an aid in the management of chronic, intractable pain of the trunk and limbs (low back and leg pain)
4. Baseline VAS is  $\geq 50$  mm for low back pain



5. Baseline VAS is  $\geq 50$  mm for leg pain
6. ODI score of 21 to 80 out of 100
7. On stable (no change in dose, route, or frequency) pain medications (prescribed and over-the-counter) being used for back and leg pain, as determined by the investigator, for at least 28 days prior to enrolling in the study
8. Willing and able to attend visits and comply with the study protocol
9. Willing and able to not increase their pain medications (prescribed and over-the-counter) being used specifically for back or leg pain through the 3-Month Visit

#### Additional Inclusion Criterion (evaluated at Device Trial - Implant)

1. After paresthesia mapping to confirm proper location at Device Trial, final lead placement spans the T9/T10 disc space
2. After paresthesia mapping to confirm proper location at permanent implant, final lead placement spans the T9/T10 disc space

## 8.4. Exclusion Criteria

1. Previously trialed or implanted with spinal cord stimulator, peripheral nerve stimulator, or an implantable intrathecal drug delivery system
2. Expected to be inaccessible for follow-up
3. Subject is currently participating, or plans to participate, in another investigational study unless written approval is provided by the Medtronic study team
4. Current diagnosis of moderate to severe central lumbar stenosis with neurogenic claudication, as determined by the investigator
5. Major psychiatric comorbidity or other progressive diseases that may confound study results, as determined by the investigator
6. Serious drug-related behavioral issues (e.g. alcohol dependency, illegal substance abuse), as determined by the investigator
7. Pregnant or planning on becoming pregnant (if female and sexually active, subject must be using a reliable form of birth control, be surgically sterile, or be at least 2 years post-menopausal)
8. Unable to achieve supine position

## 9. Study Procedures

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### 9.1. Summary of Visits

Specific data and procedure requirements per visit are summarized in Table 4 and a flow diagram of the device trial is available in Figure 1. A summary of required visits are as follows:

- Baseline Visit
- Device Trial Day 0 – Lead Placement and initial programming
- Device Trial Day 2
- Device Trial Day 4 (if necessary)
- Device Trial Day 6 (if necessary)
- Implant



- Device Activation Visit
- 2-Week Visit
- 4-Week Visit
- 6-Week Visit
- 3-Month Visit
- 6-Month Visit
- 12-Month/Final Visit

Telephone calls will be conducted as described in Table 2 below.

All device-, therapy-, or procedure-related adverse events and device deficiencies will be collected from the point of enrollment through to study exit.

**Table 2. Protocol Visit Windows**

Visit	Visit ranges
Baseline Visit	NA
Device Trial Day 0	≤ 14 days after Baseline visit
Device Trial Day 2	2 + 2 days after Device Trial Day 0
Device Trial Day 4, if necessary	2 + 2 days after Device Trial Day 2
Device Trial Day 6, if necessary	Must occur 2 days after Device Trial Day 4 Visit and before or on Device Trial Day 10
Implant Visit	≤ 30 days after end of device trial
Device Activation Visit ( <b>Day 0</b> )	9 -16 days after implant; pending wound healing
1-Week Telephone Call	7 ± 3 days after <b>Day 0</b>
2-Week Clinic Visit	14 days ± 3 days after <b>Day 0</b>
3-Week Telephone Call	21 ± 3 days after <b>Day 0</b>
4-Week Clinic Visit	28 days ± 3 days after <b>Day 0</b>
5-Week Telephone Call	35 ± 3 days after <b>Day 0</b>
6-Week Clinic Visit	42 days ± 3 days after <b>Day 0</b>
7-Week Telephone Call	49 ± 3 days after <b>Day 0</b>
8-Week Telephone Call	56 days ± 3 days after <b>Day 0</b>
9-Week Telephone Call	63 ± 3 days after <b>Day 0</b>
10-Week Telephone Call	70 days ± 3 days after <b>Day 0</b>
11-Week Telephone Call	77 ± 3 days after <b>Day 0</b>



Visit	Visit ranges
3-Month Clinic Visit	90 days ± 10 days after <b>Day 0</b>
3.5-Month Telephone Call	105 days ± 15 days after <b>Day 0</b>
4.5-Month Telephone Call	135 days ± 15 days after <b>Day 0</b>
5.5-Month Telephone Call*	165 days ± 15 days after <b>Day 0</b>
6-Month Clinic Visit	180 days ± 15 days after <b>Day 0</b>
6.5-Month Telephone Call*	195 days ± 15 days after <b>Day 0</b>
7.5-Month Telephone Call	225 days ± 15 days after <b>Day 0</b>
8.5 Month Telephone Call	255 days ± 15 days after <b>Day 0</b>
9.5-Month Telephone Call	285 days ± 15 days after <b>Day 0</b>
10.5-Month Telephone Call	315 days ± 15 days after <b>Day 0</b>
11.5-Month Telephone Call*	345 days ± 15 days after <b>Day 0</b>
12-Month/Final Clinic Visit	360 days ± 15 days after <b>Day 0</b>

\* For instances where the monthly telephone call window overlaps the clinic visit window, if the clinic visit occurs within the telephone call window, the telephone call is not required.

## 9.2. Baseline Visit

Subjects are considered enrolled at the time the study-specific informed consent/HIPAA form or other data protection form as required by local regulations is signed. At the Baseline visit, subjects will be consented and if they agree to participate they will be assessed for eligibility to the study-specific inclusion/exclusion criteria. Each subject must be in compliance with all of the inclusion/exclusion criteria to be eligible to participate in this study. No study-related procedures or testing will be conducted prior to completing the consenting process of a subject. Female subjects of child-bearing potential will be administered a urine pregnancy test at this visit. A subject who has a positive urine pregnancy test will be exited from the study according to Section 9.19. Once a subject is enrolled, if they are determined to be ineligible for the study, or if they withdraw early, a study exit eCRF must be completed. Subjects will complete the VAS for overall (low back and leg) pain, low back pain, and leg pain. The VAS will be scored to assess subject eligibility per the inclusion criteria. Subjects must have a VAS score ≥ 50 mm for low back pain, a VAS score ≥ 50 mm for leg pain, and an ODI score that is between 21 to 80 to continue in the study. If subjects are in compliance with the inclusion and exclusion criteria, their low back and leg pain history and surgical history will be collected at this visit. Enrolled subjects may not be rescreened. Subjects that meet the minimum pain score criteria will also be scheduled for a device trial and complete the required assessments (see below). Subjects will also be asked to set an objective goal for their therapy related to a desired outcome or activity i.e., the ability to stand and wash dishes or walk around the block.



## Data collection requirements for the Baseline Visit:

- VAS
- Inclusion/exclusion criteria
- Demographics
- Back and leg pain/surgical history
- Urine pregnancy test results, if applicable
- EQ-5D-5L
- ODI
- Activity goal
- Pain medications
- AEs

## 9.3. Device Trial ( $\leq 14$ days post-Baseline)

The Device Trial has three phases:

- Phase I: Implant and Programming (Trial – Day 0)
- Phase II: Evaluation of HD Programming (Trial Days 0 – 4)
- Phase III: Evaluation of Physician Preference Programming (Trial Days 4 – 10), if necessary

### Implant and Programming (Trial – Day 0)

[REDACTED]

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e. For Intellis: End session, exit application, generate and obtain report  
During this visit, subjects will be provided with a patient programmer and ENS and educated on their use. During the device trial, subjects will be allowed to change the amplitude. However, changes to the frequency and pulse width by the subject will not be allowed and will be locked on the patient programmer.

## Data collection requirements for the Device Trial Day 0:

- Device information
- Fluoroscopy/x-ray images annotated with vertebral marker(s)
- Final program settings
- Initial and final device interrogation reports
- Level of conus medularis (if available)
- Pain medications
- AEs/device deficiencies

## Day 2 Visit (2 + 2 Days from Device Trial Day 0)

At the Day 2 Visit, subjects will be asked to report their improvement in overall pain compared to baseline. It is recommended that the Day 2 Visit be, at least, 48 hours after Trial Day 0.

- If a subject reports  $\geq 50\%$  improvement in overall pain compared to baseline at the Day 2 visit, the trial will be deemed successful and trial leads will be explanted.
- If a subject does not report  $\geq 50\%$  improvement in overall pain compared to baseline at the Day 2 Visit, they will be reprogrammed to move the bipole up one electrode and schedule a Day 4 Visit.

## Data collection requirements for the Day 2 Visit

- Percent Improvement in Overall Pain Assessment
- Final program settings, if reprogramming occurs
- Initial and final device interrogation reports
- Pain medications
- AEs/device deficiencies

## Day 4 Visit (2 + 2 Days from Day 2 Visit; if necessary)

At the Day 4 Visit, subjects will be asked to report their improvement in overall pain compared to baseline. It is recommended that the Day 4 Visit be, at least, 48 hours after the Day 2 Visit.

- If a subject reports  $\geq 50\%$  improvement in overall pain compared to baseline at the Day 4 visit, the trial will be deemed successful and trial leads will be explanted.
- If a subject does not report  $\geq 50\%$  improvement in overall pain compared to baseline at the Day 4 Visit, they will be programmed to physician preference settings (see Physician Preference Programming Instructions).







[REDACTED]

**Data collection requirements for the Implant Visit:**

- Device information
- Serial/lot numbers for leads and INS
- Fluoroscopy/x-ray images annotated with vertebral marker(s)
- Initial and final device interrogation reports
- Pain medications
- AEs/device deficiencies

**9.5. Device Activation Visit (Day 0; 9 – 16 days after implant)**

The Device Activation Visit will take place 9 – 16 days after implant, pending wound healing. If wound has not healed, reschedule the Device Activation Visit. Device Activation is considered Day 0 for the purpose of calculating the monthly follow-up visits and phone calls. Lead location (lateral and AP) may be captured via fluoroscopy/x-ray annotated with vertebral marker(s). Use the most current image to program the subject’s device based on Programming Algorithm below (Table 3). During this visit, subjects will be educated on the use of their patient programmer and recharger.

