Abbott	Clinical Investigation Plan Cover Page

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DELIVERY
EValuating Anatomic vErsus TaRgeted Lead Placement for BurstDR TherapY During the Trial (DELIVERY)
Study Document No: SJM-CIP-10116
Version [C]
Date: 4 October, 2019

Sponsor

Abbott
The Corporate Village
Da Vincilaan 11-boxF1
1935 Zaventem, Belgium

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6901 Preston Road
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DELIVERY
Randomized, Controlled, Single Blind, Prospective, Multicenter Study Evaluating Anatomic versus Targeted Lead Placement for BurstDR Therapy During the Trial Evaluation Period.
CRD_767
Study Document No: SJM-CIP-10116
Version [C]
Date: 21-JUN-2017
Clinical Investigation Plan (CIP)

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[redacted]

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:

Table of Contents

1 Introduction

This document is a clinical investigation plan (CIP) for the clinical investigation of the SJM™ Invisible Trial System with market-approved lead(s). This clinical investigation is intended to evaluate anatomic versus targeted lead placement for BurstDR™ therapy during the trial evaluation period.

This clinical investigation is sponsored by Abbott (ABT).

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.

2 Background and Justification for Clinical Investigation

Spinal cord stimulation (SCS) reduces pain and improves function and quality of life for patients with chronic, intractable pain[1]. Typically, patients, who are candidates for SCS have failed other treatment options, are recommended by their physician to participate in a SCS trial evaluation period with percutaneously implanted leads powered by an external generator. The trial evaluation period can span from 3 to 30 days (or more) depending on the patient needs, physician's discretion, and regional reimbursement requirements. Successful trial evaluation of the SCS device is contingent upon adequate pain relief and/or functional improvements as assessed by the patient and the physician. Standard of care for "successful" trial evaluations is driven by reimbursement in most countries, which typically includes, but may not be limited to, patient assessment of 50% pain relief and willingness to proceed to a permanent implantable pulse generator (IPG).

Until recently, SCS trials and permanent systems delivered tonic stimulation (See Figure 1), which delivers a stream of pulses at consistent amplitude, pulse width and frequency. Tonic stimulation produces paresthesia, a tingling sensation, in the areas of stimulation coverage. Outcomes during the trial evaluation are thought to predict long-term success with therapy, though evidence in the literature is sparse due to poor reporting of trial experiences. Rates of successful trial evaluations leading to permanent implant vary in the literature (41% to 71% or more).[2,3]

Recently, BurstDR™ stimulation mode was approved in Europe and the US for use in permanently implanted systems (CE mark: March 2014 and PMA: October 2016). BurstDR™ programmable parameters include (A) the burst train, (B) the time of onset of the burst train to the time of onset of the next burst train (burst rate), and (C) the rate of pulses within each train (intra-burst rate) (See Figure 2). While BurstDR™ features a group of pulses that are repeated in an on/off pattern, it is unlike cycle mode because it mimics the natural signaling of burst neurons utilizing closely spaced stimuli. The amplitudes used for BurstDR™ stimulation are reported to be significantly lower than those traditionally used for tonic stimulation which results in pain suppression that is generally sensation free (e.g., does not produce paresthesia).

The St. Jude Medical™ Invisible Trial System, capable of delivering both tonic and BurstDR™ stimulation, was approved (CE mark: June 2015 and PMA: July 2015). The Invisible Trial System consists of an External Pulse Generator (EPG) and a Patient Controller. The EPG is smaller than other systems on the market and is designed to be bandaged to the patient's back, which eliminates access to connector wires to reduce dislodgement and lead migrations. Furthermore, the EPG is controlled wirelessly via Bluetooth™ low energy technology with the Patient Controller.

Lead placement for BurstDR™ has proceeded to use temporary tonic stimulation such that the sensory qualities of tonic programming (paresthesias) can be used to elicit feedback from patients and ensure the leads are properly placed and programmed. Because BurstDR™ results in sensation-free therapy for most patients, it has been proposed that anatomic placement of the leads could result in effective therapy while

reducing procedure times during both the trial evaluation and permanent system implants. No studies have investigated this procedural variation, to date.

Additionally, there is no published literature for the use of BurstDR™ or the Invisible Trial System during the trial evaluation period, and, thus, no quantitative examination of the rate of successful qualification for permanent implant when this therapy mode and device is used during the trial evaluation period.

Therefore, the aims of the proposed clinical investigation are to evaluate the qualification rate of BurstDR™ in conjunction with the Invisible Trial System during the trial evaluation period for BurstDR™ therapy via anatomic versus targeted lead placement.

Figure 1: tonic pattern

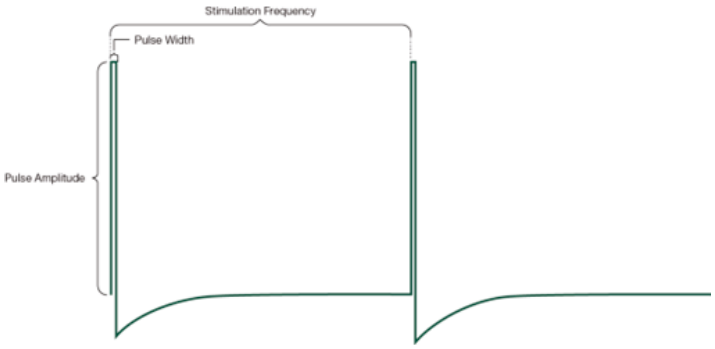
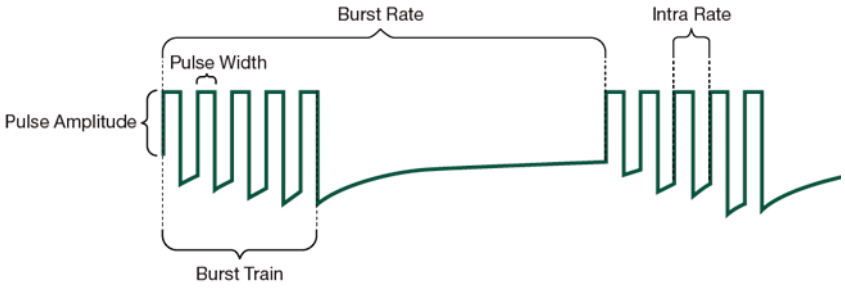


