BurstDR™ micrOdosing stimuLation in De-novo patients

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BOLD
BurstDR™ micrOdosing stimuLation in De-novo patients
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Clinical Investigation Plan (CIP)

Sponsor	Abbott 6901 Preston Road Plano, TX 75024 USA
Coordinating Investigator	Name/Title Hospital Department/function Address City Country

PRINCIPAL INVESTIGATOR SIGNATURE PAGE

I have read and agree to adhere to the clinical investigation plan and all regulatory requirements applicable in conducting this clinical investigation.

Principal Investigator

Printed name:
Signature:
Date:

Coordinating Investigator/ National Investigator

SIGNATURE PAGE

I have read and agree to adhere to the clinical investigation plan and all regulatory requirements applicable in conducting this clinical investigation.

Coordinating Investigator/ National Investigator

Printed name:
Signature:
Date:

Table of Contents

1 Synopsis

The purpose of this study is to evaluate the therapeutic efficacy of microdosing BurstDR™ stimulation in spinal cord stimulation (SCS) patients with chronic intractable back and/or leg pain. Microdosing BurstDR™ consists of periods during which stimulation is delivered with standard BurstDR™ stimulation parameters alternated with periods during which no stimulation is being delivered. Previous results show that patients using standard BurstDR™ can be programmed with microdosing with no changes to therapeutic efficacy (Vesper et. al, 2017). In this study we propose to evaluate therapeutic efficacy of BurstDR™ microdosing, and determine optimal microdosing programming parameters in chronic pain patients, who are eligible for SCS therapy.

1.1 Objective(s)

- The primary objective is to evaluate the efficacy of BurstDR™ microdosing stimulation in patients with chronic intractable back and/or leg pain with no prior history of SCS therapy.
- The secondary objectives are to evaluate the optimal microdosing program, evaluate the long term efficacy of BurstDR™ stimulation on patient's pain intensity, and evaluate the improvements in quality of life, disability, anxiety, depression, catastrophizing and overall satisfaction.

1.2 Devices Used

The following devices will be used in this clinical investigation:

Table 1: Identification of Devices under Investigation

Device name	Model/Type	Manufacturer	Region/ Country	Investigational or Market Released
Abbott Invisible trial external pulse generator (EPG)	3599 (Base), 3032 (Header)	Abbott	US/OUS	Released
Abbott Invisible trial Clinician Programmer	3870, 3872	Abbott	US/OUS	Released
Abbott Invisible trial Patient Controller	3871, 3873	Abbott	US/OUS	Released
Abbot Percutaneous trial lead	31XX	Abbott	US/OUS	Released
Abbott Lead extension	33XX	Abbott	US/OUS	Released
Abbott Prodigy internal pulse generator (IPG)	3799	Abbott	US/OUS	Released
Abbott Prodigy MRI IPG	3772	Abbott	US/OUS	Released
Abbott Prodigy Charger	3730	Abbott	US/OUS	Released
Abbott Prodigy Patient Programmer	3856	Abbott	US/OUS	Released
Abbott Rapid Programmer programming device	3835	Abbott	US/OUS	Released
Abbott Proclaim IPG	3660, 3662	Abbott	US/OUS	Released
Abbott Clinician Programmer App	3874	Abbott	US/OUS	Released
Abbott Patient Controller App	3875	Abbott	US/OUS	Released
Abbott commercially available percutaneous leads	31X6, 318X, 314X, 315X, 316X	Abbott	US/OUS	Released
Abbott commercially available paddle leads	322X, 321X, 328X, 324X, 326X, 3240	Abbott	US/OUS	Released
Abbott Cinch™ Lead Anchor	1194	Abbott	US/OUS	Released
Abbott Swift-Lock™ Anchor	1192	Abbott	US/OUS	Released

1.3 Design

This is a prospective, open label, multicenter feasibility trial to evaluate the therapeutic efficacy of different BurstDR™ microdosing patterns in patients with chronic intractable pain.

Subjects, eligible for SCS therapy, who are diagnosed with chronic intractable back and/or leg pain, will be considered for inclusion in this study. After baseline evaluation, subjects will undergo a SCS trial using the Abbott Invisible Trial system. During the trial implant phase, SCS leads will be implanted in the dorsal column based on physician discretion. According to standard clinical practices performed in the United States (US), the trial phase will last around 3-7 days. At the start of the trial phase, patients will be programmed with the first ON/OFF stimulation pattern (30 second STIM ON, 90 seconds STIM OFF). Patients who do not achieve adequate pain relief (at least 50% reduction in back and/or leg VAS from baseline) within the first 3-4 days will be reprogrammed to a new ON/OFF stimulation pattern (5 seconds ON/ 15 seconds OFF). Patients, who still do not achieve adequate pain relief within 2 to 3 days from reprogramming, will be reprogrammed to a continuous mode of BurstDR™ stimulation and their trial evaluation will continue. These patients will be evaluated for an additional 2 days. At the end of the SCS trial, all subjects that experience at least 50% pain relief (according to average back and/or leg VAS) using one of the two microdosing burst stimulation paradigms will be considered further participation in the study. See Figure 1.

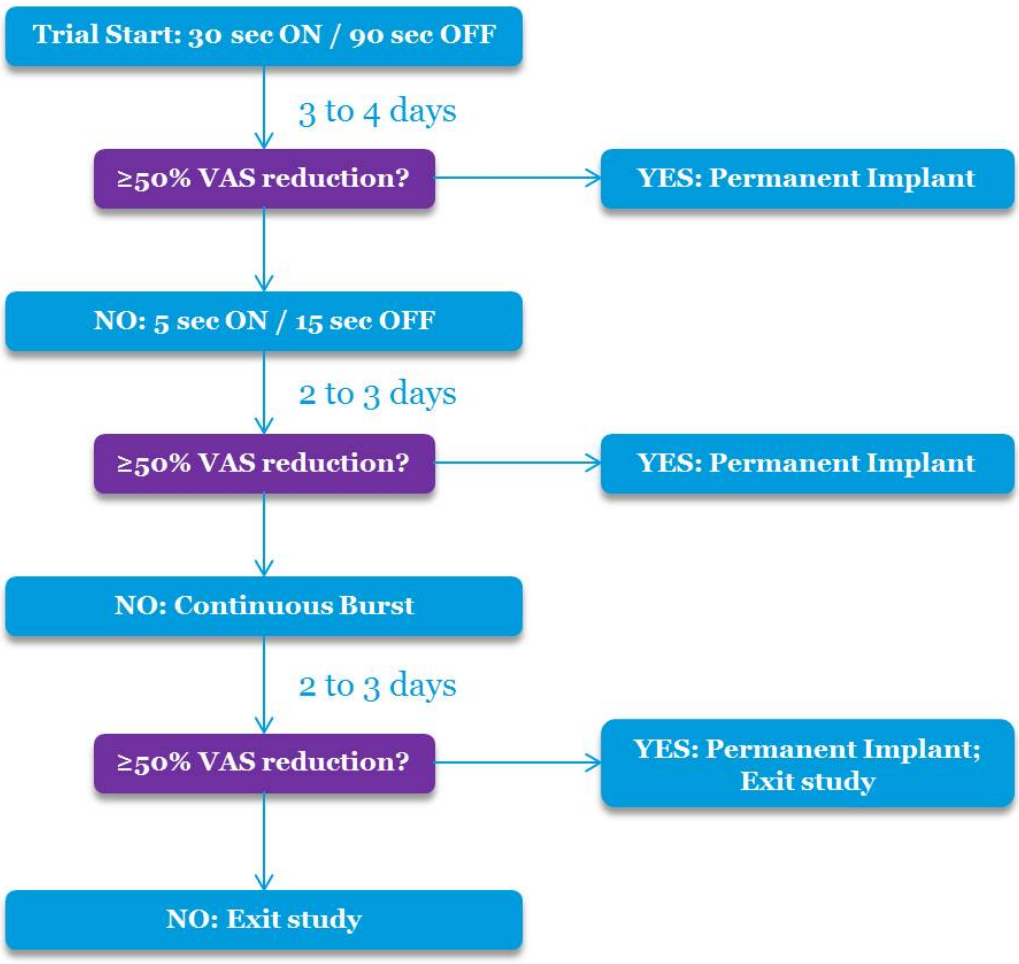


Fig 1: Representation of the decision making algorithm for the SCS trial phase of the study

Patients who have passed the trial phase and have received permanent implantation will be programmed based on the stimulation mode used for their trial success. Pain intensity, quality of life, disability, anxiety, depression, pain catastrophizing, satisfaction, and medication usage will be assessed at baseline, after SCS trial and at the 1, 3 and 6 month follow up. Adverse events will be collected throughout the study period.

During the month leading to the 1 month follow up visit, patients' pain relief will be evaluated on a weekly basis according to Figure 2. Briefly, patients who do not achieve adequate pain relief (greater or equal to pain relief achieved during the trial phase) will try lower stimulation ON/OFF ratios to determine the lowest possible stimulation ratio whilst maintaining adequate pain relief. This stimulation ON/OFF ratios will start from a ratio of 1:12 (Program 1) and increase to a potential ON/OFF ratio of 1:3 (Program 5) – Once the most optimal microdosing program is determined (as per algorithm in Figure 2), the patient will continue the rest of the study with that program. If inadequate pain relief is experienced anytime during the study, the BurstDR™ microdosing parameters will be altered as per the algorithm in Figure 2.