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**Table 3. Recommended Permanent Implant Programming Algorithm**

[Redacted table header]

[Redacted]	[Redacted]	[Redacted]	[Redacted]
[Redacted]	[Redacted]	[Redacted]	[Redacted]
[Redacted]	[Redacted]	[Redacted]	[Redacted]
[Redacted]	[Redacted]	[Redacted]	[Redacted]
[Redacted]	[Redacted]	[Redacted]	[Redacted]
[Redacted]	[Redacted]	[Redacted]	[Redacted]
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[Redacted]	[Redacted]	[Redacted]	[Redacted]
[Redacted]	[Redacted]	[Redacted]	[Redacted]

**Data collection requirements for the Device Activation Visit:**

- Fluoroscopy/x-ray images annotated with vertebral marker(s), if collected
- Initial and final device interrogation reports
- Pain medications
- AEs/device deficiencies

## 9.6. 2-Week, 4-Week, 6-Week and 3-, 6-, and 12-Month Clinic Visits

Visits will occur at 2, 4 and 6 weeks and 3, 6 and 12 months post-device activation. At the 2-Week Visit or 4-Week Visit, if the 2-Week Visit is not at least 30 days after implant, the subject will have the accelerometer in their device oriented in all positions and AdaptiveStim enabled. VAS will be collected at all visits. EQ-5D-5L, ODI, PGIC, and SSA will be assessed at the 3-, 6- and 12-Month Visits. The Paresthesia Assessment, and Recharging Questionnaire will be collected at the 3- and 12-Month Visits. The Activity Goal Assessment will be collected at 2-Week, 4-Week, 6-Week and 3-Month Visits. Data for the primary endpoint will be collected at the 3-Month Visit.



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[REDACTED]

#### Data collection requirements for the 2-Week, 4-Week, 6-Week and 3-, 6-, and 12-Month Clinic Visits:

- VAS (all follow-up visits)
- EQ-5D-5L (3-, 6- 12-Months)
- ODI (3-, 6-, 12-Months)
- SSA (3, 6-, 12 Months)
- PGIC (3-, 6-, 12 Months)
- Activity Goal Assessment (2-Week, 4-Week, 6-Week, and 3-Month)
- Paresthesia Assessment (3-, 12-Months)
- Recharger Questionnaire (3-, 12-Months)
- Fluoroscopy/x-ray annotated with vertebral marker(s), if applicable
- Initial and final device interrogation reports
- Pain medications
- AEs/device deficiencies

#### **9.7. Telephone Calls (1, 3, 5, 7, 8, 9, 10 and 11 weeks post-device activation; Monthly Telephone Calls at 3.5, 4.5, 5.5, 6.5, 7.5, 8.5, 9.5, 10.5, 11.5 Months post-3-Month Visit)**

Subjects will be assessed for AEs (new or existing) and asked about any pain medication changes. They will also be asked to confirm that their stimulator is on and the amplitude reported on their patient



programmer. If the subject is not satisfied with their pain relief, they will come in for an unscheduled visit.

#### Data collection requirements for the Telephone Calls:

- Pain Relief Assessment
- Amplitude for active group
- Pain medications
- AEs/device deficiencies

### 9.8. Unscheduled Visits:

Unscheduled visits may occur if programming changes are required to correct programming errors, to reprogram to optimize pain control (see Reprogramming Instructions in section 9.6), or for an AE. Whenever feasible, subjects should have their devices interrogated. If a subject was experiencing  $\geq 50\%$  reduction in pain at a previous visit and no longer is, a fluoroscopy/x-ray annotated with vertebral marker(s) may be taken to assess for possible lead migration.

#### Data collection requirements for the Unscheduled Visit:

- VAS
- Reason for the visit
- Initial and final device interrogation reports, if applicable
- Fluoroscopy/x-ray annotated with vertebral marker(s), if applicable
- Pain medications
- AEs/device deficiencies

### 9.9. System Modifications:

System modifications (e.g. lead or device revision, replacement, or explant) may occur due to ineffective or loss of therapy, adverse event, device deficiency, or subject concerns that are not correctable by programming. In the event of a system modification, the follow-up schedule for the subject will remain unchanged. If the neurostimulator requires replacement, contact a member of the Medtronic study team as the decision to allow re-implant will be handled on a case-by-case basis. If the system is explanted, the explanted system should be returned to Medtronic (Refer to Device Product Return, Section 7.8).

#### Data collection requirements for a system modification:

- Initial and final interrogations from old and new INS uploaded to NPU, if replaced and subject remains in the study
- If any portion of the implanted system is replaced, record all changes in source documentation and on the system modification eCRF (e.g. new lead model/serial number)
- AEs/device deficiencies



## 9.10. Study Exit

Normal study completion occurs when the subject has completed the required study visits through the 12-Month Visit (refer to required procedures described in Section 9.6), at which time the subject will end their participation in the study and site personnel will then complete a study exit eCRF. If the subject is an early withdrawal, refer to Withdrawal of Subjects, Section 9.19.

## 9.11. Schedule of Events

**Table 4: Schedule of Events**

Study Procedures, Tasks, and Data Collection (row) by Visit (column)	Baseline Visit	Device Trial (Trial Day 0) Visit	Device Trial Day 2 Visit	Device Trial Day 4 Visit	Device Trial Day 6 Visit	Implant Visit	Device Activation Visit (Day 0)	2-, 4-, 6-week, 3-, 6-, and 12-Month/Final Visit	Post-implant Phone Calls	Unscheduled Visits
Informed Consent Process	√									
Demographics	√									
Inclusion/Exclusion Criteria	√									
Urine Pregnancy Test	√									
VAS – overall, low back, and leg	√							√		√
Low back and Leg Pain/Surgical History	√									
Activity Goal	√							√ <sup>a</sup>		
EQ-5D-5L	√							√ <sup>b</sup>		
ODI	√							√ <sup>b</sup>		
Level of conus medularis <sup>f</sup>		√								
Final Program Settings		√	√ <sup>c</sup>	√ <sup>c</sup>	√ <sup>c</sup>					
Percent Improvement in Overall Pain			√	√ <sup>d</sup>	√ <sup>d</sup>					
Pain Relief Assessment									√	
Fluoroscopy/x-ray annotated with vertebral marker(s)		√ <sup>e</sup>				√	√ <sup>f</sup>	√ <sup>f</sup>		√ <sup>f</sup>
Amplitude of Active Group									√	
Device information (model, serial/lot number)		√				√				
Paresthesia Assessment								√ <sup>g</sup>		
Recharging Questionnaire								√ <sup>g</sup>		
PGIC								√ <sup>b</sup>		
Subject Satisfaction Assessment (SSA)								√ <sup>b</sup>		



Study Procedures, Tasks, and Data Collection (row) by Visit (column)	Baseline Visit	Device Trial (Trial Day 0) Visit	Device Trial Day 2 Visit	Device Trial Day 4 Visit	Device Trial Day 6 Visit	Implant Visit	Device Activation Visit (Day 0)	2-, 4-, 6-week, 3-, 6-, and 12-Month/Final Visit	Post-implant Phone Calls	Unscheduled Visits
Initial and final device interrogation reports		√	√	√ <sup>c</sup>	√ <sup>c</sup>	√	√	√		√ <sup>c</sup>
Collect AE/DD	√	√	√	√	√	√	√	√	√	√
Pain Medications	√	√	√	√	√	√	√	√	√	√

<sup>a</sup>Activity goal performed at 2, 4, 6-week and 3-month visit

<sup>b</sup>EQ-5D-5L, ODI, PGIC and SSA performed at 3, 6 and 12-month visits

<sup>c</sup>Perform activity only if unit reprogrammed

<sup>d</sup>If visit performed

<sup>e</sup>At trial implant and if acquired in recovery room

<sup>f</sup>If acquired

<sup>g</sup>Paresthesia questionnaire and recharging questionnaire performed at 3 and 12-month visit

## 9.12. Subject Screening

Subjects may be recruited through the investigator’s practice and referring physicians. It is recommended to recruit subjects who live within a reasonable distance from the site.

Potential subjects may be identified through chart reviews or as new or existing patients attend clinic visits. If subjects are recruited from outside the investigator’s practice, sites are to ensure that appropriate release for access to the subject’s records (paper and/or electronic) is obtained. Any subject recruitment materials disseminated to subjects (advertisements, handouts, posters, social media) must be approved by the IRB/EC prior to use.

Recruited subjects will be screened by the Principal Investigator or authorized site personnel by reviewing the study inclusion and exclusion criteria. All subjects must be consented in accordance with the protocol prior to any study-specific procedures. Subjects who do not meet all of the inclusion criteria or who meet any of the exclusion criteria cannot be rescreened.

## 9.13. Prior and Concomitant Medications

Only medications used for the treatment of back and/or leg pain will be collected during the study. Only subjects who are on a stable dose (no new medications, discontinued, or changes in dose, route, or frequency) of all prescribed and over the counter pain medications for low back and/or leg pain, in the opinion of the PI, for at least 28 days prior to screening will be eligible for participation in the study. Subjects will not be allowed to increase their pain medications (including prescribed and over-the-counter) specifically for back and leg pain, as defined above, through the 3-Month Visit unless there is a need to mitigate a safety concern (e.g. adverse event). Decreases in pain medications are allowed after



enrollment. Any changes to subject's pain medications while they are enrolled in the study will be documented in the subject's medical records and the pain medications eCRF.

The addition of pain medications for the relief of surgical discomfort after device trial and implant procedures is allowed. Pain medications prescribed for post-operative pain management are not considered an increase in pain medications if the medication is ceased prior to the date of the Device Activation Visit.

## 9.14. Subject Consent

Investigators shall consider for enrollment all subjects who meet eligibility requirements for study participation to avoid any bias in the subject population. Prior to enrolling subjects, each investigational site's IRB/EC will be required to approve the CIP, the informed consent form (ICF) and HIPAA/data protection authorization or other privacy language (where required by law), and any other written study information to be provided to the subjects (e.g. CA Bill of Rights if applicable, subject assessments etc.). The document(s) must be controlled (i.e. version number and date) to ensure it is clear which version(s) were approved by the IRB/EC. Any adaptation of the informed consent form must be reviewed by Medtronic and approved by the IRB/EC prior to enrolling subjects. The ICF will be provided under separate cover.

Patient informed consent is defined as legally effective, documented confirmation of a subject's voluntary agreement to participate in a clinical study after information has been given to the subject on all aspects of the clinical study that are relevant to the subject's decision to participate. The informed consent process will be performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and in accordance with 21 CFR Part 50 or applicable local regulation.