Figure 2: BurstDR™ pattern



3 Device(s) Under Investigation

3.1 Identification and Description of the Devices under investigation

3.1.1 Identification

In this clinical investigation, the SJM™ Invisible Trial System is being used and consists of an External Pulse Generator (EPG), a Clinician Programmer and a Patient Controller. The components communicate with each other via wireless Bluetooth™ communication.

Table 1: Identification of Devices under Investigation

Device name	Model/Type	Manufacturer	Region/ Country	Investigational or Market Released
SJM™ Invisible Trial System	3599, 3032	SJM	EMEA/ANZ/CA/US	Market Released
Clinician Programmer (iPad Mini)	3872	SJM	EMEA/ANZ/CA/US	Market Released
Patient Controller (iPod Touch)	3873	SJM	EMEA/ANZ/CA/US	Market Released

3.1.2 Device Description and Intended Purpose

The SJM™ Invisible Trial System is indicated for use in subjects as an aid in the management of chronic, intractable pain of the trunk and/or limbs and is used during the trial system evaluation period. It consists of an External Pulse Generator (EPG), a Clinician Programmer and a Patient Controller. The components communicate with each other via wireless Bluetooth™ Low Energy (BLE) communication.

3.1.3 Device Handling and Storage

The devices used during this clinical investigation are commercially available and will be handled and stored according to the applicable product manuals and standard site practices.

3.2 Devices Accountability

The devices used during this clinical investigation are commercially available and device accountability is not required.

4 Clinical Investigation Design

4.1 Clinical Investigation Design

This is a randomized, controlled, single blind, multi-center clinical investigation comparing success rates for anatomically placed leads to conventional, targeted lead placement for BurstDR™ during the trial evaluation period with the SJM™ Invisible Trial System. Subjects will be blinded to treatment group and randomized in a 1:1 ratio as follows:

- Group 1 (AB): anatomic lead placement followed by BurstDR™ stimulation during an initial trial evaluation period
- Group 2 (TB): targeted lead placement followed by BurstDR™ stimulation during an initial trial evaluation period

If the subject qualifies for permanent system implant as defined in section 4.3.1 after the initial trial evaluation period, the subject will exit the clinical investigation and continue their treatment per the physician's standard of care. Subjects who do not qualify for permanent system implant as defined in section 4.3.1 after the initial trial evaluation period may participate in an extended trial evaluation period, per physician discretion, during which they will be programmed with tonic stimulation. Subjects continuing to an extended trial evaluation period will be followed through the completion of the extended trial period. At the end of the extended trial evaluation period, subjects will exit the clinical investigation.

The randomization diagram (Figure 3) and the study flow chart (Figure 4) are shown below.