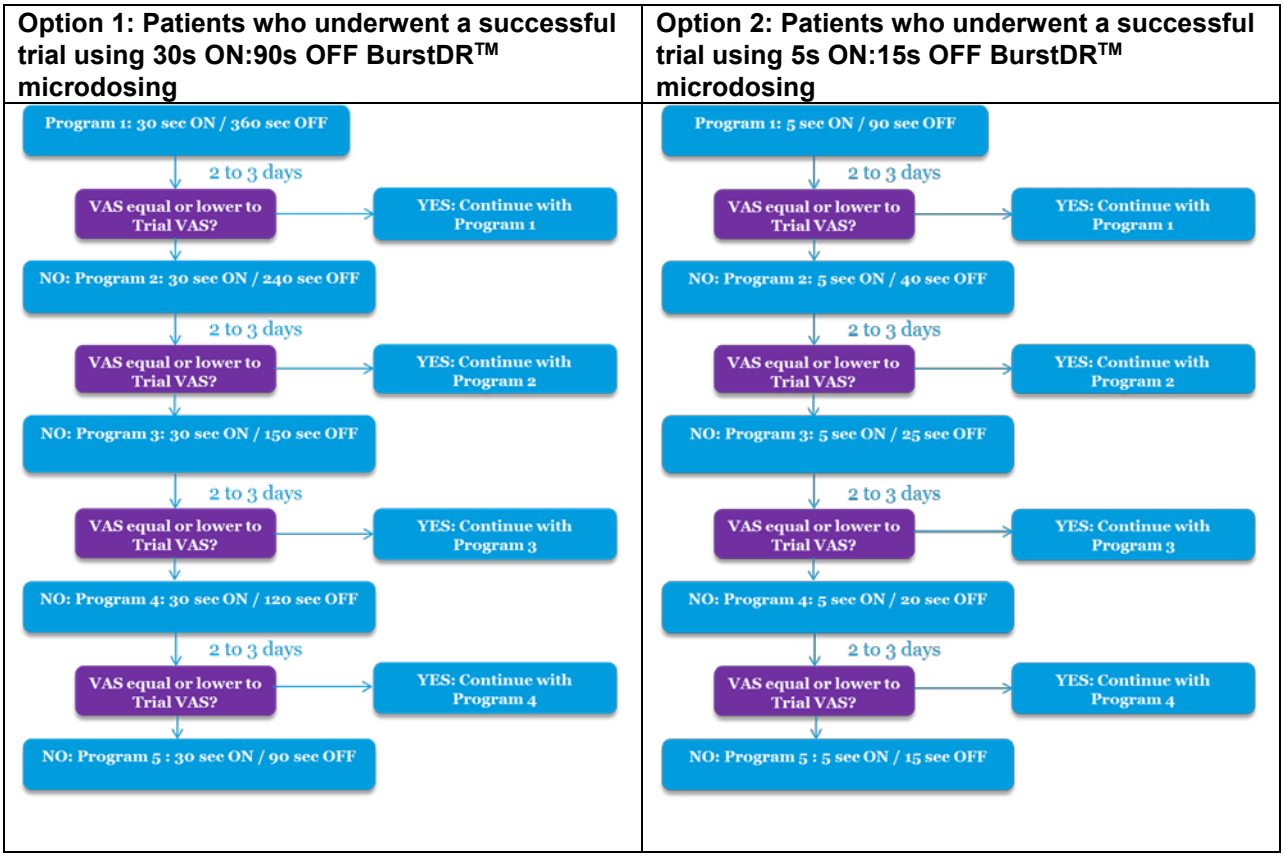


Figure 2: Representation of the decision making algorithm for the SCS 1 month post permanent implant phase of the study

The total duration of the study is expected to be 2 years.

The clinical study will be conducted in up to 6 centers in the United States

Up to 60 subjects will be enrolled in this study.

1.4 Endpoints

There is 1 primary endpoint and 3 secondary endpoints in this clinical investigation.

1.4.1 Primary Endpoints

- Evaluate the change in pain intensity between baseline, trial and long-term follow up evaluations using the Visual Analog Scale (VAS) assessments.

1.4.2 Secondary Endpoints

- Evaluate the optimal microdosing program required to maintain optimal pain relief on a patient specific basis
- Evaluate the change in European Quality of life – 5 Dimensions (EQ-5D) scores between baseline, SCS trial and follow up visits
- Evaluate the change in Oswestry Disability Index (ODI) scores between baseline, SCS trial and follow up visits
- Evaluate the change in Hospital Anxiety and Depression scale (HADS) scores between baseline, SCS trial and follow up visits
- Evaluate the change in Pain Catastrophizing Scale (PCS) scores between baseline, SCS trial and follow up visits
- Evaluate the change in Patient Global Impression of Change (PGIC) between SCS trial and follow up visits
- Evaluate the change in medication usage between baseline, SCS trial and follow up visits

1.4.3 Descriptive Endpoint(s)

Descriptive endpoints are reported using only summary statistics and no hypothesis tests will be performed.

- Optimal microdosing program
- Medication Usage

1.5 Study Population

The intended population of this clinical investigation consists of patients diagnosed with chronic intractable back and/or leg pain with no prior history of neuromodulation therapies.

1.6 Inclusion/Exclusion Criteria

1.6.1 Inclusion Criteria

- Subject is able to provide informed consent to participate in the study;
- Subject diagnosed with chronic intractable pain associated with back and/or limbs;
- Subject is 18 years of age or older;
- Subject has failed to respond to at least 6 months of conventional treatment which may include pharmacological treatment, physical therapy, epidural injections;
- Subject has a back and/or leg pain intensity of at least 6.0 cm out of 10.0 cm on the average back and/or leg pain VAS at baseline;
- Subject's medical record has been evaluated by the Investigator to ensure that the subject is a good candidate for a neurostimulation system;
- Subject is on stable pain medications with a total opioid for at least 28 days prior to enrolling in this study, and is willing to stay on those medications with no dose increase until the 3 month visit;
- Subject is willing to cooperate with the study requirements including compliance with the regimen and completion of all office visits;

- Female candidates of child-bearing potential agree to commit to the use of an effective method of contraception (including but not limited to sterilization, barrier devices, oral contraceptives, intrauterine devices (IUDs), condoms, rhythm method, or abstinence) for the duration of the study

1.6.2 Exclusion Criteria

- Subject has a current diagnosis of a coagulation disorder, bleeding diathesis, progressive peripheral vascular disease, post-herpetic neuralgia or uncontrolled diabetes mellitus;
- Subject is currently participating in a clinical investigation that includes an active treatment arm;
- Subject has been implanted with or participated in a trial period for a neurostimulation system;
- Subject has an infusion pump;
- Subject has evidence of an active disruptive psychological or psychiatric disorder as determined as per standard of care;
- Subject has a current diagnosis of a progressive neurological disease as determined by the Investigator;
- Subject is immunocompromised;
- Subject has an existing medical condition that is likely to require repetitive MRI evaluation in the future (i.e. epilepsy, stroke, multiple sclerosis, acoustic neuroma, tumor);
- Subject has history of cancer requiring active treatment in the last 12 months;
- Subject has an existing medical condition that is likely to require the use of diathermy in the future;
- Subject has documented history of allergic response to titanium or silicone;
- Subject has a documented history of substance abuse (narcotics, alcohol, etc.) or substance dependency in the 6 months prior to baseline data collection;
- Subject is a female candidates of child bearing potential that are pregnant (confirmed by positive urine/blood pregnancy test);
- Subject has life expectancy of less than 6 months;
- Subject is involved in an injury claim under current litigation

1.7 Enrollment

A patient becomes a subject once he/she has been fully informed about the study, has agreed to participate, signed & dated the consent.

1.8 Study Assessments

Subjects will undergo a baseline assessment to collect primary and secondary outcome measures prior to the SCS trial. Specifically, baseline assessments will include: pain rating as assessed by the VAS, quality of life as assessed by EQ-5D, disability as assessed by ODI, anxiety and depression as assessed by the HADS, and pain catastrophizing as assessed by the PCS. Medication usage will also be collected during the baseline visit.

Subjects will be implanted with trial SCS system according to clinical practice and practitioner's discretion. At the end of the SCS trial period, subjects who experienced a reduction of 50% or more in average pain back and/or leg VAS scores with one of the two microdosing stimulation paradigms will be offered permanent implant and further participation in the study. The same primary and secondary outcomes measures will be collected at the end of the SCS trial period as well as at the 1, 3 and 6 months follow up visit, with the inclusion of patient satisfaction as assessed by the PGIC. Programming parameters will also be assessed during these visits.

2 Introduction

This document is a clinical investigation plan (CIP) for the BOLD clinical investigation. This clinical investigation is intended to evaluate the therapeutic efficacy of microdosing BurstDR™ stimulation in

spinal cord stimulation (SCS) patients with chronic intractable back and/or leg pain. This clinical investigation is sponsored by Abbott.