Prior to entering the study, the principal investigator, or appropriately delegated designee, will explain to each subject all aspects of the clinical investigation that are relevant to the subject's decision to participate throughout the clinical investigation including, but not limited to, the following: purpose and nature of the study, study procedures, expected study duration, available alternative therapies, and the benefits and risks involved with study participation and the potential treatment.

The investigator shall seek such consent only under circumstances that provide the prospective subject sufficient opportunity to consider whether to participate, and that minimize the possibility of coercion or undue influence. No informed consent, whether oral or written, may include any exculpatory language through which the subject is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence.

Subjects are considered enrolled at the time the study-specific ICF is signed. Informed consent must be obtained from the subject prior to initiation of any study-specific procedures. Subjects must be able to



personally sign and date the consent form to participate in this study. Signing and dating of the ICF or HIPAA authorization or other data protection form by a legally authorized representative will not be permitted for this study. Subjects will be required to sign and date a HIPAA authorization or other data protection form as required by local regulations before participating sites can collect, use and submit subject information to the study sponsor. The Consent Form and Authorization to Use and Disclose Personal Health Information/ Research Authorization/other legally required privacy language must be given to the subject in a language he/she is able to read and understand.

If the informed consent form is obtained the same day the subject begins participating in study-related procedures, it will be documented in the subject's case history that consent was obtained prior to participation in any study-related procedures

The original signed ICF must be filed in the hospital/clinical chart and/or with the subject's study documents. A copy of the informed consent form and signed Authorization to Use and Disclose Personal Health Information/Research Authorization/other legally required privacy language must be provided to the subject.

The informed consent form and Authorization to Use and Disclose Personal Health Information/Research Authorization/other legally required privacy language must be available for monitoring and auditing.

Any changes to a previously approved informed consent form throughout the course of the study must be submitted and approved by Medtronic and the IRB/EC reviewing the application before being used to consent a prospective study subject. The document(s) must be controlled (i.e. versioned and dated) to ensure it is clear which version(s) were approved by the IRB/EC.

The investigator must notify the subject of any significant new findings about the study that become available during the course of the study which are pertinent to the safety and well-being of the subject, as this could impact a subject's willingness to participate in the study. If relevant, approval may be requested from subjects to confirm their continued participation.

## **9.15. Assessment of Efficacy**

Subject assessments will be performed by appropriately trained, qualified and delegated site personnel according to the usual practices of the site.

### **9.15.1. Single-day Visual Analog Scale (VAS)**

Pain will be assessed by a single-day VAS (0 – 100 mm). The VAS will be used to evaluate the primary and two secondary study endpoints with 0 mm meaning "no overall, low back, or leg pain" and 100 mm meaning "worst overall, low back, or leg pain imaginable." Subjects will be asked to report pain intensity "in the last 24 hours" by marking a line perpendicular to the VAS line at the point that represents their pain intensity. Site personnel will determine the score by measuring the distance (mm) on the 100-mm line between the left, "no pain" anchor and the subject's mark, measuring the total



distance of the line (to ensure that it is 100 mm) and dividing the distance from the “no pain” mark to the subject’s mark by the total distance of the line. The scored VAS ranges from 0 – 100. The VAS will be administered at the Baseline, Follow-up Visits (2-Week, 4-Week, 6-Week and 3-, 6- and 12-Month Visits), and Unscheduled Visits. The VAS data will be the basis for verification of certain study entry criteria at the Baseline Visit and for calculation of the primary study endpoint.

## 9.15.2. Percent Improvement in Overall Pain Assessment

Subjects will be asked their percent improvement in overall pain from 0 – 100% at Device Trial Day 2, Device Trial Day 4, and Device Trial Day 6.

## 9.15.3. Patient Global Impression of Change (PGIC)

The Patient Global Impression of Change (PGIC) version 2, which measures the subject’s impression of change<sup>12</sup>, will be administered at the 3-, 6-, and 12-Month Visits prior to device interrogation. The PGIC is a 7-point scale used by patients to report their overall assessment of change in status since beginning treatment which will be defined as when the device was turned on. The PGIC consists of the following question:

Since beginning treatment, at this clinic (in this study), how would you describe the change (if any) in ACTIVITY LIMITATIONS, SYMPTOMS, EMOTIONS, and OVERALL QUALITY OF LIFE related to your painful condition? (tick ONE box)

1. No change (or condition has gotten worse)
2. Almost the same, hardly any change at all
3. A little better, but no noticeable change
4. Somewhat better, but the change has not made any difference
5. Moderately better, and a slight but noticeable change
6. Better, and a definite improvement that has made a real and worthwhile difference
7. A great deal better, and a considerable improvement that has made all the difference

## 9.15.4. Pain Relief Assessment

Subjects will be asked if they are satisfied with pain relief on the weekly and monthly phone calls following device activation. Verbal responses will be documented by qualified, trained, and delegated site personnel during the call.

## 9.15.5. Recharging Questionnaire

This questionnaire will be administered at the 3- and 12-Month visits and is designed to capture information about the frequency and typical duration of recharging sessions experienced by subjects.

## 9.15.6. Paresthesia Assessment

This assessment will be administered at 3- and 12-Month Visits and is utilized to obtain subject feedback on whether or not they have experienced the sensation of paresthesia, and if so, whether or not it was uncomfortable.



## 9.15.7. Subject Satisfaction Assessment (SSA)

This assessment will be administered at the 3-, 6- and 12-Month Visits and is utilized to obtain subject feedback on whether they would recommend the therapy to other patients suffering from similar pain, and to obtain feedback on their overall satisfaction with the therapy.

## 9.15.8. European Quality of Life-Five Dimensions

This assessment will be administered at the Baseline Visit and 3-, 6- and 12-Month Visits. The European Quality of Life – Five Dimensions (EQ-5D), version 5L, is a standardized measure of health status developed by the EuroQol Group and a widely used validated tool to determine health-related quality of life.<sup>13</sup> The EQ-5D-5L descriptive system consists of 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has 5 levels of severity: no problems, slight problems, moderate problems, severe problems, extreme problems. The subject will be asked to indicate his/her health state by selecting the most appropriate statement in each of the 5 dimensions.

## 9.15.9. ODI

This assessment will be administered at the Baseline Visit and 3-, 6- and 12-Month Visits. The ODI (version 2) is one of the most highly recommended measures for patients with spinal disorders.<sup>14</sup> The validated questionnaire consists of 10 subject-reported sections on the ability to perform activities of daily living.

## 9.15.10. Activity Goal

The Activity Goal will be administered at the Baseline Visit, 2-Week, 4-Week, 6-Week and 3-Month Visits. It is used to assess progress towards a specific, realistic activity goal chosen by the subject at the Baseline Visit. If Baseline goal is obtained, then the subject will be asked to set a new goal and so on through the 3-Month Visit.

## 9.15.11. Back Pain/Surgical History and Demographics

Subject demographics, back and leg pain/surgical history and primary pain diagnosis will be collected at the Baseline visit. This information must be documented within their medical records and reported on the study eCRFs.

## 9.16. Assessment of Safety

Subjects will be assessed from enrollment through the end of the study for AEs related to the following:

- The implanted SCS system, accessories and surgical procedures
- SCS therapy

In addition, all device deficiencies reported during the study will be collected.

## 9.17. Recording Data

This study will be utilizing a remote data capture (RDC) system to collect study required Case Report Form (CRF) information. Electronic CRFs (eCRFs) will be provided by the sponsor; required data will be taken from source documents and entered into the study database via the eCRFs by the appropriately



delegated site personnel, in accordance with applicable regulations. Source documentation for VAS and subject assessments will be captured in a paper format and completed confidentially by the subject only. Data from the paper assessments will be entered into the database by delegated site personnel after ensuring the completeness and accuracy of the data.

The Principal Investigator or appropriately delegated individuals are responsible for entering data for the study on the eCRFs. The Principal Investigator or delegated Sub-Investigator (physician only) is required to approve all data on eCRFs via electronic signature.

### 9.17.1. Programming Data

Through device interrogations with the 8840 N'Vision® Clinician Programmer for RestoreSensor SureScan MRI Neurostimulation system and the 8880T2 Communicator for the Intellis AdaptiveStim Neurostimulation system, parameter data (e.g., session data files) will be collected from the neurostimulator.

Report Link is a commercially available tool, which will be used during this study for the RestoreSensor SureScan MRI Neurostimulation system, that allows clinicians to electronically transfer and save session data files as a PDF document from the 8840 N'Vision® Clinician Programmer to a computer at their study site. The Intellis AdaptiveStim Neurostimulation system uses an app, Clinical Data Upload, on the 8880T2 Communicator to electronically transfer session data files as PDF documents to a computer at their study site. The PDF files can be printed to local or network printer and stored in electronic medical record systems and uploaded into the Neuro Programmer Upload (NPU) application.

NPU is an application designed to capture and store programmer interrogation output reports (e.g., session data reports) from the 8840 N'Vision Clinician Programmer or the Intellis AdaptiveStim Neurostimulation system, extract and store the data in the Medtronic NPU database for analysis and reporting.

### 9.17.2. Fluoroscopy/x-ray imaging

Fluoroscopy/x-rays will be obtained at Device Trial Implant and Permanent Implant. Fluoroscopy/x-rays may be obtained at the Device Trial in the recovery room (after subject is dressed prior to programming), at the Device Activation visit, or at any time the investigator feels is necessary. Any images collected for the study will be annotated with a vertebral marker. [REDACTED]

[REDACTED]

[REDACTED]



An imaging Manual with instructions on how to transfer the images to Medidata Solutions will be provided to the study sites. Medidata Solutions will send de-identified images to Medtronic. Medtronic will store the images in a secure document management system, and a qualified reader will evaluate the images to define and characterize the locations of the lead and active contacts with respect to anatomical landmarks as well as for future evaluation by Medtronic.

## 9.18. Deviation Handling

A deviation is defined as an instance(s) of failure to follow, intentionally or unintentionally, the requirements of the clinical investigational plan. The investigator is not allowed to deviate from the CIP, except under emergency circumstances to protect the rights, safety and well-being of human subjects.

All study deviations must be reported on the eCRFs regardless of whether medically justifiable, pre-approved by Medtronic, an inadvertent occurrence, or taken to protect the subject in an emergency.

Study deviations must be reported to Medtronic as soon as possible upon the site becoming aware of the deviation. Reporting of deviations must comply with IRB/EC policies, local laws, and/or regulatory agency requirements.