Figure 3: Randomization Diagram

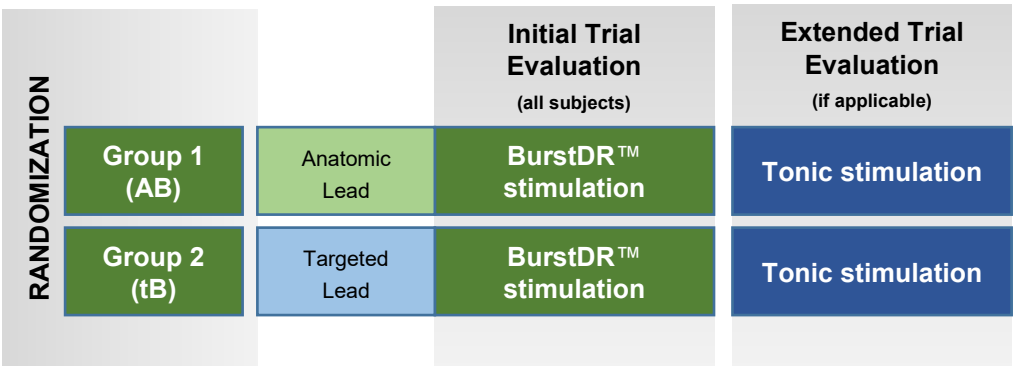
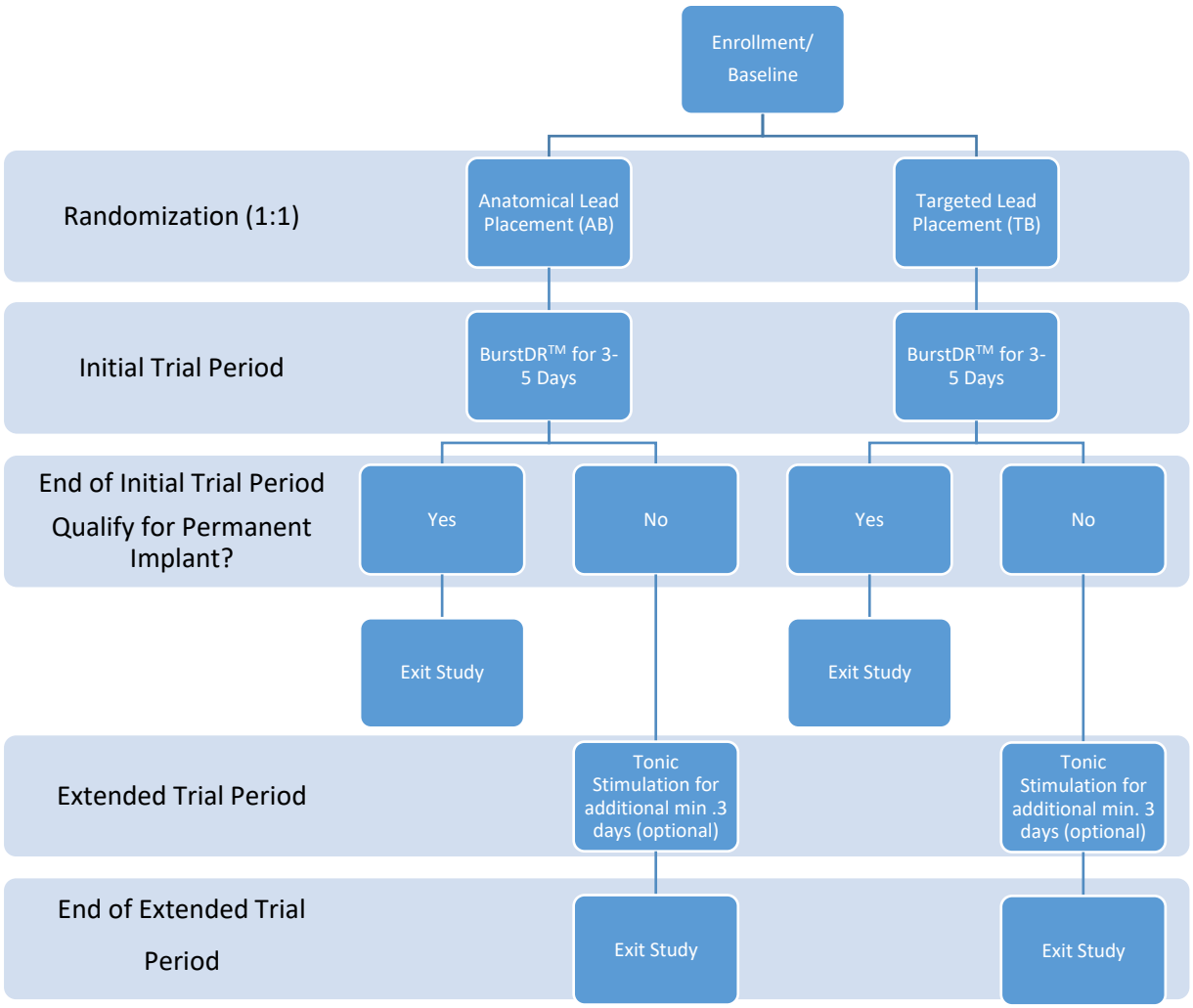


Figure 4: Study Flow Chart



[redacted]

4.2 Objectives

4.2.1 Primary Objective

The primary objective in this clinical investigation is to demonstrate that the qualification rate with anatomic lead placement is non-inferior to the qualification rate with targeted lead placement (tonic paresthesia guided) for the BurstDR™ stimulation trial evaluation period.

4.2.2 Secondary Objective

The secondary objective of this clinical investigation is to establish a higher rate of physician preference for anatomic lead placement procedure.

4.3 Endpoints

There is one primary endpoint and one secondary endpoint in this clinical investigation.

4.3.1 Primary Endpoint

The primary endpoint is the qualification rate for permanent system implant at the end of the initial trial evaluation period.

Qualification for permanent system implant is defined by a composite in which a subject meets all of the following conditions:

- >50% patient reported pain relief (PRP) at the end of the trial evaluation
- Trial evaluation period lasted for a minimum of 3 days
- Physician recommends subject for permanent system implant
- Subject reports a willingness to pursue a permanent system implant

Subjects are not qualified for permanent system implant if they meet **both** of the following:

- ≤50% PRP (patient reported pain relief) at the end of the trial evaluation
- Trial evaluation period lasted for a minimum of 5 days

4.3.2 Secondary Endpoint

The secondary endpoint is the rate of physician preference for anatomic placement versus targeted placement at the end of the study.

4.3.3 Descriptive Endpoint(s)

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

1. Overall procedure time (in-room to out-room), implant procedure time (needle-in to needle-out), and total time of intra-operative fluoroscopy exposure for each randomized group and stratified by number of leads and lead type (permanent lead or temporary lead).
2. Programming time required for each randomized group.
3. Change from pre-implant Numerical Rating Scale (NRS) in each randomized group to end of initial trial evaluation period and to the end of the extended trial evaluation period, as applicable.
4. Number of subjects in each randomized group who have affirmative assessment for each of the independent criteria required for qualification for permanent implant.

[redacted]

5. Proportion of subjects in each randomized group who do not qualify for permanent implant, however do proceed with permanent implant per physician discretion.
6. Time from trial system implant to >50% PRP measured by the number of days (also known as "wash-in period").
7. Rate of serious adverse device effects (SADE) in each group.
8. Number and proportion of meaningful lead migrations* during the initial trial evaluation periods by treatment group.
9. Number and proportion of meaningful lead migrations* during the initial trial evaluation period in subjects who have a temporary trial lead implant compared to subjects who have a permanent trial lead implant.
10. Clinician assessment of anesthesia related difficulty (assessed primarily in the procedure room for the trial) on a 5 point likert scale for each randomized group.
11. Clinician assessment of lead placement difficulty on a 5 point likert scale for each randomized group.
12. Clinician affinity (liking) for lead placement technique at the end of the trial implant procedure.
13. Permanent system qualification rate at the end of extended trial period.