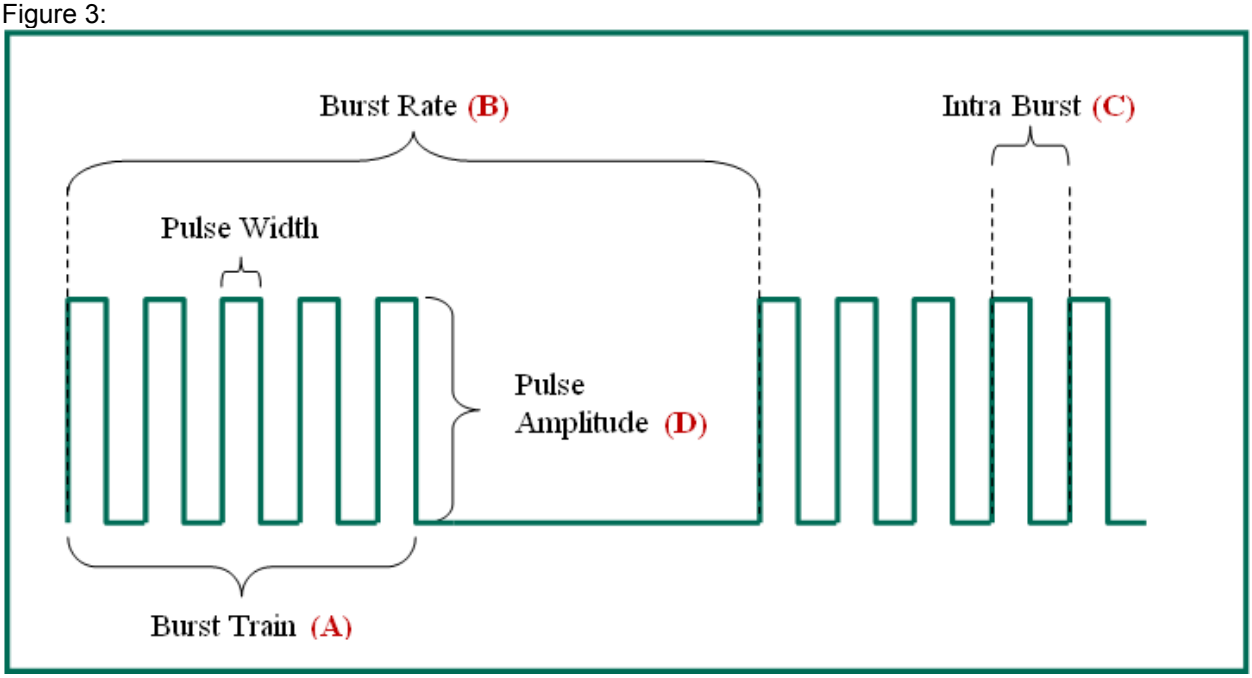
This clinical investigation will be conducted in accordance with this CIP. All parties involved in the conduct of the clinical investigation will be qualified by education, training, or experience to perform their tasks and this training will be documented appropriately.

3 Background and Justification for Clinical Investigation

Spinal cord stimulation (SCS) is increasingly being used as an alternative for the treatment of chronic, intractable pain. In a systematic meta-analysis of the literature, Taylor et al. (2006) reported that SCS reduces pain, improves quality of life, reduces analgesic use, allows some patients to return to work and may also result in significant cost savings over time, while having minimally significant adverse events in patients with neuropathic back and/or leg pain.

Patients receiving conventional tonic SCS (electrical pulses delivered in the 40-60Hz stimulation frequency range) experience paresthesia or a tingling sensation. Burst SCS is a newer paradigm that is currently approved worldwide. Burst stimulation eliminates or greatly reduces the incidence of paresthesia (Courtney et al. 2014), and it entails delivering groups of pulses called burst trains (A) repeated at a burst rate (B); within each burst train, several pulses are issued at an intra-burst rate (C) (See Figure 3). Individual pulses are characterized by a pulse amplitude (D) and pulse width.

Figure 3:



While the efficacy of standard burst stimulation parameters is known (Courtney et al. 2014, DeRidder et al., 2010, 2013), its comparison to more energy efficient settings is unknown.

Burst microdosing consists of delivery of intermittent doses of burst stimulation. Preliminary evidence supports that the therapeutic efficacy of burst microdosing results in a similar clinical outcome compared to standard burst stimulation (Vesper et al. 2017). Use of these new energy efficient stimulation parameters has the potential to prolong the battery life of a non-rechargeable, primary cell Implantable

Pulse Generator (IPG). It also has the potential to improve patient convenience by decreasing the frequency with which the patient has to recharge a non-primary cell IPG.
In this study, we aim to evaluate the therapeutic efficacy of different BurstDR™ microdosing patterns in patients with chronic intractable pain

4 Device(s) Under Investigation

4.1 Identification and Description of the Devices under investigation

4.1.1 Identification

Table 2: Identification of Devices under Investigation

Device name	Model/Type	Manufacturer	Region/ Country	Investigational or Market Released
Abbott Invisible trial external pulse generator (EPG)	3599 (Base), 3032 (Header)	Abbott	US/OUS	Released
Abbott Invisible trial Clinician Programmer	3870, 3872	Abbott	US/OUS	Released
Abbott Invisible trial Patient Controller	3871, 3873	Abbott	US/OUS	Released
Abbot Percutaneous trial lead	31XX	Abbott	US/OUS	Released
Abbott Lead extension	33XX	Abbott	US/OUS	Released
Abbott Prodigy internal pulse generator (IPG)	3799	Abbott	US/OUS	Released
Abbott Prodigy MRI IPG	3772	Abbott	US/OUS	Released
Abbott Prodigy Charger	3730	Abbott	US/OUS	Released
Abbott Prodigy Patient Programmer	3856	Abbott	US/OUS	Released
Abbott Rapid Programmer programming device	3835	Abbott	US/OUS	Released
Abbott Proclaim IPG	3660, 3662	Abbott	US/OUS	Released
Abbott Clinician Programmer App	3874	Abbott	US/OUS	Released
Abbott Patient Controller App	3875	Abbott	US/OUS	Released
Abbott commercially available percutaneous leads	31X6, 318X, 314X, 315X, 316X	Abbott	US/OUS	Released
Abbott commercially available paddle leads	322X, 321X, 328X, 324X, 326X, 3240	Abbott	US/OUS	Released
Abbott Cinch™ Lead Anchor	1194	Abbott	US/OUS	Released
Abbott Swift-Lock™ Anchor	1192	Abbott	US/OUS	Released

4.1.2 Device Description and Intended Purpose

Abbott Invisible trial external pulse generator (EPG): a 16 channels, software controlled, battery powered, and external stimulator that generates the electrical pulses to be used during the trial phase of the study

Abbott Invisible trial Clinician Programmer: software compatible with iOS™ App 8.1 or later to be used on iPad mini™; enables the clinician to program the Abbott Invisible trial EPG
Abbott Invisible trial Patient Controller: software compatible with iOS™ App 8.1 or later to be used on iPad touch™; enables patient-controlled therapy adjustment of the Abbott Invisible trial EPG
Abbott Percutaneous trial lead: sterile stimulating electrode placed in the epidural space of the spinal cord and connected to the EPG
Abbott Lead extension: sterile extension that connects the pulse generator to the stimulating electrode
Abbott Prodigy: a 16 channels, software controlled, rechargeable battery powered, internal stimulator to be used during the follow up phase of the study that generates the electrical pulses.
Abbott Prodigy MRI: a 16 channels, software controlled, rechargeable battery powered, internal stimulator to be used during the follow up phase of the study that generates the electrical pulses.
Abbott Prodigy Charger: The IPG Charging System provides the capability to recharge the IPG battery while stimulation is either on or off. The charging system has several main parts: AC line cord, AC power supply, power cable, and charger antenna. The charger transmits RF energy through the antenna to the IPG battery to recharge it.
Abbott Patient Programmer: the patient programmer allows subjects to adjust stimulation intensity and to select a different stimulation programs in the Prodigy MRI IPG.
Abbott Rapid Programmer: the rapid programmer enables the clinician to program the Prodigy IPG.
Abbott Proclaim internal pulse generator (IPG): a 16 channels, software controlled, battery powered, internal stimulator to be used during the follow up phase of the study that generates the electrical pulses
Abbott Clinician Programmer App: software compatible with iOS™ App 8.3 or later to be used on iPad mini™; enables the clinician to program the Proclaim IPG
Abbott Patient Controller App: software compatible with iOS™ App 8.1 or later to be used on iPad touch™; enables patient-controlled therapy adjustment of the Proclaim IPG
Abbott percutaneous leads lead: sterile stimulating electrode that are placed in the epidural space of the spinal cord and connected to the Proclaim or Protégé IPG
Abbott paddle leads: sterile stimulating electrodes that are placed in the epidural space of the spinal cord and connected to the Proclaim or Protégé IPG
Abbott Cinch™ Lead Anchor: securing device designed to reduce lead migration and breakage
Abbott Swift-Lock™ Anchor: securing device designed to reduce lead migration and breakage

4.1.3 Device Handling and Storage

Sponsor requires all investigational products be stored, according to the labeling and Instructions for Use, in a secure area to prevent unauthorized access or use.

4.1.4 Identification

4.2 Devices Accountability

Device accountability not required in post market studies

5 Clinical Investigation Design

5.1 Clinical Investigation Design

This is a prospective, open label, multicenter feasibility trial to evaluate the therapeutic efficacy of different BurstDR™ microdosing patterns in patients with chronic intractable pain.

Subjects diagnosed with chronic intractable back and/or leg pain, with no prior history of SCS therapy, will be considered for inclusion in this study. After baseline evaluation, subjects will undergo a SCS trial using the Abbott Invisible Trial system. During the trial implant phase, SCS leads will be implanted in the dorsal column based on physician discretion. According to standard clinical practices performed in the United States (US), the trial phase will last around 3-7 days. At the start of the trial phase, patients will be

programmed with the first ON/OFF stimulation pattern (30 second STIM ON, 90 seconds STIM OFF). Patients who do not achieve adequate pain relief (at least 50% reduction in back and/or leg VAS from baseline) within the first 3-4 days will be reprogrammed to a new ON/OFF stimulation pattern (5 seconds ON/ 15 seconds OFF). Patients, who still do not achieve adequate pain relief within 2 to 3 days from reprogramming, will be reprogrammed to a continuous mode of BurstDR™ stimulation and their trial evaluation will continue. These patients will be evaluated for an additional 2 days. At the end of the SCS trial, all subjects that experience at least 50% pain relief (according to average back and/or leg VAS) using one of the two microdosing burst stimulation paradigms will be considered further participation in the study. See Figure 1.