In the event the deviation involves a failure to obtain a subject's consent or is made to protect the life or physical well-being of a subject in an emergency, the deviation must be reported to the IRB/EC as well as Medtronic within five (5) working days.

In situations where the investigator anticipates, contemplates, or makes a conscious decision to deviate from the CIP, the Investigator must submit in writing to Medtronic, his/her request to deviate from the CIP. Prior written approval from Medtronic is expected. In such situations, if the deviation affects a subject's rights, safety and well-being, or the scientific integrity of the study, prior approval from IRB/EC is also required.

Prior approval from Medtronic is not required when a deviation is necessary to protect the rights, safety or well-being of a subject in an emergency or in unforeseen situations beyond the investigator's control (e.g. subject failure to attend scheduled follow-up visits, inadvertent loss of data due to computer malfunction, inability to perform required procedures due to subject illness).

Medtronic is responsible for analyzing deviations, assessing their significance, and identifying any additional corrective and/or preventive actions (e.g. amend the Clinical Investigation Plan, conduct additional training, or terminate the investigation). Repetitive or serious investigator compliance issues may result in initiation of a corrective action plan with the investigator and site, and in some cases,



necessitate suspending enrollment until the problem is resolved or ultimately terminating the investigator's participation in the study.

Examples of study deviations include but are not limited to the following:

- Failure to obtain informed consent or HIPAA authorization prior to study enrollment, failure to re-consent when new risks/procedures added, use of an outdated consent, or unqualified or non-delegated personnel performing consent process
- Violation of inclusion/exclusion criteria
- Failure to collect protocol required assessments or failure to perform protocol required procedures (e.g., VAS data, subject assessment missing)
- Missed visits
- Visits outside of window
- Lack of programmer data upload or device interrogation printout
- Use of expired device or unapproved device
- Unauthorized personnel performing study procedures

## 9.19. Subject Withdrawal or Discontinuation

A subject has the right to withdraw from the study at any time and for any reason without prejudice to his/her future medical care by the principal investigator or institution. Subjects will be provided standard medical care by their physician after their study participation ends.

The study sample size accounts for expected attrition, thus subjects that discontinue after implant will not be replaced.

If a subject is withdrawn from the study, the reason for withdrawal shall be recorded on a study exit eCRF and in the subject's medical record. Examples of reasons for study discontinuation include, but are not limited to, the following:

- Eligibility criteria not met
- Pregnancy
- Failure to follow study requirements
- Subject death
- Subject lost to follow-up (LTFU)
- Subject voluntarily withdraws from the study
- Adverse events
- Normal study completion

A study exit eCRF will be completed for any enrolled subject who permanently discontinues from the study or completes the protocol-required study follow-up and has completed the study.

In the case that the subject is determined to be lost to follow-up, details of a minimum of three attempts and the method of attempt (e.g., two by phone and one by certified letter) to contact the subject must be recorded in the subject's medical records. In addition, requirements set forth by the governing IRB/EC must be followed.



The investigator should make all attempts to conduct a discontinuation visit prior to subject withdrawal if the subject is withdrawn after the Device Activation Visit and outside of a protocol-required visit. All eCRFs should be completed for visits that occurred prior to the subject’s withdrawal. In addition, regardless of when the discontinuation occurs, the subject should be asked to complete all 12-Month/Final Visit procedures, if the subject is willing, in order to obtain final assessments for the study. A study exit eCRF must also be completed.

**Table 5. Data collection requirements for subject withdrawal**

Time of Early Withdrawal	Procedures Required
Prior to Device Activation	Complete appropriate visit eCRFs based on the visits completed (e.g. Baseline, Device Trial etc.) prior to discontinuation and the study exit eCRF.
After Device Activation and prior to the 12-Month/Final Visit	Complete all appropriate visit eCRFs based on visits completed prior to the discontinuation, the 12-Month/Final Visit eCRF (if subject is willing), and study exit eCRF.

## 9.20. Pregnancy

The safety of SCS has not been established for pregnant women, for an unborn fetus, or during childbirth. If a subject is able to become pregnant and is sexually active, documentation of medically acceptable birth control must be present in the medical records. In the event that a subject becomes pregnant during the study, it is not considered an AE; however, the study center must immediately inform Medtronic study personnel and perform the following activities:

- The investigator will instruct the subject to turn the stimulator “OFF” and to return to the site for a visit as soon as possible. The subject will be exited from the study.
- The study center must complete a Study Exit eCRF and final interrogation and upload reflecting therapy suspension.
- The Principal Investigator should notify the IRB per the study center’s specific requirements.

## 10. Risks and Benefits

### 10.1. Potential Risks

Spinal Cord Stimulation therapy is a reversible procedure (i.e., the system can be turned off or removed in most cases) with stimulation parameters that are adjustable to minimize or reverse complications and maximize therapeutic effects. The RestoreSensor SureScan MRI and Intelis AdaptiveStim Neurostimulation systems are commercially available for treatment of chronic intractable pain. The risks associated with the RestoreSensor SureScan MRI and Intelis AdaptiveStim Neurostimulation systems are included in commercial product information. Systems will only be used in geographies where they are commercially available. There are no expected new or increased risks associated with this clinical study.



There may be additional risks related to the use of Medtronic neurostimulation systems, other than the ones described below, that are not yet known.

### **10.1.1. Risks of Surgery**

Implanting a neurostimulation system has risks similar to spinal procedures, including spinal fluid leak (spinal fluid collection under the skin), headaches, swelling, bruising, bleeding, infection, or paralysis.

Subjects on anticoagulation therapy may be at higher risk for problems after surgery such as hematomas that could result in paralysis.

### **10.1.2. Spinal Cord Stimulation Risks**

The implantation of a spinal cord stimulation system involves risks that are similar to other spinal procedures. In addition to those normally associated with surgery, implantation or use of a neurostimulation system includes, but is not limited to, the following risks:

- Allergic or immune system response to the implanted materials
- Infection
- Lead or neurostimulator erosion through the skin or migration
- Leakage of cerebrospinal fluid
- Loss of pain relief may return patients to their underlying pain condition
- Persistent pain at the neurostimulator site
- Placement of the epidural lead is a surgical procedure that may expose patients to risks of epidural hemorrhage (bleeding), hematoma, or paralysis
- Radicular chest wall stimulation
- Seroma (fluid collection in pocket where stimulator is placed) or hematoma at the neurostimulator site
- Change in stimulation, possibly related to cellular changes around the electrode(s), shifts in electrode position, loose electrical connections, lead fractures, which has been described by some patients as uncomfortable stimulation (jolting or shocking sensation)
- Over time there could be changes in the level of symptom control. In most cases, the physician can correct these changes without surgery.
- Formation of excessive tissue around the lead in the epidural space can result in delayed spinal cord compression and paralysis, requiring surgical intervention. Time to onset can range from weeks to many years after implant.
- The safety of this therapy is unknown for pregnancy, unborn fetus, or delivery
- Stimulation-dependent gastrointestinal symptoms such as diarrhea, incontinence or constipation
- Stimulation-dependent bladder symptoms such as urinary retention, incontinence or frequency
- Unexpected changes in stimulation - Electromagnetic interference, changes in posture, and other activities can cause a perceived increase in stimulation

# Vectors Post Market Clinical Investigation Plan



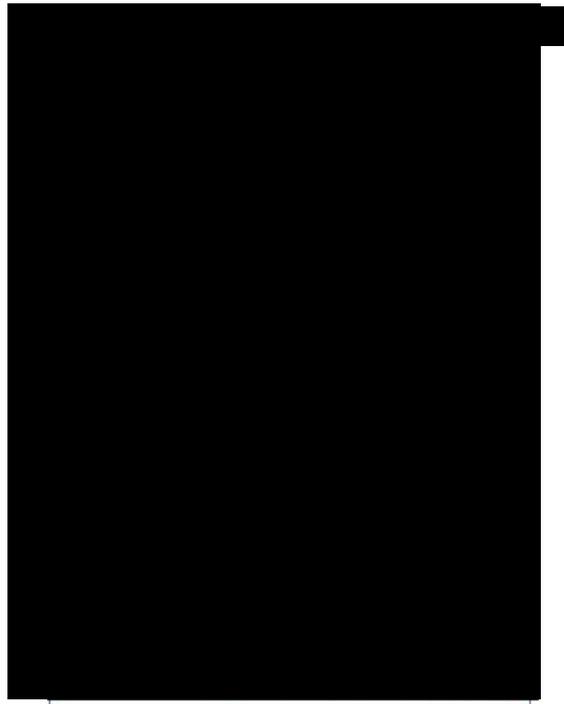
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**Low battery charge level** – Charge the neurostimulator when you see a **Low battery** screen displayed on the patient programmer or **recharger**. If the battery charge level is at 0, the device should be recharged to avoid therapy delivery falling to 0. For RestoreSensor SureScan MRI Neurostimulator if the battery remains in a discharged state, it continues to lose charge and it will become overdischarged. If the RestoreSensor SureScan MRI Neurostimulator battery is allowed to overdischarge, the recharger may not be able to recharge or communicate with the neurostimulator; however, your doctor may be able to restore the battery function. For RestoreSensor SureScan MRI Neurostimulator, follow the instructions in the model 37751 Recharger Charging System Manual to recharge the neurostimulator battery.

**Recharger use** – Check for skin irritation or redness near the neurostimulator during recharging. Do not sit or lie on the antenna or apply excessive pressure to the antenna. Take periodic breaks during prolonged recharging. Although no direct cause and effect has been established, some patients have reported heating sensation, discomfort, blistering not caused by heating, skin irritation, or redness near the implanted neurostimulator during or after recharging.

**Frequency of recharging**- per the patient programmer labeling subjects should check the battery level of their INS on a daily basis. Due to the higher pulse density of HD stimulation setting the recharging intervals may need to be more frequent. Daily activities may be disrupted based on the fact that subjects may need to recharge more frequently as a result of the programmed parameters used in this study. Subjects should pay particular attention to **Charging Efficiency** and **Battery Charge Level** indicators on the recharger.