*A meaningful lead migration is defined as a lead migration resulting in the inability to program for therapeutic response.

4.4 Study Population

The intended population for this clinical investigation is patients over the age of 18 years that have chronic, intractable pain of the trunk and/or lower limbs and have been recommended by a physician for spinal cord stimulation therapy.

4.4.1 Inclusion Criteria

To participate in this clinical investigation, the patient must meet all of the following inclusion criteria:

1. Patient indicated for SCS therapy in accordance with the approved labeling.
2. Patient's pain profile indicates appropriate lead placement would be at one or more levels from T7 to T10, to achieve pain coverage.
3. Patient has a baseline score on the NRS ≥6 over the past 24 hours for 'average overall pain' specific to the area(s) of chronic pain that will be treated with spinal cord stimulation.
4. Patient is considered by the Study Investigator as a candidate for implantation of a spinal cord stimulator system according to the system Instructions for Use.
5. Patient is >18 years of age at the time of enrollment.
6. Patient is willing to adhere to the study requirements, including compliance with and completion of all study visits.
7. Patient has signed and received a copy of the EC/IRB approved informed consent.

4.4.2 Exclusion Criteria

Patients are not eligible for clinical investigation participation if they meet any of the following exclusion criteria:

1. Patient currently has a spinal cord stimulation system implanted.
2. Patient has previously failed a spinal cord stimulation therapy (either trial system evaluation or permanent system implant).
3. Patient has a primary diagnosis of Peripheral Vascular Disease (PVD), Angina Pectoris, or Chronic Migraine.
4. Patient is scheduled to undergo an on-the-table trial evaluation (aka all-in-one procedure)
5. Patient is scheduled to be implanted with (a) surgical paddle trial lead(s).

6. Patient is currently participating in another clinical investigation with an active treatment arm.
7. Patient is unable to read and/or write.

5 Procedures

Approval from the Sponsor must be received prior to initiating study procedures.

Patients are considered enrolled in the study and become subjects from the moment the patients have provided written Patient Informed Consent.

Enrolled subjects will be randomized before any study procedure is performed. Subjects will undergo a trial system implant procedure with lead placement according to their randomization group. Follow-up of subjects will be according to the site's practice. Upon completion of the initial trial evaluation period, the subject will be considered to have completed the study if he/she qualifies for permanent implant. In case the subject does not qualify for permanent implant, the trial evaluation period may be extended, per physician discretion. The extended trial evaluation period will continue for an additional minimum of 3 days and will end per standard of care. Subjects who do not choose to enter the extended trial evaluation period will exit the study.

The Principal Investigator should arrange for appropriate care of subjects following study completion.
The Principal Investigator is responsible for ensuring all clinical investigation data are collected as required per CIP scheduled procedures.

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

5.1 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.

5.2 Screening

The Principal Investigator or delegated study personnel is responsible for screening all potential patients to determine patient eligibility for the clinical investigation.

If a patient meets all inclusion criteria and does not meet any of the exclusion criteria, he/she is eligible for the clinical investigation.

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.

5.3 Point of Enrollment

Patients are considered enrolled in the clinical investigation and become subjects from the moment the patients have provided written Patient Informed Consent.

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.

5.4 Scheduled Procedures

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

The list of clinical investigation specific tests and procedures (Table 2) below summarize visit flow and requirements of this clinical investigation.

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

Visit / Study Activity	Enrollment / Baseline	Trial System Implant (Initial Trial Evaluation Period Start)	End of Initial Trial Evaluation Period Begin Extended Trial Evaluation (If applicable)	End of Extended Trial Evaluation Period (if applicable)	Unscheduled Visit
Informed Consent	X				
Subject Eligibility	X				
Demographics, Pain History & Diagnosis	X				
Numerical Rating Scale	X		X	(X)	

PROMIS-29	X				
Pain Catastrophizing Scale	X				
Patient satisfaction and PRP			X	(X)	
Randomization	X	(X)			
Implant procedure and system data		X			
Patient Trial Diary		X	X	(X)	
Email Programming Details		X	X	(X)	(X)
Stimulation Assessment		X	X	(X)	(X)
Qualify for permanent implant			X	(X)	
Reason for Visit					X
Procedure Time		X			
Programming Time		X			(X)
Subject's Feedback			X		
Clinician Assessment		X			
Physician's Preference			X*		
Imaging		X	X	(X)	(X)
Lead Location		X	X	(X)	(X)
SADEs, SAEs ADEs		(X)	(X)	(X)	(X)
Deviation(s)	(X)	(X)	(X)	(X)	(X)
Withdrawal	(X)	(X)	(X)	(X)	(X)
Death	(X)	(X)	(X)	(X)	(X)

(X) If applicable
* only after last subject's last End of Initial Trial Period Visit- for a single site

5.4.1 Enrollment/Baseline Visit

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

- Demographics, pain history, pain diagnosis
- Numerical Rating Scale (NRS)
- Patient Reported Outcomes Measurement Information System-29 (PROMIS-29)
- Pain Catastrophizing Scale (PCS)
- Deviations (if applicable)
- Withdrawal (if applicable)
- Death (if applicable)

5.4.2 Randomization and Blinding

Randomization may occur at the end of the baseline visit or just prior to surgery for trial system implant (Initial Trial Evaluation Period Start) Visit.