Patients who have passed the trial phase and have received permanent implantation will be programmed based on the stimulation mode used for their trial success. Pain intensity, quality of life, disability, anxiety, depression, pain catastrophizing, satisfaction, and medication usage will be assessed at baseline, after SCS trial and at the 1, 3 and 6 month follow up. Adverse events will be collected throughout the study period.

During the month leading to the 1 month follow up visit, patients' pain relief will be evaluated on a weekly basis according to Figure 2. Briefly, patients who do not achieve adequate pain relief (greater or equal to pain relief achieved during the trial phase) will try lower stimulation ON/OFF ratios to determine the lowest possible stimulation ratio whilst maintaining adequate pain relief. This stimulation ON/OFF ratios will start from a ratio of 1:12 (Program 1) and increase to a potential ON/OFF ratio of 1:3 (Program 5) – Once the most optimal microdosing program is determined (as per algorithm in Figure 2), the patient will continue the rest of the study with that program. If inadequate pain relief is experienced anytime during the study, the BurstDRTM microdosing parameters will be altered as per the algorithm in Figure 2.

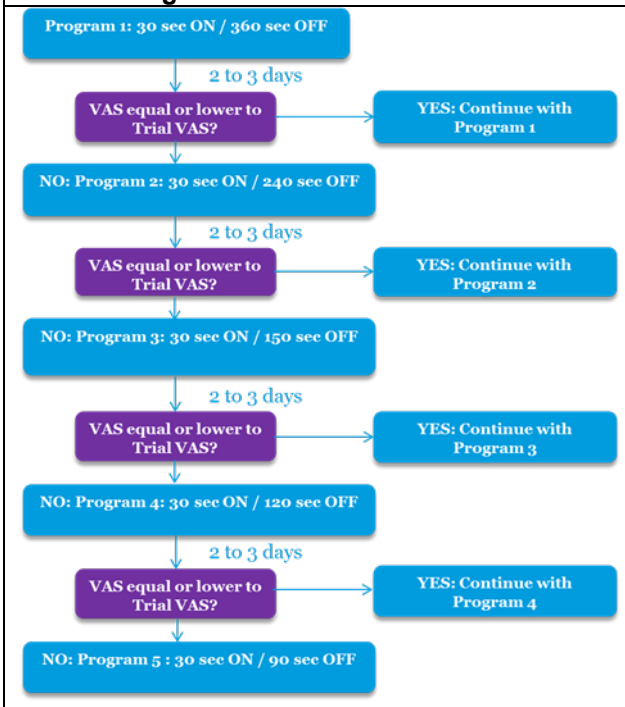
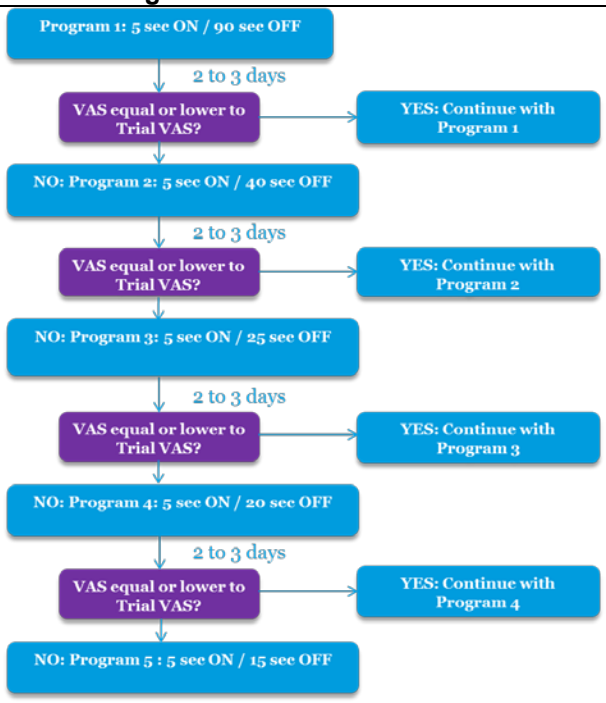
Option 1: Patients who underwent a successful trial using 30s ON:90s OFF BurstDR™ microdosing	**Option 2: Patients who underwent a successful trial using 5s ON:15s OFF BurstDR™ microdosing**
	

Figure 2: Representation of the decision making algorithm for the SCS 1 month post permanent implant phase of the study

The total duration of the study is expected to be 2 years.

The clinical study will be conducted in up to 6 centers in the United States.

Approximately 60 subjects will be enrolled in this study.

5.2 Objectives

The objective of this clinical investigation is to evaluate the therapeutic efficacy of microdosing BurstDR™ stimulation in spinal cord stimulation (SCS) patients with chronic intractable back and/or leg pain.

5.2.1 Primary Objectives

- To evaluate efficacy of microdosing BurstDR™ stimulation in patients with chronic intractable back and/or leg pain that have never received neuromodulation treatments before.

5.2.2 Secondary Objectives

- Evaluate the optimal microdosing program required to maintain optimal pain relief on a patient specific basis
- Evaluate the long term efficacy of BurstDR™ stimulation on patients' pain intensity
- Evaluate the improvements in quality of life, disability, anxiety, depression, catastrophizing, medication and overall satisfaction of patients using microdosing BurstDR™ stimulation

5.3 Endpoints

There is 1 primary endpoints and 7 secondary endpoints in this clinical investigation.

5.3.1 Primary Endpoint

- Evaluate the change in pain intensity between baseline, trial and long-term follow up evaluations using the Visual Analog Scale (VAS) assessments.

5.3.2 Secondary Endpoint

- Evaluate the optimal microdosing program required to maintain optimal pain relief on a patient specific basis
- Evaluate the change in European Quality of life – 5 Dimensions (EQ-5D) scores between baseline, SCS trial and follow up visits
- Evaluate the change in Oswestry Disability Index (ODI) scores between baseline, SCS trial and follow up visits
- Evaluate the change in Hospital Anxiety and Depression Scale (HADS) scores between baseline, SCS trial and follow up visits
- Evaluate the change in Pain Catastrophizing Scale (PCS) scores between baseline, SCS trial and follow up visits
- Evaluate the change in Patient Global Impression of Change (PGIC) between SCS trial and follow up visits
- Evaluate the change in medication usage between baseline, SCS trial and follow up visits

5.3.3 Descriptive Endpoint(s)

Descriptive endpoints are reported using only summary statistics and no hypothesis tests will be performed.

- Optimal microdosing program
- Medication Usage

5.4 Study Population

The intended population of this clinical investigation consists of patients diagnosed with chronic intractable back and/or leg pain with no prior history of neuromodulation therapies.

5.4.1 Inclusion Criteria

- Subject is able to provide informed consent to participate in the study;
- Subject diagnosed with chronic intractable pain associated with back and/or limbs;
- Subject is 18 years of age or older;
- Subject has failed to respond to at least 6 months of conventional treatment which may include pharmacological treatment, physical therapy, epidural injections;
- Subject has a back and/or leg pain intensity of at least 6.0 cm out of 10.0 cm on the average back and/or leg pain VAS at baseline;
- Subject's medical record has been evaluated by the Investigator to ensure that the subject is a good candidate for a neurostimulation system;
- Subject is on stable pain medications with a total opioid for at least 28 days prior to enrolling in this study, and is willing to stay on those medications with no dose increase until the 3 month visit;
- Subject is willing to cooperate with the study requirements including compliance with the regimen and completion of all office visits;
- Female candidates of child-bearing potential agree to commit to the use of an effective method of contraception (including but not limited to sterilization, barrier devices, oral contraceptives, intrauterine devices (IUDs), condoms, rhythm method, or abstinence) for the duration of the study

5.4.2 Exclusion Criteria

- Subject has a current diagnosis of a coagulation disorder, bleeding diathesis, progressive peripheral vascular disease, post-herpetic neuralgia or uncontrolled diabetes mellitus;
- Subject is currently participating in a clinical investigation that includes an active treatment arm;
- Subject has been implanted with or participated in a trial period for a neurostimulation system;
- Subject has an infusion pump;
- Subject has evidence of an active disruptive psychological or psychiatric disorder as determined as per standard of care;
- Subject has a current diagnosis of a progressive neurological disease as determined by the Investigator;
- Subject is immunocompromised;
- Subject has an existing medical condition that is likely to require repetitive MRI evaluation in the future (i.e. epilepsy, stroke, multiple sclerosis, acoustic neuroma, tumor);
- Subject has history of cancer requiring active treatment in the last 12 months;
- Subject has an existing medical condition that is likely to require the use of diathermy in the future;
- Subject has documented history of allergic response to titanium or silicone;
- Subject has a documented history of substance abuse (narcotics, alcohol, etc.) or substance dependency in the 6 months prior to baseline data collection;
- Subject is a female candidates of child bearing potential that are pregnant (confirmed by positive urine/blood pregnancy test);

- Subject has life expectancy of less than 6 months;
- Subject is involved in an injury claim under current litigation

6 Procedures

The clinical study will be conducted in accordance with the CIP. All parties participating in the conduct of the clinical study will be qualified by education, training, or experience to perform their tasks and this training will be documented appropriately. Approval from the Sponsor must be received prior to initiating study procedures.