- Check the neurostimulator battery charge level once a day or more frequently as needed.
- Keep the neurostimulator sufficiently charged to maintain therapy. It can be charged at any time; you do not need to wait for a low battery message.
- During neurostimulator recharging, monitor the Charging Efficiency row and adjust the antenna to obtain as many solid black boxes as possible. If only two boxes are filled in (6 or more boxes are empty) adjust the antenna to improve the signal strength between the neurostimulator and recharger.
- During recharging, ensure the neurostimulator Battery Charge Level is at least 25% before ending the charge session. However, a full battery charge is ideal.

### 10.1.5. Pregnancy Risks

Pregnant women are not able to take part in this study. Female subjects must agree to not become pregnant during the study by using a medically acceptable method of birth control. If a subject becomes pregnant during this study, there may be risks to the unborn child that are not yet known. The study doctor should be notified immediately if the patient thinks they are or have become pregnant. The stimulator will be turned "OFF" and the patient will be exited from the study.

### 10.1.6. Radiographic Imaging

As part of the study, subjects will be required to have fluoroscopic or X-ray images taken of their thoracic spine 1 time in addition to the imaging conducted to implant the leads. This may be beyond what is standard of care. The risk associated with these additional images has been considered and determined to be minimal since the total radiation dose will be approximately the same as one CT scan of the abdomen.

## 10.2. Study Risk Control Measures

The following will be done to mitigate risks associated with the implanted system:

- Investigators who are experienced with spinal cord stimulation implantation techniques will be utilized
- Instructions will be given to the study participants to ensure they can properly use the patient programmer and recharger system
- Subjects can turn off stimulation at any time during the study with the patient programmer or recharger
- Periodic monitoring of the study participants
- Labeling that contains precautions, warnings, and contraindications, as well as instructions on the use of the devices will be available and/or provided to the clinicians and subjects

## 10.3. Potential Benefits

Spinal cord stimulation may reduce low back or leg pain intensity, return the patient to a more fully functional status, and/or improve quality of life. Additionally, with stimulation delivered at comfort threshold amplitudes, subjects may avoid uncomfortable or even intolerable stimulation sensations, such as painful paresthesia. During the study subjects will have increased interaction with physicians or medical staff compared to routine clinical care, which may provide some indirect health benefits.



Data from this study may have the anticipated benefit of helping Medtronic with the understanding of SCS therapy and assisting with the design of future studies and product improvements. The information gathered from this study could also help clinicians optimize therapy for their patients.

## 10.4. Risk-Benefit Rationale

Neurostimulation therapies, such as SCS, are used as an aid in the management of chronic, intractable pain that cannot be effectively managed with medications and/or other conservative treatments alone. Patients considered for neurostimulation therapy have typically had pain of long duration and have failed multiple therapeutic paths. Findings from clinical studies documented in published literature suggest that T9/T10 has been a common location to target stimulation for chronic back and leg pain.

Medtronic has carefully designed and tested the RestoreSensor SureScan MRI and Intellis AdaptiveStim Neurostimulation Systems to ensure the safety and performance for the treatment of chronic, intractable pain. Medtronic has completed an extensive risk analysis to ensure the identification of potential hazards and subsequent mitigation of these hazards to eliminate them entirely or reduce them to an acceptable level.

The risks associated with the surgical implantation of the device, device use, and device failures are the same those observed for commercially available SCS devices. With an existing pre-market application approval for the commercially available RestoreSensor SureScan MRI and Intellis AdaptiveStim Neurostimulation Systems, an established safety profile of probable benefit outweighing risk already exists for SCS Therapy for chronic back and/or leg pain. In most cases implantation of SCS is a reversible procedure and the system can be turned off or removed. Moreover, stimulation parameters are adjustable to minimize or reverse complications and maximize therapeutic effects. System output and programming parameters used with the proposed HD stimulation parameters are within the range of the commercially available RestoreSensor SureScan MRI and Intellis AdaptiveStim Neurostimulation Systems. However, some subjects may not receive effective pain relief with the proposed HD stimulation parameters. HD stimulation non-responders will be managed in the same manner as commercial patients, and their devices may be programmed to any combination of parameters chosen by their physician. The anticipated benefits of the clinical outcomes of SCS therapy per the study design outweigh the overall risk.

## 11. Adverse Events and Device Deficiencies

### 11.1. Definitions/Classifications

Each adverse event is classified according to ISO 14155:2011 Where the definition indicates “device”, it refers to any device used in the study. See geography-specific addenda for applicable OUS information.

Term	Definition
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<p><b>Adverse Event (AE):</b> (ISO 14155:2011 3.2)</p>	<p>Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device.</p> <p><i>NOTE 1:</i> This definition includes events related to the investigational medical device or the comparator.</p> <p><i>NOTE 2:</i> This definition includes events related to the procedures involved.</p> <p><i>NOTE 3:</i> For users or other persons, this definition is restricted to events related to investigational medical devices.</p>
<p><b>Adverse Device Effect (ADE):</b> (ISO 14155:2011 3.1)</p>	<p>Adverse event related to the use of an investigational medical device.</p> <p><i>NOTE 1:</i> This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device.</p> <p><i>NOTE 2:</i> This definition includes any event resulting from use error or from intentional misuse of the investigational medical device.</p>
<p><b>Device Deficiency (DD):</b> (ISO 14155:2011 3.15)</p>	<p>Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance.</p> <p><i>NOTE:</i> Device deficiencies include malfunctions, use errors, and inadequate labeling.</p>
<p><b>Malfunction:</b> (ISO 14155:2011 3.27)</p>	<p>Failure of an investigational medical device to perform in accordance with its intended purpose when used in accordance with the instructions for use or (CIP).</p>
<p><b>Use Error:</b> (ISO 14155:2011 3.43)</p>	<p>Act or omission of an act that results in a different medical device response than intended by the manufacturer or expected by the user.</p> <p><i>NOTE 1:</i> Use error includes slips, lapses, and mistakes.</p> <p><i>NOTE 2:</i> An unexpected physiological response of the subject does not in itself constitute a use error.</p>
<p><b>Term</b></p>	<p><b>Seriousness</b></p>
<p><b>Serious Adverse Event (SAE):</b> (ISO 14155:2011 3.37)</p>	<p>Adverse event that</p> <ul style="list-style-type: none"> <li>a) led to death,</li> <li>b) led to serious deterioration in the health of the subject, that either resulted in             <ul style="list-style-type: none"> <li>1) a life-threatening illness or injury, or</li> <li>2) a permanent impairment of a body structure or a body function, or</li> <li>3) in-patient or prolonged hospitalization, or</li> <li>4) medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function,</li> </ul> </li> <li>c) led to foetal distress, foetal death or a congenital abnormality or birth defect.</li> </ul>



	<i>NOTE:</i> Planned hospitalization for a pre-existing condition, or a procedure required by the CIP, without serious deterioration in health, is not considered a serious adverse event.
<b>Serious Adverse Device Effect (SADE):</b>  (ISO 14155:2011 3.36)	Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event
<b>Unanticipated Serious Adverse Device Effect (USADE):</b>  (ISO 14155:2011 3.42)	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.  <i>NOTE:</i> 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.
<b>Term</b>	<b>Relatedness</b>
<b>Device Related</b>	An adverse event that results from the presence or performance (intended or otherwise) of the Neuromodulation System
<b>Therapy Related</b>	Event related to therapy delivery by device. Normally therapy-related events resolve when the device is turned off or reprogrammed. This category should not include events that resulted from a malfunction of the device (i.e. hardware-related events).
<b>Procedure Related</b>	An adverse event that occurs due to any procedure related to the implantation, surgical modification of the system or programming.

## 11.2. Foreseeable Adverse Events and Anticipated Adverse Device Effects

All anticipated adverse events and adverse device effects are the same as those foreseeable risks listed in Section 10.1.

## 11.3. Recording of Adverse Events

In this study, only device-, therapy- and procedure-related adverse events (AEs) and device deficiencies that occur from enrollment through subject discontinuation from the study will be collected. Adverse event and device deficiency information will be reported to Medtronic on an adverse event or device deficiency eCRF, one for each AE and/or device deficiency.

It is the responsibility of the investigator to identify the occurrence of device-, therapy- or procedure-related adverse events and device deficiencies and to ensure all required information is accurately recorded on the eCRF. Refer to the applicable eCRF for the information to be reported for each adverse event and device deficiency.



For adverse events that require immediate reporting, initial reporting to Medtronic may be done by phone, or e-mail, or on the eCRF by completing as much information as is available. The adverse event eCRF must be completed as soon as possible.

In case the investigator requires information from the sponsor in an emergency situation, the investigator can contact Medtronic using the contact details provided in the synopsis and Section 11.7.

The clinical course of each adverse event must be followed until the adverse event is resolved, the subject is in a stable condition, or until the subject discontinues from the study. "Ongoing" adverse events and device deficiencies must be assessed at each study visit. The adverse event eCRF should be updated when there is a change to the information provided on the form (e.g. change in intervention, outcome, relatedness, etc.).

At the last scheduled visit, the investigator will instruct the subject to provide an update on the status of any ongoing events and report any adverse event or issue with the device that they believe might be related to participation in the study.

## 11.4. Recording of Device Deficiencies

Device deficiency information will be collected throughout the study and reported to Medtronic on a device event eCRF, one for each device deficiency. The investigator must determine and document on the eCRF device deficiencies that did not lead to an adverse event but could have led to a serious adverse device effect:

- If either suitable action had not been taken
- If intervention had not been made, or
- If circumstances had been less fortunate

## 11.5. Adverse Event and Device Deficiency Reporting Requirements

only those Adverse Events (AEs) which are related to the following will be collected:

- The implanted SCS system, accessories and surgical procedures
- SCS therapy

In addition, all device deficiencies reported during the study will be collected.

It is the responsibility of the Investigator to adhere to the adverse event reporting requirements as stated within the protocol or in the applicable country-specific addenda and to their IRB/EC reporting requirements. Unanticipated Serious Adverse Device Effects (USADE) must be reported to Medtronic within 24 hours of learning of the effect, and to the IRB/EC as required. Medtronic is also responsible to report these events to participating investigators, IRBs/ECs, the FDA and or other regulatory agencies based on applicable local laws.



Upon receipt of notification of adverse events and device deficiencies at Medtronic, a Medtronic study team member will review for completeness and accuracy and when necessary, will request clarification and/or additional information from the investigator. If Medtronic disagrees with the Investigator’s assessment of the adverse event, Medtronic study personnel will document the disagreement and report or ensure reporting of both opinions to IRB/EC and regulatory agencies as required. Medtronic will utilize the Medical Dictionary for Regulatory Activities (MedDRA) to assign a MedDRA term for each adverse event and device deficiency based on the information provided by the investigator.