Subjects will be randomized (1:1) using random permuted blocks of varying length and stratified by site. Subjects will be blinded to treatment group and treated in two groups as follows:

1. Group 1 (AB): anatomic lead placement followed by BurstDR™ stimulation during initial trial evaluation period
2. Group 2 (TB): targeted lead placement followed by BurstDR™ stimulation during initial trial evaluation period

Randomization assignment will be communicated to the site via the Randomization Application available in the EDC Site Portal.

Regardless of sedation, subjects will not be able to distinguish what implant technique (anatomic or targeted) is utilized without intimate knowledge of SCS programming, and with standardizing subject

interactions, the subjects will remain blinded to the treatment group. Implanting physicians and surgical support staff must follow the specific guidelines for the lead placement techniques and therefore cannot be blinded, but will be provided with a standardized script to assist with subject interaction as a way to minimize the risk of disclosing randomization assignments. Additionally, sites will be instructed to schedule study visits to restrict study subjects from being in the clinic at the same time, which aims to minimize subject to subject communication. Prior to study exit and before being unblinded, subjects will be asked about their memory for intra-operative testing as an assessment of the blind. Intra-operative testing is the key distinguishing feature between the techniques, so assessment of memory for experience will help to establish the status of the blind for each subject.

A Blinding Plan will be maintained separately which will include a listing of all parties involved in the study to manage workflow and identification of blinded and unblinded information.

5.4.3 Trial System Implant (Initial Trial Evaluation Period Start)

Record the required information on the applicable CRF:

- Implant procedure and system data
- Stimulation assessment
- Clinician assessment
- Procedure time
- Programming time
- Adverse events (if applicable)
- Deviations (if applicable)
- Withdrawal (if applicable)
- Death (if applicable)

Upload and attach the following documentation to the applicable CRF:

- Images

[redacted]

The subject will complete a Patient Trial Diary once a day utilizing an application located on the Patient Controller during the trial evaluation period. The subject will record areas of pain, stimulation therapy goals and percentage of pain relief in the diary. At the end of the trial evaluation period, the End of Trial Summary report will be submitted to the sponsor.

The following section of the protocol provides a guideline for surgical implantation and programming of the trial evaluation system.

Lead Placement Technique:

Anatomic lead placement (Randomization Group 1)

Physicians may implant one or two leads as per their preference/standard of care at the site. Guidance for placement of the leads is provided below:

Placement of 1 lead:

- Lead 1 – Place lead tip at the rostral end of T8 segment
- No tonic mapping/confirmation required
- Confirm position using fluoroscopy (X-ray) and reposition lead if needed

[redacted]

Placement of 2 leads:

- Lead 1 – Place lead tip at the rostral end of T8 segment
- Lead 2 – Place lead tip at the rostral end of T9 segment
- No tonic mapping/confirmation required
- Confirm position using fluoroscopy (X-ray) and reposition lead if needed

Targeted Lead Placement Technique (Randomization Group 2)

- Physicians may implant one or two leads as per their preference/standard of care at the site
- Utilize the standard lead placement technique as per standard of care for BurstDR stimulation.
- Position lead(s) at the appropriate thoracic segment in the epidural space – dictated by pain coverage required by patient
- Confirm adequate coverage of pain areas using tonic stimulation
- Adjust lead position as needed to attain adequate coverage of pain areas

[redacted]

Anchoring Technique:
Securing the SCS leads during this investigation is critical to evaluate the anatomic versus targeted lead placement through the course of the trial period. Acceptable methods to secure the leads include suturing and utilization of anchors. Methods that are not allowed during this investigation include include steri-strips and pre-manufactured bandages.

Postoperative Programming:
After the trial system implant procedure is complete, all subjects will be programmed with BurstDR™ stimulation programs by trained personnel and/or an Abbott representative using the Clinician Programmer. Subjects will be given a Patient Controller and instructed how to use the Patient Controller to adjust stimulation as needed to produce the best results and to complete the Patient Trial Diary daily during the trial evaluation period

[redacted]

During the initial trial evaluation period, the stimulation parameters may be optimized. If this is needed, the subject would return to the clinic for adjustments to the programming parameters. Study personnel performing programming activities will utilize the same methods as the post-op programming to ensure the subject remains blinded to treatment group. This visit should be documented as an unscheduled visit. If a lead revision is needed during the trial period, the subject should be withdrawn from the study.

[redacted]

5.4.4 End of Initial Trial Evaluation Visit

The initial trial evaluation period will be a minimum of 3 days. At the end of the initial trial evaluation period, the subject will be evaluated for qualification for permanent implant. If the subject qualifies for permanent implant, the subject will exit the study and continue their treatment per the physician's standard of care.

If the subject does not qualify for permanent system implant after a minimum of 5 days, the subject may be re-programmed with tonic stimulation, per physician discretion, and may enter the extended trial evaluation period. The extended evaluation period must continue for an additional minimum of 3 days.

[redacted]

Subjects will be re-programmed by trained personnel and/or an Abbott representative using the Clinician Programmer. Subjects will be instructed how to use the Patient Controller to adjust stimulation as needed to produce the best results and to complete the Patient Trial Diary daily during the extended trial evaluation period

For subjects continuing with the extended trial evaluation period record the required information on the applicable CRF:

- NRS
- Patient satisfaction and PRP
- Stimulation assessment
- Subject's feedback
- Lead location
- Physician preference (if applicable- only after End of Initial Trial Period Visit for the last subject for a single site)
- Adverse events (if applicable)
- Deviations (if applicable)
- Withdrawal (if applicable)
- Death (if applicable)
- Qualify for permanent implant

[redacted]

Upload and attach the following documentation to the applicable CRF:

- Images

The subject will continue to complete the Patient Trial Diary daily during the extended trial evaluation period (if applicable). The subject will record areas of pain, stimulation therapy goals and percentage of pain relief. At the end of the extended trial evaluation period, the End of Trial Summary report will be submitted to the sponsor.