Patients will be informed about the study to determine if he/she is interested in participating. Eligible patients will read, sign and date the informed consent and will continue to participate in the study as subjects. Subjects diagnosed with chronic intractable back and/or leg pain, with no prior history of SCS therapy, will be considered for inclusion in this study and will be assessed at baseline and all follow up visits.

The assessments will include:

- Pain intensity as assessed by the Visual Analog Scale (VAS)
- Quality of life as assessed by the European Quality of Life – 5 Dimensions (EQ-5D)
- Disability as assessed by the Oswestry Disability Index (ODI)
- Anxiety and Depression as assessed by the Hospital Anxiety and Depression Scale (HADS)
- Pain Catastrophizing as assessed by the Pain Catastrophizing Scale (PCS)
- Satisfaction as assessed by the Patient Global Impression of Change (PGIC)
- Medication Usage
- Adverse Events

After baseline evaluation, subjects will undergo a SCS trial using the Abbott Invisible Trial system. During the trial implant phase, SCS leads will be implanted in the dorsal column based on physician discretion. According to standard clinical practices performed in the United States (US), the trial phase will last around 3-7 days. At the start of the trial phase, patients will be programmed with the first ON/OFF stimulation pattern (30 second STIM ON, 90 seconds STIM OFF). Patients who do not achieve adequate pain relief (at least 50% reduction in back and/or leg VAS from baseline) within the first 3-4 days will be reprogrammed to a new ON/OFF stimulation pattern (5 seconds ON/ 15 seconds OFF). Patients, who still do not achieve adequate pain relief within 2 to 3 days from reprogramming, will be reprogrammed to a continuous mode of BurstDR™ stimulation and their trial evaluation will continue. These patients will be evaluated for an additional 2 days. At the end of the SCS trial, all subjects that experience at least 50% pain relief (according to average back and/or leg VAS) using one of the two microdosing burst stimulation paradigms will be considered further participation in the study. See Figure 1.

Patients who have passed the trial phase and have received permanent implantation will be programmed based on the stimulation mode used for their trial success. Pain intensity, quality of life, disability, anxiety, depression, pain catastrophizing, satisfaction, and medication usage will be assessed at baseline, after SCS trial and at the 1, 3 and 6 month follow up. Adverse events will be collected throughout the study period.

During the month leading to the 1 month follow up visit, patients' pain relief will be evaluated on a weekly basis according to Figure 2. Briefly, patients who do not achieve adequate pain relief (greater or equal to pain relief achieved during the trial phase) will try lower stimulation ON/OFF ratios to determine the lowest possible stimulation ratio whilst maintaining adequate pain relief. This stimulation ON/OFF ratios will start from a ratio of 1:12 (Program 1) and increase to a potential ON/OFF ratio of 1:3 (Program 5) – Once the most optimal microdosing program is determined (as per algorithm in Figure 2), the patient will continue

the rest of the study with that program. If inadequate pain relief is experienced anytime during the study, the BurstDRTM microdosing parameters will be altered as per the algorithm in Figure 2.

The following sections provide a detailed description of procedures required by this CIP.

6.1 Informed Consent Process

The Principal Investigator or his/her authorized designee will conduct the Informed Consent Process, as required by applicable regulations and the center's IRB/EC. This process will include a verbal discussion with the subject on all aspects of the clinical investigation that are relevant to the subject's decision to participate, such as details of clinical investigation procedures, anticipated benefits, and potential risks of clinical investigation participation. During the discussion, the Principal Investigator or his/her authorized designee will avoid any improper influence on the subject and will respect subject's legal rights. The subject shall be provided with the informed consent form written in a language that is understandable to the subject and has been approved by the center's IRB/EC. The subject shall have adequate time to review, ask questions and consider participation.

If the subject agrees to participate, the Informed Consent form must be signed and dated by the subject and by the person obtaining the consent. The signed original will be filed in the subject's hospital or research charts, and a copy will be provided to the subject.

The Principal Investigator or his/her authorized designee will document the informed consent process in the subject's hospital and/or research charts. The date of signature will be entered on an applicable Case Report Form (CRF).

Failure to obtain informed consent from a subject prior to clinical investigation enrollment should be reported to Sponsor within 5 working days and to the reviewing center's IRB/EC according to the IRB's/ EC's reporting requirements.

If, during the clinical investigation, new information becomes available that can significantly affect a subject's future health and medical care, the Principal Investigator or his/her authorized designee will provide this information to the subject. If relevant, the subject will be asked to confirm their continuing informed consent in writing.

6.2 Screening

Potential patients presenting at the investigational sites will be fully informed about the clinical investigation, following the established Informed Consent process (described in section 6.1). Once a duly dated and signed Informed Consent Form is obtained, the screening procedures may begin.

Records of patients who are screened must be maintained.

In case the subject does not meet all inclusion criteria or meets any of the exclusion criteria, the subject is considered a screening failure. The Principal Investigator or the delegated study personnel will record the screening failure in the hospital records and on a screening log as required.

6.3 Point of Enrollment

Subject is considered enrolled in the clinical investigation from the moment the subject has provided a written Informed Consent and has been confirmed to meet all inclusion criteria and none of the exclusion criteria.

The Principal Investigator or delegated study personnel will record enrollment information (name of the clinical investigation, date of consent and Inclusion/exclusion information) in the hospital records and complete and submit an applicable CRF in a timely manner.

Notification of enrollment to the Sponsor is considered to have occurred when the Sponsor has received the applicable CRF.

6.4 Scheduled Procedures

The Principal Investigator is responsible for ensuring all clinical investigation data is collected as required per CIP scheduled procedures.

6.4.1 Baseline

Baseline visit activities can occur at the same visit of enrollment after the informed consent has been obtained.

The following assessments and information will be collected at the baseline visit

- Demographics- include subject's Age and Gender
- Physical examination- include subject's height and weight
- Indication for device/ procedure
- Previous therapies tried for indications
- Clinical investigation specific examinations
    - Pain intensity as assessed by the VAS
    - Quality of life as assessed by the EQ5D
    - Disability as assessed by the ODI
    - Anxiety and Depression as assessed by the HADS
    - Pain Catastrophizing as assessed by the PCS
    - Medication Usage

Timing of visit	Activities at visit	Case Report Form
Screening/Baseline	• Subject assesses pre-trial pain levels, quality of life, disability, anxiety, depression, pain catastrophizing, and medication usage.	• VAS Form • EQ-5D Form • ODI Form • HADS Form • PCS Form • Medication Usage Form

6.4.2 SCS Trial

During the trial implant phase, SCS leads will be implanted in the dorsal column based on physician discretion. According to standard clinical practices performed in the United States (US), the trial phase will last around 3-7 days. At the start of the trial phase, patients will be programmed with the first ON/OFF stimulation pattern (30 second STIM ON, 90 seconds STIM OFF). Patients who do not achieve adequate pain relief (at least 50% reduction in back and/or leg VAS from baseline) within the first 3-4 days will be reprogrammed to a new ON/OFF stimulation pattern (5 seconds ON/ 15 seconds OFF). Patients, who still do not achieve adequate pain relief within 2 to 3 days from reprogramming, will be reprogrammed to a continuous mode of BurstDR™ stimulation and their trial evaluation will continue. These patients will be evaluated for an additional 2 days. At the end of the SCS trial, all subjects that experience at least 50% pain relief (according to average back and/or leg VAS) using one of the two microdosing burst stimulation paradigms will be considered further participation in the study. Patients who still do not achieve adequate

pain relief will be reprogrammed to a continuous mode of BurstDR™ stimulation and their trial evaluation will continue. These patients will be evaluated for an additional 2 days.

The following assessments and information will be collected at the SCS Trial visit

- Surgery Form
- Clinical investigation specific examinations
    - Programming Form

The following activities will be performed at the SCS Trial visit:

- SCS Trial Lead(s) Implant
- EPG Device programming

Timing of visit	Activities at visit	Case Report Form
SCS Trial	• SCS trial lead implant • EPG programming	• Surgery Form • Programming Form

6.4.3 End of Trial

During the End of Trial visit, subjects will complete the same questionnaires completed during the baseline visit. If the VAS score is < 50% of the VAS collected during the screening visit and is not using the two microdosing burst stimulation paradigms, the subject will exit the study. Subjects whose VAS score at the end of the trial is >50% of the VAS collected during the screening visit and is using one of the two microdosing burst stimulation paradigms, will be considered for permanent lead and IPG implantation.

The following assessments and information will be collected at the End of Trial visit:

- Clinical investigation specific examinations
    - Pain level as assessed by the VAS
    - Quality of life as assessed by the EQ-5D
    - Disability as assessed by the ODI
    - Anxiety and Depression as assessed by the HADS
    - Pain Catastrophizing as assessed by the PCS
    - Satisfaction as assessed by the PGIC
    - Medication usage;
    - Programming Form

Timing of visit	Activities at visit	Case Report Form
End of Trial	• Subject assess pain levels, quality of life, disability, anxiety, depression, pain catastrophizing, satisfaction, medication usage, and programming	• VAS Form • EQ-5D Form • ODI Form • HADS Form • PCS Form • PGIC Form • Medication Usage Form • Programming Form

6.4.4 Permanent Implant

Permanent implant will be performed according to standard clinical practice.

The following assessments and information will be collected at the Permanent Implant visit

- Surgery Form

The following activities will be performed at the Permanent Implant visit:

- SCS Permanent Lead(s) Implant
- IPG Implant

Timing of visit	Activities at visit	Case Report Form
SCS Permanent Implant	• SCS permanent lead implant • IPG implant	• Surgery Form

6.4.5 Activation

IPG will be programmed using burst stimulation according to standard programming techniques.