## 11.6. Non-Reportable Events

Events that are not reportable for this study are:

- Lack of pain relief
  - Pain symptoms will be collected as part of the efficacy measures
- Sensation of stimulation (paresthesia)
  - Sensation of stimulation (e.g. tingling, buzzing) will not be reported as this may occur as part of this therapy. **Exception: Sensation or stimulation events that are uncomfortable to the subject (e.g. shocking, jolting) will be reported.**
- Adverse events unrelated to
  - Implanted SCS system, accessories or surgical procedure
  - Spinal cord stimulation therapy

Table 6 provides a list of common expected surgical adverse events. An expected surgical event will not be considered reportable unless it worsens or is present outside the stated timeframe post-procedure.

**Table 6: Expected Surgical Adverse Events and Durations**

Event description	Time frame after the surgical procedure
Anesthesia-related nausea/vomiting	24 hours
Mild to moderate pain at surgical site	7 days
Low-grade fever (<100°F or < 37.8°C)	48 hours
Mild to moderate bruising / ecchymosis	7 days
Pocket site / incisional pain	14 days
Seroma	72 hours
Sleep problems (insomnia)	72 hours

## 11.7. Emergency Contact Details

For emergency contact regarding an SADE/DD, contact the Clinical Study Manager immediately. Refer to the country specific addenda for OUS information.

**24-hour Medtronic contact information for reporting SADEs/DD:**

Email: [rs.neuadverseeventreporting@medtronic.com](mailto:rs.neuadverseeventreporting@medtronic.com)



Phone (US) : +1 (765) 505 - 9036

## 11.8. Deaths

The investigator must notify Medtronic immediately and the IRB/EC, as required, after learning of a subject's death, regardless of whether or not the death is related to the device system, therapy or procedure. The investigator should also attempt to determine, as conclusively as possible, whether such deaths are related to the device system, therapy, or procedure. If the death is evaluated as device-, therapy-, or procedure-related, and unanticipated, the event will be reported as a USADE by Medtronic to the appropriate regulatory authorities.

If it is determined that the cause of death was device-, therapy-, or procedure-related:

- And an autopsy is conducted, a copy of the report should be provided to Medtronic.
- Medtronic requests that all device system components that were being used at the time of the death be returned to Medtronic for analysis per Section 7.8.
- Requested death certificates and/or source documentation if obtained should be redacted and sent to Medtronic.
- If the death occurs at a location remote from the study site, it is the study site's responsibility to make three attempts to retrieve all pertinent information related to the subject's death and submit the investigator's death summary of the known events surrounding the death to Medtronic.

## 12. Data Review Committees

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This study will not use a Clinical Events Committee (CEC), Adverse Events Advisory Committee (AEAC) or an independent Data Monitoring Committee (DMC). Instead, all reported adverse events and device deficiencies will be reviewed by a Medtronic Medical Advisor to ensure consistent reporting.

## 13. Statistical Design and Methods

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### 13.1. General Statistical Considerations

Data analysis will be performed by Medtronic-employed statisticians or designees. A validated statistical software package (e.g., SAS version 9.4 or higher) will be used to analyze the study results.

The Statistical Analysis Plan (SAP) will be developed prior to data analysis and will include a comprehensive description of the statistical methods and reports to be included in the final study report. Any change to the data analysis methods described in the CIP will require an amendment only if it changes a principal feature of the CIP. Any other change to the data analysis methods described in the CIP, and the justification for making the change, will be described in the clinical study report.



All analyses will be pooled by neurostimulator model unless otherwise specified.

PASS11 was used to calculate the sample size for the primary objective.

### 13.1.1. Analysis populations

There will be 4 population sets for the purposes of analysis in this study:

**Enrolled Analysis Set:** All consented subjects.

**Trialed Analysis Set:** All subjects who are implanted with trialing leads at T9/T10 and programmed at the Device Trial Day 0 Visit.

**Implanted Analysis Set:** All subjects who have a positive device trial with HD parameters at T9/T10 and are implanted with a neurostimulation system.

**Treated Analysis Set:** All subjects in the Implanted Analysis Set whose devices are activated at the Device Activation Visit.

### 13.1.2. Handling of missing data

The primary and secondary efficacy objectives will be evaluated for the Treated Analysis Set. For subjects in the Treated Analysis Set with missing outcome data, the missing outcome measure will be imputed using multiple imputations (MI). [REDACTED]

[REDACTED]

Following imputation, the objectives will be evaluated using MI analysis methods.

Imputation for missing data may be implemented for the long-term additional measures analyses.

### 13.1.3. Interim efficacy analyses

An interim analysis providing preliminary characterization of the secondary objectives will be performed in late 2018 with the intent of presenting the results in early 2019. The details of these analyses will be specified in the SAP.

Analyses of the efficacy outcomes and safety assessment will be performed after 100 subjects have reached the 3-Month Visit, as described in section 13.1.6. The primary efficacy objective will not be evaluated. These analyses will be specified in the SAP and are not intended to be used to modify the study.



### 13.1.4. Center pooling

All investigators in the proposed study will conduct the study according to a common protocol and utilize the same CRFs to collect study data. In addition, site study personnel training will be conducted prior to initiation of the study in each site and periodic monitoring will be conducted by Medtronic to ensure compliance with protocol requirements.

Data will be pooled across centers for all analyses. No single site will be allowed to implant more than 25 subjects. This is intended to reduce the possibility that a site with atypical results will be overly influential in the study results based on pooled data.

### 13.1.5. Multiple testing adjustment

The study has one primary objective that will be evaluated with statistical testing. The primary objective will be evaluated at an alpha level of 0.05 after all subjects in the Treated Analysis Set have completed the 3-Month Visit.

Therapy efficacy will be demonstrated by successfully passing the primary objective analysis. The secondary objectives are not alpha-controlled; they will be characterized but not evaluated with statistical testing.

### 13.1.6. Reports

[REDACTED]

## 13.2. Demographics

Demographics and baseline characteristics will be summarized for all enrolled subjects, as well as the subset of subjects in the Treated Analysis Set.

## 13.3. Primary Objective

### 13.3.1. Primary objective

To demonstrate a significant improvement in overall (low back and leg) pain intensity using HD stimulation starting at 90 - 200  $\mu$ sec and 1000 Hz with lead placement spanning the T9/T10 disc space, as measured by the Visual Analog Scale (VAS), from Baseline to the 3-Month Visit.

### 13.3.2. Hypothesis

The mean change in overall pain in implanted subjects ( $\mu_c$ ) from baseline to 3 months will be statistically significantly different from no change on the VAS scale 0-100 mm:

$$H_0: \mu_c = 0$$

$$H_A: \mu_c \neq 0$$



### 13.3.3. Endpoint definition

The change in overall pain will be calculated for all subjects in the Treated Analysis Set as:

$$\text{Baseline overall pain} - \text{3-Month overall pain}$$

The baseline and 3-month overall pain scores will be collected on the Visual Analog Scale (VAS) at the Baseline and 3-Month Visits, respectively.

### 13.3.4. Study sample size justification

The Tests for One Mean in PASS11 was used to calculate the sample size. The assumptions of  $\alpha = 0.05$ , power = 0.9, null mean (Mean0) = 0, alternative mean (Mean1) = 20, standard deviation = 30, alternative hypothesis = Mean0  $\neq$  Mean1, and Infinite population size, results in a sample size of 26 subjects. However, a sample size of 100 subjects derived for the secondary objectives (section 13.4) ensures over 99% power under those same assumptions.

Up to 215 subjects will be enrolled to ensure at least 100 subjects reach the 3-month endpoint.

### 13.3.5. Analysis methods

The two-sided, one sample t-test will be used to test the hypothesis of the primary objective. The main analysis will include all subjects in the Treated Analysis Set. In addition to the hypothesis test, the two-sided 95% confidence interval for the average change in overall pain will be calculated and reported.

### 13.3.6. Handling of missing data

The primary analysis for this efficacy objective will be evaluated for all subjects in the Treated Analysis Set. The method for handling missing data for the primary endpoint is described in section 13.1.2.

### 13.3.7. Sensitivity analyses

Sensitivity analyses will be conducted for the primary efficacy objective using the methods described below:

- Completers analysis:
  - Only subjects in the Treated Analysis Set with complete paired data at the Baseline and 3-Month Visits will be included in the analysis.

█ [REDACTED]

█ [REDACTED]



[Redacted]

[Redacted]

## 13.4. Secondary Objectives

### 13.4.1. Secondary objective 1: Overall pain responder rate

To characterize the overall (low back and leg) pain efficacy responder rate, as measured by the VAS, from Baseline to the 3-Month Visit, with a confidence interval within  $\pm 10\%$ .

#### Endpoint definition

The responder rate will be calculated as the proportion of subjects in the Treated Analysis Set who demonstrate at least a 50% improvement in overall pain from baseline to 3 months. For each subject, percentage improvement will be calculated as:

$$\frac{(\text{Baseline overall pain} - \text{3-Month overall pain}) \times 100}{\text{Baseline overall pain}}$$

The baseline and 3-month overall pain scores will be collected on the VAS at the Baseline and 3-Month Visits, respectively. Subjects who report at least a 50% improvement in overall pain will be considered responders.

#### Study sample size justification

Calculations were performed using PASS11, Confidence Intervals for One Proportion, with Confidence Level = 0.95, P = 0.5, Confidence Interval Formula = Score (Wilson), Interval Type = Two-Sided. Table 7 shows the 95% confidence interval for a 50% responder rate for 50-100 subjects. A sample size of 100 subjects provides a 95% confidence interval within 9.6% of the responder rate estimate, if the observed responder rate is 50%. The confidence interval is the widest with a responder rate of 50%; a lower or higher responder rate will have a narrower confidence interval.

**Table 7. 95% Confidence Interval (CI) for Responder Rate = 50%**

N	Lower Limit	Upper Limit	CI Width	+/- Range
50	36.6%	63.4%	26.7%	13.4%
60	37.7%	62.3%	24.5%	12.3%
70	38.6%	61.4%	22.8%	11.4%
80	39.3%	60.7%	21.4%	10.7%
90	39.9%	60.1%	20.2%	10.1%
100	40.4%	59.6%	19.2%	9.6%



## Analysis methods

The responder rate as defined above will be calculated for subjects in the Treated Analysis Set. The score (Wilson) method will be used to calculate the 95% confidence interval of the responder rate. In this analysis, missing data will be imputed as described above in section 13.3.6. Sensitivity analyses will be performed as described in section 13.4.4.