Subjects who do not continue with the extended trial evaluation will exit the study and continue their treatment per the physician's standard of care.

Record the required information on the applicable CRF:

- NRS
- Patient satisfaction and PRP
- Stimulation assessment
- Clinician assessment
- Lead location
- Adverse events (if applicable)
- Deviations (if applicable)
- Withdrawal (if applicable)
- Death (if applicable)
- Qualify for permanent implant

Upload and attach the following documentation to the applicable CRF:

- Images

5.4.5 End of Extended Trial Evaluation Period (if applicable)

Subjects will return to the clinic at the end of the extended trial evaluation period, at which time the subject's participation in the clinical investigation is completed regardless of qualification for permanent implant. Once the subject exits the study, the subject will continue their treatment per the physician's standard of care.

[redacted]

Record the required information on the applicable CRF:

- NRS
- Patient satisfaction and PRP
- Stimulation assessment
- Lead Location
- Adverse events (if applicable)
- Deviations (if applicable)
- Withdrawal (if applicable)
- Death (if applicable)
- Qualify for permanent implant

Upload and attach the following documentation to the applicable CRF:

- Images

[redacted]

During the extended trial evaluation period, the stimulation parameters may be optimized. If this is needed, the subject would return to the clinic for adjustments to the programming parameters.

5.5 Unscheduled Visits

An unscheduled visit is defined as any visit where the subject returns to the participating study site for medical care outside of a specified study visit. Reasons for unscheduled visits may include an adverse event, wound check, or programming change (not protocol specific).

During the trial evaluation period(s), the stimulation parameters may be optimized. If this is needed, the subject would return to the clinic for adjustments to the programming parameters.

Record the required information on the applicable CRF:

- Reason for visit
- Programming time (if applicable)
- Lead Location (if applicable)
- Adverse events (if applicable)
- Deviations (if applicable)
- Withdrawal (if applicable)
- Death (if applicable)

[redacted]

5.6 Patient Reported Outcome (PRO) measures

The Study Coordinator or designee will give the subject questionnaire to complete on his or her own or apply an interview technique. 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 and only one response is chosen for each question unless otherwise noted.

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

[redacted]

5.6.1 Numerical Rating Scale (NRS)

The pain NRS consists of 1 question that will be asked by interviewing the subjects. The subjects will be asked to rate their average pain specific to the area(s) of chronic pain being treated over the past 24 hours on a 0 (no pain) to 10 (worst imaginable pain) scale. A higher score indicates a higher pain level. The NRS is implemented in the Baseline CRF, the End of Initial Trial Evaluation Period CRF or the End of Extended Trial Evaluation Period CRF.

5.6.2 Patient Reported Pain relief (PRP)

Subjects are asked to directly estimate the percentage of pain relief experienced during the trial period from 0% (no pain relief) to 100% (total pain relief). (e.g. “I have 60% pain relief”).

5.6.3 29-Item Adult Scale of the Patient Reported Outcomes Measurement Information System (PROMIS-29) (Deyo, Ramsay, Buckley, et al., 2016)

The PROMIS-29 is an adult scale developed in partnership with the National Institutes of Health (NIH) to estimate overall quality of life by assessing the following domains known to impact activities of daily living: physical function, sleep disturbance, depression, anxiety, fatigue, pain interference, pain intensity, and social role satisfaction. The scale requires subjects to rate the frequency and/or severity of symptoms and experiences related to each of these domains; a numerical rating scale for pain intensity (0-10) is included on the scale. A total score is calculated and transformed against normative data into a t score indicating global quality of life in relation to population norms. Subscales are defined by each domain described above and can be examined separately to parse separate symptoms or deficiencies in quality of life. Additionally, an impact score for chronic low back pain was developed by the NIH Research Task Force (Deyo, Dworkin, Amtmann,et al., 2014), which is computed using the pain intensity, pain interference, and physical function subscales. Data captured in this scale can be used in a variety of ways to establish patient characteristics and track changes over time.

5.6.4 Pain Catastrophizing Scale (PCS) (Sullivan, Bishop, & Pivik, 1995)

The PCS is a validated scale that measures the magnitude of catastrophizing (negative thoughts and feelings while a patient is experiencing pain). Subjects answer questions about how they feel and what they think about when they are in pain (i.e., not at the current moment). The scale includes 13 statements concerning pain experiences that are rated on a scale between 0 ‘not at all’ and 4 ‘always’. The scale is self-administered, takes 5 minutes to complete and examines the following three domains: Rumination, Magnification and Helplessness. A higher score indicates a higher level of catastrophizing. The PCS is implemented in the Baseline CRF.

5.6.5 Stimulation Assessment

The Stimulation Assessment Form includes questions to identify the sensations experienced when stimulation is used. Subjects identify the intensity and areas of sensations, if experienced. Intensity is rated on a scale of 0 (no feeling) to 10 (very intense). A map of the body is labeled with different numbered quadrants to identify the areas of sensations. The subject will be requested via interview technique to indicate the area he/she is feeling sensations. The form will be implemented at Trial System Implant (Initial Trial Evaluation) Visit CRF, End of Initial Trial Evaluation Visit CRF and End of Extended Trial Visit CRF.