The following assessments and information will be collected at the Activation visit

- Clinical investigation specific examinations
  - Programming Form

Timing of visit	Activities at visit	Case Report Form
Activation	• IPG programming	• Programming Form

6.4.6 Scheduled Follow-ups

Subjects will be followed up for 6 months post-activation visit with follow-up assessments at 1, 3 and 6 months. During each visit, subjects will complete the same questionnaires completed during the end of trial visit.
The following assessments and information will be collected at the End of Trial visit:

- Clinical investigation specific examinations
  - Pain level as assessed by the VAS
  - Quality of life as assessed by the EQ-5D
  - Disability as assessed by the ODI
  - Anxiety and Depression as assessed by the HADS
  - Pain Catastrophizing as assessed by the PCS
  - Satisfaction as assessed by the PGIC
  - Medication usage;
  - Programming Form

Timing of visit	Activities at visit	Case Report Form
End of Trial	• Subject assess pain levels, quality of life, disability, anxiety, depression, pain catastrophizing, satisfaction, medication usage, and programming	• VAS Form • EQ-5D Form • ODI Form • HADS Form • PCS Form • PGIC Form • Medication Usage Form • Programming Form

6.5 Patient Reported Outcome (PRO) Measures

The Study Coordinator or designee will administer patient-reported outcome questionnaires. It is important the subject understands the meaning of all words and instructions in the questionnaires. The subject should be instructed to ask any questions about the questionnaires if further explanation is needed. Once the questionnaires are completed, the Study Coordinator or designee will review for completeness to verify that all questions have been answered according to the directions provided.

The following PRO measures will be collected according to the study requirements.

- Pain level as assessed by the VAS
- Quality of life as assessed by the EQ-5D
- Disability as assessed by the ODI
- Pain Catastrophizing as assessed by the PCS
- Anxiety and Depression as assessed by the HADS

6.6 Unscheduled Visits

An Unscheduled Visit is defined as any visit where an active study subject returns to the participating study site for medical care outside of a specified study visit. Unscheduled visits may include subjects returning to the office for an adverse event. The visit should be documented by completing the Unscheduled Visit Form and any other applicable forms (Adverse Event, Deviation, Death and/or Withdrawal Form.

6.7 Study Flow Chart

The Study Flow Chart and the Table 2 below summarize subject flow and requirements of this clinical investigation.

Figure 1: Study Flow Chart

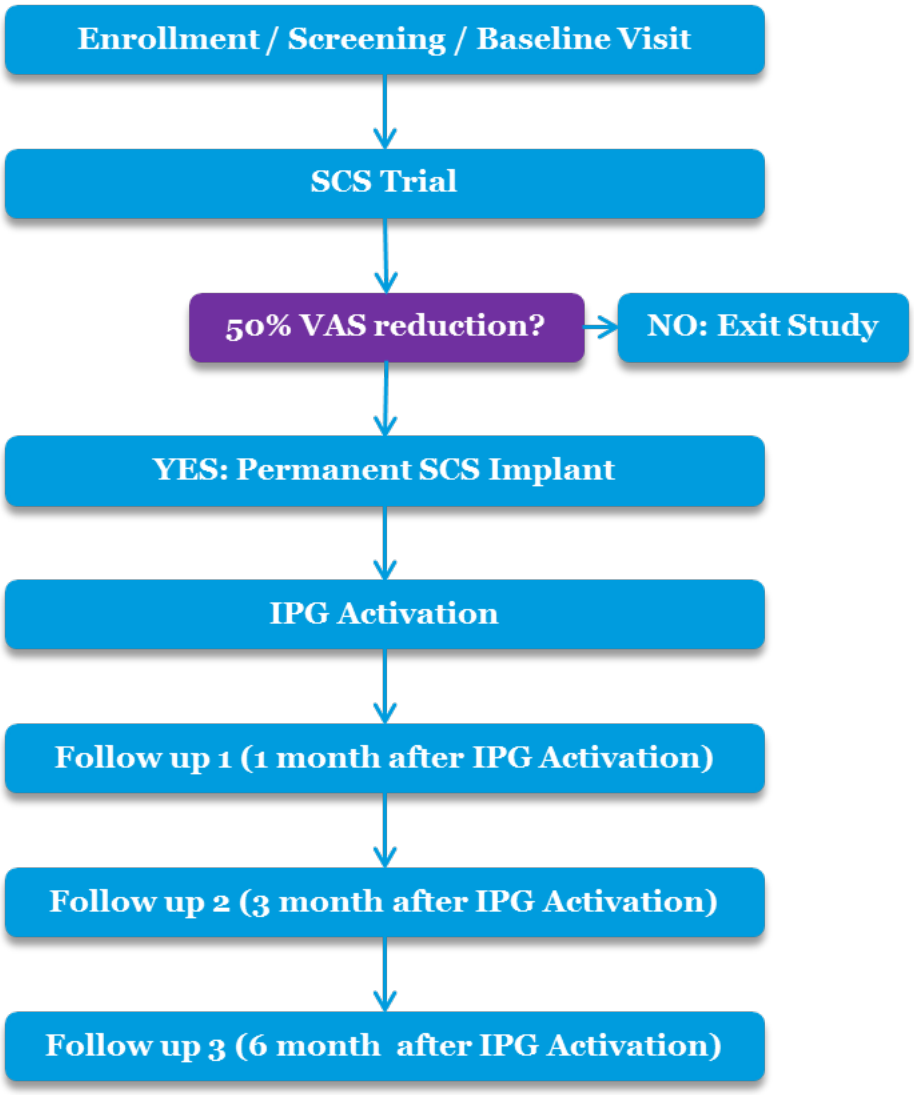


Table 2: List of all clinical investigation specific tests and procedures

Visit Study Activity	Enrollment	Baseline	SCS Trial	End of Trial	SCS Implant	Activation	Follow-up Visits*
Informed Consent Process	X						
Inclusion/Exclusion Criteria Screening	X						
VAS Assessment		X		X			X
Enrollment Form	X						
EQ-5D Assessment		X		X			X
ODI Assessment		X		X			X
HADS Assessment		X		X			X
PCS Assessment		X		X			X
PGIC Assessment				X			X
Trial System Implant			X				
Permanent System Implant					X	X	
Adverse Event	(X)	(X)	(X)	(X)	(X)	(X)	(X)
Deviation	(X)	(X)	(X)	(X)	(X)	(X)	(X)
Termination	(X)	(X)	(X)	(X)	(X)	(X)	(X)
Death	(X)	(X)	(X)	(X)	(X)	(X)	(X)

(X) If applicable
* Follow up visit assessments will be performed at months 1(30 ± 21 days), 3(90 ± 21 days) and (180 ± 21 days)

6.8 Description of Activities Performed by Sponsor Representatives

Trained sponsor personnel may perform certain activities to ensure compliance to the clinical investigational plan and may provide technical expertise.

Sponsor personnel may:

- Provide technical support to the Investigators during trial

Sponsor personnel will not:

- Perform the informed consent process
- Provide medical diagnosis or treatment to subjects
- Discuss a subject's condition or treatment with a subject without the approval and presence of a health care practitioner
- Independently collect clinical investigational data

While Sponsor representatives may perform these activities, the Principal Investigator remains responsible for ensuring all clinical investigation data is collected as required per CIP.

6.9 Subject Study Completion

Subject participation in the clinical investigation will conclude upon completion of the 6-month visit. Upon completion of subject participation in the clinical investigation, the subject will return to standard of care.

6.10 Subject Withdrawal

Subjects must be informed about their right to withdraw from the clinical investigation at any time and for any reason without sanction, penalty or loss of benefits to which the subject is otherwise entitled. Withdrawal from the clinical investigation will not jeopardize their future medical care or relationship with the investigator. Subjects will be requested to specify the reason for the request to withdraw. The investigator must make all reasonable efforts to retain the subject in the clinical investigation until completion of the clinical investigation.

The investigator may decide to withdraw a subject from the study at any time with reasonable rationale. The subject's future care will not be influenced by a decision, voluntary or otherwise, to withdraw from the study. All reasonable efforts should be made to retain the subject in the clinical study until completion of the study.

Reasons for subject's withdrawal include, but are not limited to:

- Subject refuses to continue participating in the study
- Subject does not meet the inclusion/exclusion criteria and does not require additional follow-up for safety reasons.
- Subject is deceased (cause must be documented)
- Subject's non-compliance
- Subject's participation is terminated by the PI or investigator, although the subject consented, since participation is no longer medically appropriate
- Subject is 'lost to follow up': Subject does not adhere to the scheduled follow up visits but has not explicitly requested to be withdrawn from the clinical study. (This does not apply to missed visits). Site personnel should at all times make all reasonable efforts to locate and communicate with the subject in order to achieve subject compliance to the scheduled follow up visits:
    - A subject will be considered 'Lost to Follow Up' after a minimum of 2 phone calls of a physician or delegate at the investigational site to the subject or contact. These 2 phone calls need to be documented in the subject's hospital records.
    - If these attempts are unsuccessful, a letter should be sent to the subject's last known address or general practitioner (GP) and a copy of this letter should be maintained in the subject's hospital records.

Note: If a subject misses one or more of the scheduled follow up visits (inclusive of the assigned visit windows), this will be considered as a missed visit. The subject may therefore still return for subsequent visits and will not be excluded from the study.

If a subject withdraws from the clinical study, the site will record the subject's reasons for withdrawal, on a Withdrawal CRF.

When subject withdrawal from the clinical study is due to an adverse event the subject will be followed until resolution of that adverse event or determination that the subject's condition is stable. The status of the subject's condition should be documented at the time of withdrawal.