### 13.4.2. Secondary objective 2: Low back pain responder rate

To characterize the low back pain efficacy responder rate, as measured by the VAS, from Baseline to the 3-Month Visit, with a confidence interval within  $\pm 10\%$ .

#### Endpoint definition

The responder rate will be calculated as the proportion of subjects in the Treated Analysis Set who demonstrate at least a 50% improvement in low back pain from baseline to 3 months. For each subject, percentage improvement will be calculated as:

$$\frac{(\text{Baseline low back pain} - \text{3-Month low back pain}) \times 100}{\text{Baseline low back pain}}$$

The baseline and 3-month low back pain scores will be collected on the VAS at the Baseline and 3-Month Visits, respectively. Subjects who report at least a 50% improvement in low back pain will be considered responders.

#### Study sample size justification

Calculations were performed using PASS11, Confidence Intervals for One Proportion, with Confidence Level = 0.95, P = 0.5, Confidence Interval Formula = Score (Wilson), Interval Type = Two-Sided. Table 8 shows the 95% confidence interval for a 50% responder rate for 50-100 subjects. A sample size of 100 subjects provides a 95% confidence interval within 9.6% of the responder rate estimate, if the observed responder rate is 50%. The confidence interval is the widest with a responder rate of 50%; a lower or higher responder rate will have a narrower confidence interval.

**Table 8. 95% Confidence Interval (CI) for Responder Rate = 50%**

N	Lower Limit	Upper Limit	CI Width	+/- Range
50	36.6%	63.4%	26.7%	13.4%
60	37.7%	62.3%	24.5%	12.3%
70	38.6%	61.4%	22.8%	11.4%
80	39.3%	60.7%	21.4%	10.7%
90	39.9%	60.1%	20.2%	10.1%
100	40.4%	59.6%	19.2%	9.6%

## Analysis methods

The responder rate as defined above will be calculated for subjects in the Treated Analysis Set. The score (Wilson) method will be used to calculate the 95% confidence interval of the responder rate. In



this analysis, missing data will be imputed as described above in section 13.1.2. Sensitivity analyses will be performed as described in section 13.4.4.

### 13.4.3. Secondary objective 3: Leg pain responder rate

To characterize the leg pain efficacy responder rate, as measured by the VAS, from Baseline to the 3-Month Visit, with a confidence interval within ±10%.

#### Endpoint definition

The responder rate will be calculated as the proportion of subjects in the Treated Analysis Set who demonstrate at least a 50% improvement in leg pain from baseline to 3 months. For each subject, percentage improvement will be calculated as:

$$\frac{(\text{Baseline leg pain} - 3\text{-Month leg pain}) \times 100}{\text{Baseline leg pain}}$$

The baseline and 3-month leg pain scores will be collected on the VAS at the Baseline and 3-Month Visits, respectively. Subjects who report at least a 50% improvement in leg pain will be considered responders.

#### Study sample size justification

Calculations were performed using PASS11, Confidence Intervals for One Proportion, with Confidence Level = 0.95, P = 0.5, Confidence Interval Formula = Score (Wilson), Interval Type = Two-Sided. Table 9 shows the 95% confidence interval for a 50% responder rate for 50-100 subjects. A sample size of 100 subjects provides a 95% confidence interval within 9.6% of the responder rate estimate, if the observed responder rate is 50%. The confidence interval is the widest with a responder rate of 50%; a lower or higher responder rate will have a narrower confidence interval.

**Table 9. 95% Confidence Interval (CI) for Responder Rate = 50%**

N	Lower Limit	Upper Limit	CI Width	+/- Range
50	36.6%	63.4%	26.7%	13.4%
60	37.7%	62.3%	24.5%	12.3%
70	38.6%	61.4%	22.8%	11.4%
80	39.3%	60.7%	21.4%	10.7%
90	39.9%	60.1%	20.2%	10.1%
100	40.4%	59.6%	19.2%	9.6%

#### Analysis methods

The responder rate as defined above will be calculated for subjects in the Treated Analysis Set. The score (Wilson) method will be used to calculate the 95% confidence interval of the responder rate. In this analysis, missing data will be imputed as described above in section 13.1.2. Sensitivity analyses will be performed as described in section 13.4.4.





[REDACTED]

Summary statistics will be presented for continuous measures (N, means, medians, standard deviations, minimums and maximums) and categorical measures (N, percent, frequency distributions) with 95% confidence intervals as appropriate. Missing data imputation may be performed on long-term outcome measures. No multiplicity adjustment will be performed for characterizations of the additional study measures.

### 13.6. Safety Assessment

All device-, therapy-, or procedure-related adverse events and device deficiencies from enrollment to study exit will be summarized. Adverse events and device deficiencies will be coded and summarized using the Medical Dictionary for Regulatory Affairs (MedDRA). Summaries will be presented as the number of events, the number of subjects who experienced the event, and the percent of subjects who experienced the event. Adverse events and device deficiencies will be summarized by study phase (e.g., Baseline, Trialing, Implant), with the appropriate number of corresponding subjects as the denominator within each study phase.

## 14. Ethics

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### 14.1. Statements of Compliance

This study will be conducted in compliance with this CIP and good clinical practice according to the International Conference on Harmonization (ICH GCP E6), the ethical principles that originate from the Declaration of Helsinki and in the United States (US), the Code of Federal Regulations (CFR) on Electronic records (21 CFR§11), Protection of human subjects (21 CFR§50), Institutional review boards (21 CFR §56), Medical Device Reporting (21CFR§803), and applicable local regulatory requirements and laws in the states and geographies in which the study will be conducted. Refer to the geography-specific addendum for more information. This study will be posted on <http://www.ClinicalTrials.gov> as part of Medtronic's commitment to full disclosure for ongoing studies that meet the requirements for public posting.

The principles of the Declaration of Helsinki have been implemented through the patient informed consent (IC) process, IRB/EC approval, study training, clinical trial registration, preclinical testing, risk-benefit assessment and publication policy.



Prior to enrolling subjects in this study, each study site's IRB/EC will be required to approve the current CIP or CIP amendments, the subject ICF, including any other written information to be provided to the subjects and, if applicable, any materials used to recruit subjects. IRB/EC approval letters must contain sufficient information to identify the version and/or date of the documents that were approved, or the information must be retrievable from the corresponding submission letter. Sites must also receive written approval from Medtronic prior to initiating subject enrollments. Any additional requirements imposed by the IRB/EC or regulatory authority will be followed and documented, if appropriate.

Investigators will be required to sign a Statement of Investigator Commitment form stating their intent to adhere to applicable regulations.

The sponsor shall avoid improper influence on, or inducement of, the subject, monitor, any investigator(s) or other parties participating in, or contributing to, the clinical investigation. All investigators shall avoid improper influence on or inducement of the subject, sponsor, monitor, other investigator(s) or other parties participating in or contributing to the clinical investigation.

## 15. Study Administration

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### 15.1. Monitoring

Medtronic is responsible for ensuring the proper conduct of this study in terms of adherence to applicable regulations, protocol compliance, and the validity and accuracy of the study data entered on eCRFs. As such, investigational sites will be monitored to ensure the safety and well-being of study subjects is preserved, and to ensure site compliance with the study protocol, applicable regulations, and the study data is accurate and complete.

Monitoring and monitoring oversight will be provided by Medtronic personnel or by representatives of Medtronic (i.e. contractors and other designees) who will support the study investigation including site qualification, site initiation, interim monitoring and study closure visits.

Contact information for the study monitoring:

Core Clinical Solutions Monitor Group  
8200 Coral Sea Street, N.E., MVS33  
Mounds View, MN 55112

The principal investigator and study staff will provide the Medtronic monitors with complete and direct access to source data (e.g., paper and electronic hospital/clinical charts, appointment books, laboratory records) that support the data on the eCRFs, as well as other documentation supporting the conduct of the study. Monitors will perform source data verification, routine reviews of study-related regulatory documents, including product accountability during scheduled monitoring visits, and work to secure compliance should any deficiencies be observed. The monitoring plan is maintained as a separate



document on file at Medtronic and contains the procedure and strategy for frequency of monitoring visits and extent source data verification to be performed for this study.

The principal investigator must make every effort to meet with the monitor during each monitoring visit.

## 15.2. Medtronic Representative Role

Medtronic representatives who are qualified and trained on the protocol may participate in the conduct of the study under the direct supervision of the principal investigator as described below. The principal investigator or other study site personnel designated on the delegation of authority form must collect all required data, record the study activities, and be responsive to the subject's needs during an activity performed by a Medtronic representative.

Medtronic representatives may provide technical support to the investigator and other health care personnel as needed during study visits. This support may include the training of site personnel on use of the Medtronic equipment or the protocol-related procedures and data collection.

In addition, Medtronic personnel may perform certain activities to ensure study quality. These activities may include:

- Provide technical support during device trial, implant and follow-up visits.
- Perform device programming, device interrogation, device download while under the direction of the investigator.
- Discuss any issues with programming or subject compliance with the principal investigator or site personnel.
- Clarify and/or troubleshoot device behavior, operation, or diagnostic output as requested by the Principal Investigator or other health care professional
- Perform device interrogation, printing or uploading of device information while under the direction of the investigator or study site personnel delegated responsibility for device programming and assist with the collection of study data from equipment and upload into the NPU database

Medtronic personnel may not perform the following:

- Practice medicine, provide medical diagnoses or make decisions related to subject treatment/care
- Discuss a subject's condition or medical treatment with the subject or a member of the subject's family
- Express opinions about the product/feature under study
- Assist the subject by direct physical contact except as required by the specific protocol-related task to be conducted
- Provide the subject with any form/questionnaires related to the products under investigation
- Enter data on eCRFs, with the exception of Medtronic Use Only fields/forms



## 15.3. Data Management

This study will use the Oracle Clinical Remote Data Capture (RDC) system, which allows the study centers to enter data directly on the eCRF within the sponsor's database over a secure internet connection. This system is a 21CFR§11 Part E compliant, fully-validated system that controls user access, ensures data integrity, and maintains an audit trail of entries, changes or corrections made to the eCRFs. User access will be granted by Medtronic to each applicable individual at a site based upon his or her delegation of authority for the study and only upon completion of the required training. The Investigator and applicable study site personnel will be given access to the electronic eCRF system; user IDs and passwords may not be shared.