5.7 Clinician Assessments

The clinician assessment of the two lead implant techniques will be performed at the end of each trial implant procedure and again at the end of the study.

At the end of each trial implant procedure, clinicians will be asked to rate the magnitude of anesthesia-related difficulty experienced during the procedure, the magnitude of difficulty in placing the leads, and their affinity (liking) for the trial implant procedure performed compared to their usual practice.

Anesthesia-related difficulty and Lead Placement difficulty will be assessed with a 5-item Likert scales (No Difficulty, Little Difficulty, Moderate Difficulty, Severe Difficulty, Extreme Difficulty – could not place leads). To assess affinity (liking), clinicians will be asked: "On a scale from 0 to 4, with 0 being 'not at all' and 4 being 'very much', how much did you like this trial implant procedure compared to your usual clinical practice." Scores will be treated as magnitude of "liking" for each procedure and will be tabulated as interval data.

At the end of the study, clinician's comparative preference for one procedure over the other will be assessed; this will serve as the secondary endpoint. Clinicians will be asked to choose either "Anatomic Lead Placement" or "Targeted Lead Placement" in response to the following question: "Considering your subjects' experiences and outcomes and your experiences with both lead placement techniques, which technique do you prefer?"

5.8 Description of Activities Performed by Sponsor Representatives

Trained Sponsor personnel will provide technical expertise and technical guidance on the use of the SCS device, including training and proctored case coverage.

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

5.9 Subject Study Completion

When the subject's participation in the clinical investigation has been completed, the subject will return to the medical care as per physician's recommendation.

5.10 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.

Examples of reasons for subject's withdrawal include, but are not limited to:

- Subject and/or family request to withdraw consent
- Subject death
- Unsuccessful trial implant resulting in ineffective stimulation
- Lead revision
- System explant

The status of the subject's condition should be documented at the time of withdrawal.

5.11 Study Committees

5.11.1 Steering Committee (SC)

A Steering Committee will advise the Sponsor on key aspects related to the development, execution, analysis and reporting, and overall conduct of the clinical investigation. A Steering Committee charter will define membership of the committee and outline the purpose, roles, responsibilities, and general rules of operation for the Steering Committee. This charter is maintained by the Sponsor and sets forth the procedures for the implementation of the Steering Committee.

A Medical Monitor will be utilized for this study. The Medical Monitor is responsible for reviewing each subject's lead placement imaging to determine if the lead placement guidelines were followed. Once the investigator completes the trial implant procedure, the images and applicable source documentation will be provided to the Medical Monitor for evaluation. If the Medical Monitor determines that the patient was implanted outside the required guidelines, a protocol deviation will be issued and the patient will be excluded from the primary endpoint analysis.

6 Statistical Considerations

The following section describes the statistical methods for the clinical investigation and justification of the design.

6.1 Hypotheses

6.1.1 Primary Endpoint Hypothesis

The primary endpoint is intended to demonstrate non-inferiority of the qualification rate at the end of the initial trial evaluation period for Group 1 (AB) compared to Group 2 (TB).

For each randomization group, the qualification rate is defined as the number of subjects who are identified as "qualified for permanent system implant" divided by total subjects who complete the initial trial evaluation period for the respective randomized group.

Qualification for permanent system implant is defined by a composite in which a subject meets all of the following conditions:

- >50% patient reported pain relief (PRP) at the end of the trial evaluation period
- Trial evaluation period lasted for a minimum of 3 days
- Physician recommends subject for permanent system implant
- Subject reports a willingness to pursue a permanent system implant
-

Subjects are not qualified for permanent system implant if they meet both of the following:

- ≤50% PRP at the end of the trial evaluation
- Trial evaluation period lasted for a minimum of 5 days

Hypothesis:
The hypothesis is formally addressed as:

H_0: $P_{AB} - P_{TB} \leq -15\%$

H_1: $P_{AB} - P_{TB} > -15\%$

where

P_{AB} = permanent system qualification rate of Group 1 (AB)
P_{TB} = permanent system qualification rate of Group 2 (TB)

[redacted]

6.1.1.1 Analysis Methodology

[redacted]

6.1.1.2 Sample Size Determination

[redacted]

6.1.1.3 Analysis Populations

The analysis population includes subjects who are randomized and either qualify for a permanent system implant or do not qualify for a permanent system implant, as defined earlier.

6.1.1.4 Subgroup Analysis

The primary endpoint will be reported separately for female and male subjects.

6.1.1.5 Missing Data

A sensitivity analysis will be carried in the same manner as the primary analysis, except the subjects who were randomized, underwent the trial system implant and did not complete the initial trial period will be included in the analysis and be treated as non-qualified subjects.

6.1.2 Secondary Endpoint Hypothesis

The secondary endpoint is intended to demonstrate physician preference for anatomic placement over targeted placement.

Hypothesis:
The hypothesis is formally addressed as:

H_0: P ≤ 60%

H_1: P > 60%

where P= percentage of physician prefer anatomic placement over targeted placement.

Analysis

[redacted]

[redacted]

6.2 Justification of Clinical Investigation Design

To date, no clinical evidence has been generated for the use of BurstDR during trial evaluation for SCS or for the Invisible Trial System with any stimulation mode. BurstDR used with permanent SCS systems has provided better patient experiences compared to tonic stimulation (e.g., pain relief and satisfaction). [4,5] The trial system, capable of delivering both BurstDR and tonic stimulation modes, may provide additional benefits by making BurstDR available during the trial evaluation and by providing an alternative stimulation mode if BurstDR fails. Furthermore, the Invisible Trial System provides a streamlined, wire-free trial experience for subjects, and establishing subject impressions of the system are integral to the marketing of this improved system.