The third follow up visit will be the final study visit. The subject will complete the questionnaires as in the previous follow up visit and will exit the study.

7 Statistical Considerations

The following section describes the statistical methods for the clinical investigation and justification of the design. Additional details on statistical analyses, including sensitivity analyses, poolability analyses, subgroup analyses and analysis of descriptive endpoint(s) may be maintained in a separate Statistical Analysis Plan (SAP).

7.1 Hypotheses

This study is an open label, multi-center, feasibility study. Thus, there is no requirement for a formal hypothesis testing. We do anticipate improvements in primary and secondary outcomes. The results obtained in this study will potentially be used to generate a level-1 evidence based study with formal statistical hypotheses testing.

7.1.1 Primary [Safety/Effectiveness] Endpoint Hypothesis(es)

7.1.1.1 Analysis Methodology

The primary analysis to assess improvement in pain intensity, using VAS, will be conducted using repeated measures ANOVA (RMANOVA). Post-hoc Tukey's pairwise comparisons will follow to determine specific differences between follow-up visits. Secondary analyses to assess improvements in quality of life, disability, anxiety, depression catastrophizing and satisfaction will be conducted using repeated measures ANOVA (RMANOVA) or the most appropriate statistical methods.

7.1.1.2 Sample Size Determination

We will enroll approximately 60 subjects in up to 4 study centers in the US. This study is a feasibility trial and no sample size calculations are required.

7.1.1.3 Missing Data

Missing data will be reported at each visit for each outcome. No imputations will be performed for missing data.

7.2 Justification of Clinical Investigation Design

This is a prospective, open label, multicenter feasibility trial to evaluate the therapeutic efficacy of different BurstDR™ microdosing patterns in patients with chronic intractable pain. Use of these new energy efficient stimulation parameters has the potential to prolong the battery life of a non-rechargeable, primary cell Implantable Pulse Generator (IPG). It also has the potential to improve patient convenience by decreasing the frequency with which the patient has to recharge a non-primary cell IPG. Thus, it is crucial to evaluate these potential energy efficient stimulation parameters in SCS eligible patients.

7.3 Multiplicity

All statistical tests will be performed with a type-1 error rate 0.05, unless otherwise stated. Family-wise error for RMANOVA will be addressed using Tukey's pairwise post-hoc comparisons.

7.4 Overall Sample Size

We will enroll up to 60 subjects.

7.5 Timing of Analysis

Interim analyses may be conducted after the end of trial visit.

7.6 Success Criteria

There are no formal success criteria. This is an observational study.

7.7 Interim Analysis

No formal interim analysis is planned for this study.

7.8 Statistical Criteria for Termination

There are no statistical criteria for termination of this clinical investigation.

7.9 Deviations from Statistical Plan

If any deviations from the original statistical plan occur, such deviations will be documented in the clinical study report or statistical report containing the analysis results.

8 Risks and Benefits

The risks associated with SCS can be found in the Instructions for Use. The study does not require any additional procedures over the standard of care. There are no additional risks introduced to study subjects.

8.1 Risks Associated with the Device Under Investigation

We do not foresee any additional risk, beyond those normally associated with SCS therapy, described below.

8.1.1 Anticipated Adverse Device Effects

In addition to those risks commonly associated with surgery, the following risks are associated with implanting or using this neurostimulation system for SCS:

- Undesirable changes in stimulation, which may be related to cellular changes in tissue around the electrodes, changes in electrode position, loose electrical connections, or lead failure
- Lead migration, causing changes in stimulation and/or reduced pain relief
- Epidural hemorrhage, hematoma, infection, spinal cord compression, or paralysis from placement of a lead in the epidural space
- Cerebrospinal fluid (CSF) leakage
- Paralysis, weakness, clumsiness, numbness, or pain below the level of the implant
- Persistent pain at the electrode or IPG site
- Seroma (mass or swelling) at the IPG site
- Infection of the lead extension at the exit zone during trial or infection of the IPG site
- Allergic or rejection response to implant materials
- Implant migration or skin erosion around the implant
- Anticipated adverse device effects
- Battery failure

These adverse events and adverse device effects are not specific to the study, but related to the approved SCS implant procedure.

8.1.2 Risks Associated with Clinical Investigation Assessments

There are no additional risks associated with the clinical investigation assessments beyond standard of care.

8.2 Risk Control Measures

Every possible effort will be taken to minimize the risks, including:

- Careful selection of experienced Investigators for the clinical investigation
- Adequate monitoring for each clinical investigation site
- Conducting the clinical investigation in accordance with the CIP, all applicable laws and regulations and any conditions of approval imposed by the appropriate IRB/EC or applicable regulatory authorities where the clinical investigation is performed
- Preparation of the SCS device and performance SCS implant procedure in accordance with the device IFUs
- Training of Investigators on the CIP

8.3 Possible interactions with concomitant treatments

There are no possible interactions with concomitant medical treatment and/or concurrent medical intervention beyond those associated with standard medical care using SCS.

8.4 Anticipated Benefits

There are no additional clinical benefits associated with the participation in this study beyond those anticipated with standard clinical SCS

8.5 Risk-to-Benefit Rationale

There are no additional risk-to-benefits associated with the participation in this study beyond those anticipated with standard clinical SCS.

9 Requirements for Investigator Records and Reports

9.1 Deviations from CIP

A deviation is defined as an instance(s) of failure to follow, intentionally or unintentionally, the requirements of the CIP. The investigator should not deviate from the CIP.

In some cases, failure to comply with the CIP may be considered failure to protect the rights, safety and well-being of subjects; such non-compliance exposes subjects to unreasonable risks. Examples: failure to adhere to the inclusion/exclusion criteria, failure to perform safety assessments intended to detect adverse events. Investigators should seek to minimize such risks by adhering to the CIP.

The PI must maintain accurate, complete, and current records, including documents showing the date of and reason for each deviation from the CIP. Relevant information for each deviation will be documented as soon as possible on the applicable CRF. The site will submit the CRF to the Sponsor.

The PI is required to adhere to local regulatory requirements for reporting deviations to IRB/EC.

Under emergency circumstances, deviations from the CIP to protect the rights, safety and well-being of subjects may proceed without prior approval of the Sponsor and the IRB/EC. Such deviations shall be documented and reported to the Sponsor and the IRB/EC as soon as possible.

9.2 Safety Reporting

Safety surveillance within this study and the safety reporting performed both by the investigator and Sponsor starts as soon as the procedure begins. This is defined as from the time the [dilator/device delivery system has been introduced into the body.

The safety surveillance and the safety reporting will continue until the last investigational visit has been performed, the subject is deceased, the subject/investigator concludes his participation into the clinical investigation or the subject withdrawal from the clinical investigation.

All adverse event data including deaths and device deficiency data (if applicable) will be collected throughout the clinical investigation and will be reported to the Sponsor on a CRF.

Adverse events will be monitored until they are adequately resolved or the subject has ended his/her participation in the trial, whichever comes first. The status of the subject's condition should be documented at each visit.

The investigator will report the event to the IRB/EC per their reporting requirements.

Reportable events to sponsor are considered:

- All Adverse Device Effects
- All Serious Adverse Events (whether or not the event is considered device or procedure related and regardless the randomization group)
- (if applicable) device deficiencies, that 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

All events mentioned above will be reported to the Sponsor, as soon as possible, but no later than 72 hours of first learning of the event.

Reportable events shall be submitted to the Sponsor. The Sponsor will ensure that all applicable events and device deficiencies are reported to the relevant authorities as per regulations. The sites should notify the Sponsor of reportable adverse events.. Additional information may be requested by the Sponsor in order to support the reporting of AEs to regulatory authorities. The investigator must notify the IRB/EC, if appropriate, in accordance with national and local laws and regulations, of the AEs reported to the Sponsor. All adverse events will be reported as per applicable regulatory requirements.

9.2.1 Subject Death

All subject deaths are to be documented and reported to the sponsor within 72 hours after becoming aware of the event.
All subjects' deaths should be documented using the "Death Form" and a "Withdrawal Form".

9.2.2 Complaints

During the study, the investigator will be responsible for reporting all complaints. A complaint is defined as any written, electronic or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness or performance of a device after it is released for distribution.

If the complaint involves an AE, the investigator must complete an AE CRF, including the information on the complaint and submit to Abbott as soon as possible.

Should a subject death be caused by the Abbott device or the device contributed to the death, the investigator should complete a Form 3500A (MedWatch) and submit to Abbott and the FDA within 10 days after becoming aware of the event.

9.3 Source records

Source documents will be created and maintained by the investigational site team throughout the clinical investigation. The data reported on the CRFs will be derived from, and be consistent with, these source documents, and any discrepancies will be explained in writing.

The following data can be recorded directly in the CRFs:

- Pain VAS scores
- EQ-5D scores
- ODI scores
- HADS scores
- PCS scores
- PGIC scores
- Medication usage form
- Programming form
- Adverse events form

9.4 Records Retention

The Sponsor and the Principal Investigators will maintain the clinical investigation documents as required. Measures will be taken to prevent accidental or premature destruction of these documents. The Principal Investigator or the Sponsor may transfer custody of records to another person/party and document the transfer at the investigational site or the Sponsor's facility, as appropriate.

These documents must be retained by the investigational site for a period of 2 years after the conclusion of the clinical investigation and made available for monitoring or auditing by the Sponsor's representative or representatives of the applicable regulatory agencies.

All original source documents must be stored for the maximum time required by the regulations at the hospital, research institute, or practice in question. If original source documents can no longer be maintained at the site, the investigator will notify the Sponsor.