The principal investigator is responsible for the overall quality (completeness, accuracy and timeliness) of the data entered on the eCRFs and the data in all other required reports. The principal investigator or sub-investigator (physician only) must review all data for accuracy and provide his/her approval of the eCRF and sign each form with an electronic signature. Data reported on the eCRFs, must be derived from and consistent with source documents, unless otherwise stated in this section or the study monitoring plan. If discrepancies in source are identified (e.g., during monitoring), these need to be corrected or justified with a documented rationale, signed and dated by the principal investigator, or authorized delegate, to be maintained as a part of the subject's records. If a person only authorized to complete eCRFs makes changes to an already signed eCRF, the system will require the principal investigator, or authorized delegate, to re-sign the eCRF.

The eCRF may be considered source for the following data collection elements:

- Investigator assessment of adverse event relatedness and seriousness
- Details pertaining to and reason for protocol deviation

Even when the CRF may be considered as source (as noted above), an alternative method of source documentation is always strongly encouraged.

Medtronic personnel will perform routine edit and consistency checks, in-house and during monitoring visits, for items such as missing data or inconsistent data. Identified data inconsistencies will be resolved by use of data queries; investigators and site personnel will review data queries and respond to them in a timely manner. The resolved discrepancy will become a part of the eCRF record for the subject. At the end of the study, the data will be frozen (locked) and will be retained indefinitely by Medtronic.

## 15.4. Direct Access to Source Data/Documents

Source documentation is defined as the original documents, data and records and may include all clinical records, hospital records, laboratory notes, surgery reports, autopsy reports, and other documents, electronic or paper, that contain original information to support study data collections or AE



reporting. The Principal Investigator is responsible for ensuring source documentation is complete, legible and accurate; and entries are made in a timely manner by appropriately delegated study staff.

The Principal Investigator and site personnel will provide the Medtronic monitor(s) with direct access to source documentation or certified copies that supports the data on the eCRFs as well as other documentation supporting the conduct of the study.

Medtronic or third-party auditors representing Medtronic may perform clinical site audits to verify the performance of the monitoring process, study conduct, and to ensure compliance with applicable regulations. Representatives from regulatory bodies such as the FDA may also perform site inspections related to this clinical study. The Principal Investigator, site personnel, and institution will provide monitors, auditors, and FDA with direct access to source documentation and all study-related documentation.

Medtronic will investigate suspected cases of fraud or misconduct as appropriate.

## 15.5. Confidentiality

All records and other information about subjects participating in this clinical study will be treated as confidential. Subject confidentiality will be maintained throughout the clinical study to the extent permitted by law. For this purpose, a unique study-specific subject identification code (study - site - subject number) will be assigned and used to allow identification of all data reported to Medtronic for each subject. Subject confidentiality is assured through the use of the study-specific subject identification numbers, use of initials only, and the de-identifying of subjects' records obtained by or provided to the Sponsor.

For purposes of monitoring this study, access to clinic and hospital records must be available to Medtronic, representatives of Medtronic (i.e. contractors and other designees), the FDA and other regulatory agencies. Study data may be made available to third parties (e.g., in the case of an audit or inspection performed by regulatory authorities), provided the data are treated confidentially and the subject's privacy is guaranteed. The identity of a subject will never be disclosed in the event study data are published. Only anonymized data will be analyzed and published.

In addition to the review of records at the center, release of de-identified records to Medtronic may be necessary. The investigational site personnel must make every effort to de-identify and label source documentation with the subject's study-specific identification number prior to submission of the records to Medtronic.

Health Insurance Portability and Accountability Act (HIPAA) language will be required to be included at every center in the US. HIPAA language may be included within the ICF according to the center's policy. Data privacy language will be included as required by geographic regulations and described in the geography-specific addenda.



## 15.6. Liability

The compensation and covered liability associated with this study conduct will be documented in a separate financial agreement signed by Medtronic, the principal investigator, and or the management of study site/institution.

## 15.7. CIP Amendments

Protocol amendments may be initiated by Medtronic to address changes to the scope or conduct of the study. Protocol amendments, and associated documents, must be approved by Medtronic and submitted to the reviewing IRBs/ECs for approval prior to implementation except when necessary to eliminate an immediate/or apparent immediate hazard to participating subjects.

## 15.8. Record Retention

### 15.8.1. Investigator Records

Documentation for this study will be produced and maintained to ensure that a complete history of the study exists. Documents created for this study, including all versions of original documents, will be identifiable and appropriately stored to assure control and traceability of data related to this study.

The principal investigator is responsible for the ensuring that all essential study documentation is retained and accessible for a minimum of 2 years (or longer as local law or facility administration requires) after the investigation is terminated or completed. The retention period may be longer if required by Medtronic, local or global regulatory requirements. Medtronic will be responsible for notifying sites of extensions to the 2-year minimum record retention requirements. Medtronic must be notified in writing by site personnel of any transfer of study documentation. The principal investigator will ensure that essential study documents are not destroyed until written permission has been obtained from Medtronic or if allowed per contract.

At a minimum, the investigator is responsible for the preparation, review, submission to Medtronic and retention of all signed and dated case report forms, reportable adverse events, device deficiencies, subject deaths, deviations from the CIP. In addition, investigators are also responsible for maintaining all correspondence with another investigator, an IRB/EC, the sponsor, a monitor, FDA or other local regulatory authority, related to this study (including approval documentation), records of each subject's case history and exposure to the device (including signed and dated informed consent forms & HIPAA or other data privacy authorizations as required by local authority), final report, and all other study-related documentation.

### 15.8.2. Investigator Reports

The principal investigator is responsible for the preparation (review and signature) and submission to the sponsor of all case report forms, adverse events, device deficiencies, deaths, and any deviations from the Clinical Investigation Plan. If any action is taken by an IRB/EC with respect to this clinical study,



copies of all pertinent documentation must be forwarded to Medtronic in a timely manner. Reports are subject to inspection and to the retention requirements as described above for investigator records.

Investigator reporting requirements for termination or suspension are listed in Section 15.10. The investigator shall prepare and submit in a complete, accurate and timely manner the reports listed in this section.

## 15.9. Publication and Use Information

Medtronic may publish the results from the Vectors Post Market study. These publication activities may include abstracts, presentations/posters to scientific meetings, and manuscripts. Specific requirements regarding publication of study data will be provided in the publication plan. All proposed publications must be reviewed and approved by Medtronic prior to publication. If required by a publisher, the principal investigator agrees to obtain all necessary authorizations from study subjects prior to submitting study-related information for publication.

### Authorship Selection

Principal investigators who enroll subjects and comply with the protocol will be eligible to act as publication authors and may be asked to write or contribute to the writing of abstracts and manuscripts. Final authorship will be based on the Ethical Considerations in the Conduct and Reporting of Research as defined by the International Committee of Medical Journal Editors (<http://www.icmje.org>). All 4 of the following criteria must be met for authorship:

1. Substantial contribution to conception and design, or acquisition of data, or analysis and interpretation of data
2. Drafting the article or revising it critically for important intellectual content
3. Final approval of the version to be published
4. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Lead authorship will be given to the principal investigator who meets the criteria listed above and has the highest number of evaluable subjects. If there is a tie for lead authorship, the authors will be listed in alphabetical order. Medtronic personnel who meet the criteria for authorship will have the right to be listed as an author. Other significant contributors to the study who do not meet the criteria for authorship will be listed in the acknowledgement section of the publication.

## 15.10. Suspension or Early Termination

Early Termination is the closure of a clinical study that occurs prior to meeting defined endpoints. This is possible for the whole study or a single center. Suspension is a temporary postponement of study activities related to enrollment. This is possible for the whole study or a single center. Medtronic reserves the right to suspend or terminate the study or an individual study site at any time. In the event



that the study is terminated, the subject's devices will be programmed as per the Investigator's discretion and once exited from the study, subjects will be managed by their physician.

### **15.10.1. Study-wide termination or suspension**

Medtronic reserves the right to suspend or terminate the study at any time. Reasons may include, but are not limited to, the following:

- Insufficient enrollment to complete the study within the expected timeframe
- Identification of adverse events or safety issues with the product or system that may impact the safety or welfare of study subjects
- Product performance/product supply issues

### **15.10.2. Investigator/center termination or suspension**

Medtronic reserves the right to suspend or terminate the study at an individual site. Reasons may include, but are not limited to, the following:

- Noncompliance with the protocol
- IRB/EC approval lapse/expiration
- Serious or repeated deviations at the site
- Failure to implement required corrective and preventive actions
- Insufficient enrollment to complete the study within the expected timeframe
- Loss of appropriately trained site personnel
- Investigator request (e.g. no longer able to support the study)

Investigators are required to notify the IRB/EC of study suspension/termination. Subjects will be notified by the investigator of suspension/termination due to unacceptable risk or of termination due to any other cause.



## 16. References

1. Shealy CN, Mortimer JT, Reswick JB. Electrical inhibition of pain by stimulation of the dorsal columns: preliminary clinical report. *Anesth Analg*. 1967;46(4):489-491. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Citation&list\\_uids=4952225](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Citation&list_uids=4952225).
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## 17. Appendices

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### 17.1. Appendix A Additional Information for Sites

Detailed sponsor contact information not outlined in the Clinical Investigational Plan will be provided under a separate cover.

### 17.2. Appendix B: Institutional Review Boards

At the time of the completion of the Vectors Post Market Clinical Investigation Plan, site selection is not yet complete. Therefore, a complete list of participating IRB/EC names, locations, and the Chairperson(s) will be distributed under a separate cover when available.

### 17.3. Appendix C: Participating Investigators and Institutions

At the time of completion of the Vectors Post Market Clinical Investigation Plan, site selection is not yet complete. Therefore, a complete list of names, addresses, and professional positions of the clinical investigators and institutions will be distributed under a separate cover when available.

## 18. Version History

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Version	Summary of Changes	Author(s)/Title
[REDACTED]	[REDACTED]	[REDACTED]



	<p>[Redacted text]</p>	<p>[Redacted text]</p>
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