10 Clinical Data Handling

The Sponsor will be responsible for the data handling. The Sponsor and/or its affiliates will be responsible for compiling and submitting all required reports to governmental agencies. Data will be analyzed by the Sponsor and may be transferred to the Sponsor's locations worldwide and/or any other worldwide regulatory authority in support of a market-approval application.

During this study the following documents will be produced:

- Patient's ICF
- Enrollment case report form
- Inclusion/Exclusion case report form
- VAS case report form
- EQ-5D case report form
- ODI case report form
- HADS case report form
- PCS case report form
- PGIC case report form

- Medication usage form
- Programming form
- Adverse events form

10.1 Protection of Personally Identifiable Information

Abbott respects and protects personally identifiable information collected or maintained for this clinical investigation. The privacy of each subject and confidentiality of his/her information will be preserved in reports and when publishing any data. Confidentiality of data will be observed by all parties involved at all times throughout the clinical investigation. All data will be secured against unauthorized access.

10.2 Data Management Plan

A Data Management Plan (DMP) will describe procedures used for data review, database cleaning, and issuing and resolving data queries. If appropriate, the DMP may be updated throughout the clinical investigation duration. All revisions will be tracked and document controlled.

Subject data will be captured in a validated electronic data capture (EDC) system hosted by the Sponsor. CRF received data for the clinical investigation will be entered by trained Abbott personnel. An electronic audit trail will be used to track any subsequent changes of the entered data.

10.3 Document and Data Control

10.3.1 Traceability of Documents and Data

The investigator will ensure accuracy, completeness legibility and timeliness of the data reported to the Sponsor on the CRFs and in all required reports.

10.3.2 Recording Data

The CRFs will be signed and dated by the authorized site personnel. Any change or correction to data reported on a paper CRF will be dated, initialed and explained if necessary, and will not obscure the original entry.

11 Monitoring

It is the responsibility of the Sponsor to ensure the clinical investigation is conducted, recorded and reported according to the approved CIP, subsequent amendment(s), applicable regulations and guidance documents.

Centralized monitoring will occur through routine internal data review. This monitoring is designed to identify missing and inconsistent data, data outliers, and potential CIP deviations that may be indicative of site non-compliance. On-site monitoring may occur at the discretion of the Sponsor.

12 Compliance Statement

12.1 Statement of Compliance

This clinical investigation will be conducted in compliance with the most current regional and local laws and regulations. Principles of Good Clinical Practice will be followed as based on the most current version of the World Medical Association (WMA) Declaration of Helsinki.

The investigator will sign a Clinical Trial Agreement and agrees to be compliant with it. The investigator will not start enrolling subjects or requesting informed consent from any subject prior to obtaining IRB/EC approval and relevant Regulatory Authority approval, if applicable, and authorization from the Sponsor in

writing for the clinical investigation. If additional requirements are imposed by the IRB/EC or relevant Regulatory Authority, those requirements will be followed. If any action is taken by an IRB/EC or a relevant Regulatory Authority with respect to the clinical investigation, that information will be forwarded to the Sponsor.

As the Sponsor, Abbott has taken up general liability insurance in accordance with the requirements of the applicable local laws. An appropriate Abbott country representative will be utilized to understand the requirements for the type of insurance that will be provided for subjects, and such information will be incorporated into the site informed consent, as applicable. If required, additional subject coverage or a clinical investigation specific insurance will be provided by the Sponsor.

12.2 Quality Assurance Audits and Regulatory Inspections

The investigator and/or delegate should contact the Sponsor immediately upon notification of a regulatory authority inspection at the site. A monitor or designee will assist the investigator and/or delegate in preparing for the audit. The Sponsor may perform quality assurance audits, as required.

The Principal Investigator or institution will provide direct access to source data during and after the clinical investigation for monitoring, audits, IRB/EC review and regulatory authority inspections, as required. The Principal Investigator or institution will obtain permission for direct access to source documents from the subject, hospital administration and national regulatory authorities before starting the clinical investigation.

12.3 Repeated and Serious Non-Compliance

In the event of repeated non-compliance or a one-time serious non-compliance, as determined by the Sponsor, a monitor or designee will attempt to secure compliance by one or more of the following actions:

- Visiting the investigator,
- Contacting the investigator by telephone,
- Contacting the investigator in writing,
- Retraining of the investigator.

If an investigator is found to be repeatedly non-compliant with the signed agreement, the CIP or any other conditions of the clinical investigation, the Sponsor will either secure compliance or, at its sole discretion, terminate the investigator's participation in the clinical investigation. In case of termination, the Sponsor will inform the responsible regulatory authority, as required, and ensure that the IRB/EC is notified, either by the Principal Investigator or by the Sponsor.

13 Suspension or Premature Termination of the Clinical Investigation

The Sponsor reserves the right to terminate the clinical investigation at any stage, with appropriate written notice to the investigators, IRB/ECs and relevant Regulatory authorities, if required.

A Principal Investigator, IRB/EC or regulatory authority may suspend or prematurely terminate participation in a clinical investigation at the investigational sites for which they are responsible. The investigators will follow the requirements specified in the Clinical Trial Agreement.

If suspicion of an unacceptable risk to subjects arises during the clinical investigation or when so instructed by the IRB/EC or regulatory authority, the Sponsor may suspend the clinical investigation while the risk is assessed. The Sponsor will terminate the clinical investigation if an unacceptable risk is confirmed. If the Sponsor completes an analysis of the reasons for the suspension, implements the necessary corrective actions, and decides to lift the temporary suspension, the Sponsor will inform the Principal Investigators, IRB/EC, or regulatory authority, where appropriate, of the rationale, providing

them with the relevant data supporting this decision. Approval from the IRB/EC or regulatory authority, where appropriate, will be obtained before the clinical investigation resumes. If subjects have been informed of the suspension, the Principal Investigator or authorized designee will inform them of the reasons for resumption.

If the Sponsor suspends or prematurely terminates the clinical investigation at an individual investigational site in the interest of safety, the Sponsor will inform all other Principal Investigators.

If suspension or premature termination occurs, the Sponsor will remain responsible for providing resources to fulfill the obligations from the CIP and existing agreements for following up the subjects enrolled in the clinical investigation, and the Principal Investigator or authorized designee will promptly inform the enrolled subjects at his/her investigational site, if appropriate.

14 Clinical Investigation Conclusion

The clinical investigation will be concluded when:

- All sites are closed AND
- The final report has been provided to investigators or the Sponsor has provided formal documentation of clinical investigation closure.

15 Publication Policy

Publications or presentations of clinical investigation methods or results will adhere to Abbott's publication policy, which is based on Good Publication Practices and International Committee of Medical Journal Editors (ICMJE) guidelines. A copy of the policy will be provided upon request of the investigator.

Appendix A: CIP Revisions

Procedure for CIP Amendments

This CIP may be amended as appropriate by the Sponsor. Rationale will be included with each amended version in the revision history table below. The version number and date of amendments will be documented.

The acknowledgement of the amended CIP by the Coordinating Investigator (if applicable) and the Principal Investigators will be collected on the signature pages.

IRB/EC and relevant Regulatory Authorities, if applicable, will be notified of amendments to the CIP.

Revision History

Amendment Number	Version	Date	Rationale	Details
Not Applicable	VA	ddMMMyyyy	First release of CIP	NA

Appendix B: Definitions

Non-study Specific Definitions

Adverse Event (AE)
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 under clinical investigation.

This definition includes events related to the investigational medical device or the comparator.
This definition includes events related to the procedures involved.

Serious Adverse Event (SAE)
An adverse event that led to:

- Death
- A serious deterioration in the health of the subject, that either resulted in:
  - A life-threatening illness or injury OR
  - A permanent impairment to a body structure or a body function OR
  - An in-patient or prolonged hospitalization OR
  - A medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function OR
- Fetal distress, fetal death or a congenital abnormality or birth defect

A planned hospitalization for a pre-existing condition, or a procedure required by the CIP is not considered a serious adverse event.

Adverse Device Effect (ADE)
An adverse event related to the use of an investigational medical device.

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.

This definition includes any event resulting from the use error or from intentional misuse of the investigational medical device.

Serious Adverse Device Effect (SADE)
Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.

Unanticipated Adverse Device Effect (UADE)
As defined in 21 CFR §812.3, unanticipated adverse device effects (UADE) are defined as any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the CIP or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

Anticipated Serious Adverse Device Effect (ASADE)
A serious adverse device effect which by its nature, incidence, severity or outcome has been previously identified in the risk analysis report.

Unanticipated Serious Adverse Device Effect (USADE)
A 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.

Device Deficiency (DD)
A Device Deficiency is defined as an inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance. Device deficiencies include malfunctions, use errors and inadequate labeling.

Vulnerable Subject
Vulnerable subject is defined as individual whose willingness to volunteer in a clinical investigation could be unduly influenced by the expectation, whether justified or not, of benefits associated with participation or of retaliatory response from senior members of a hierarchy in case of refusal to participate.
EXAMPLE Individuals with lack of or loss of autonomy due to immaturity or through mental disability, persons in nursing homes, children, impoverished persons, subjects in emergency situations, ethnic minority groups, homeless persons, nomads, refugees, and those incapable of giving informed consent. Other vulnerable subjects include, for example, members of a group with a hierarchical structure such as university students, subordinate hospital and laboratory personnel, employees of the Sponsor, members of the armed forces, and persons kept in detention.

Appendix C: Bibliography

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Appendix D: Case Report Form

Case report forms will be kept under a separate cover and are available upon request.

Appendix F: Informed Consent Form

Study specific informed consent will be kept under a separate cover and is available upon request.