The primary aim of this clinical investigation is to establish that anatomic lead placement for BurstDR trials results in non-inferior qualification rates compared to the traditional targeted lead placement technique. The ability to anatomically place trial leads is potentially important because it should reduce procedure time, which benefits both physicians and patients. Prior to the availability of BurstDR stimulation, anatomic placement was not indicated due to the sensory experiences of tonic stimulation. Thus, the current clinical investigation will establish the feasibility of the anatomic placement procedure. Additionally, establishing the physician's preference of anatomic placement and the effect of anatomic placement on procedure time will inform clinical care. Thus, the chosen endpoints capture qualification rate, physician preference, procedure time, and descriptive information. All of these are designed to explore procedure benefits, clinical experience, and patient experience.

To limit knowledge bias, this clinical investigation will be single blinded (i.e., subjects will not be made aware of the group to which they are randomized). Additionally, a standardized script will be provided to study site personnel to assist with patient interaction as a way to minimize the risk of disclosing randomization assignments.

The primary marker of success during the typical SCS trial evaluation period is qualification for permanent implant. Qualification per standard of care for SCS devices includes a successful trial evaluation period defined by subject's assessment of 50% or more pain relief during the trial evaluation, physician's recommendation, and the subject's willingness to continue to the permanent system. As such, the current clinical investigation defines qualification for permanent implant as a composite endpoint based upon standard of care to be used as for the primary endpoint. Demonstration of non-inferiority will establish that the anatomic placement technique is similar to traditional, targeted techniques in terms of subject selection for permanent implant. Secondary and descriptive endpoints will provide evidence of the physician and patient experience with both types of implant procedures and with the Invisible Trial System, overall.

As the primary hypothesis will be tested prior to actual permanent implant status, the clinical investigation will end at the qualification stage without consideration of the actual permanent implant status for subjects. Qualification based on efficacy, subject self-selection, and physician discretion is sufficient to make inferences about the anatomic procedure and Invisible Trial System features.

Failure to qualify for this study is contingent upon a minimum of 5 days of stimulation. Anecdotal reports indicated that burst stimulation may take up to 5 days to impart full benefit; whereas, tonic stimulation does not historically have a wash-in period to reach full benefit. As such, failures occurring before 5 days may be a product of insufficient exposure to burst therapy, and the primary endpoint is contingent upon equitable treatment between randomization arms in all other aspects excepting procedure. Additionally, subjects who fail the burst trial and proceed to an extended trial evaluation with tonic stimulation will need to ensure that they are provided sufficient time to assess the alternate stimulation mode. At present, the wash-out period for burst, if any, has not been established but is suspected to be at least a few hours and up to 2 days. As such, subject's ending their trial evaluation before 5 days without meeting criteria for qualification for permanent implant will be considered a deviation and treated as missing data. Use of this criterion will also

allow exploratory analyses for potential wash-in and wash-out periods for burst stimulation, that are yet to be established in a clinical study.

6.3 Multiplicity

There is one primary endpoint and one secondary endpoint of this clinical investigation. The secondary endpoint will be tested when the primary endpoint is met. Therefore, no multiplicity adjustment is needed.

6.4 Overall Sample Size

[redacted]

6.5 Descriptive Endpoints

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

1. Overall procedure time (in-room to out-room), implant procedure time (needle-in to needle-out), and total time of intra-operative fluoroscopy exposure for each randomized group and stratified by number of leads and lead type (permanent lead or temporary lead).
2. Programming time required for each randomized group.
3. Change from pre-implant Numerical Rating Scale (NRS) in each randomized group to end of initial trial evaluation period and to the end of the extended trial evaluation period, as applicable.
4. Number of subjects in each randomized group who have affirmative assessment for each of the independent criteria required for qualification for permanent implant.
5. Proportion of subjects in each randomized group who do not qualify for permanent implant, however do proceed with permanent implant per physician discretion.
6. Time from trial system implant to >50% PRP measured by the number of days (also known as “wash-in period”).
7. Rate of serious adverse device effects (SADE) in each group.
8. Number and proportion of meaningful lead migrations* during the initial trial evaluation periods by treatment group.
9. Number and proportion of meaningful lead migrations* during the initial trial evaluation period in subjects who have a temporary trial lead implant compared to subjects who have a permanent trial lead implant.
10. Clinician assessment of anesthesia related difficulty (assessed primarily in the procedure room for the trial) on a 5 point likert scale for each randomized group.
11. Clinician assessment of lead placement difficulty on a 5 point likert scale for each randomized group.
12. Clinician affinity (liking) for lead placement technique at the end of the trial implant procedure.
13. Permanent system qualification rate at the end of extended trial period.

*A meaningful lead migration is defined as a lead migration resulting in the inability to program for therapeutic response

6.6 Timing of Analysis

Analysis will be performed when the last enrolled subject completes the initial trial evaluation or, if subject failed to qualify during the initial trial evaluation period and participated in the extended trial period, after completion of the extended trial period.

6.7 Success Criteria

The clinical investigation will be considered a success when the primary endpoint is met.

6.8 Interim Analysis

No interim analyses are planned for this study.

6.9 Statistical Criteria for Termination

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

6.10 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.

7 Risks and Benefits

The risks associated with the use of the 'Invisible Trial System' are anticipated to be comparable to those associated with the use of other currently available SCS trial systems. Subjects participating in this study are indicated for an SCS trial neuromodulation system as part of their standard medical management and are subject to the risk associated with the use of these devices. The study does not require any additional procedures or assessments over the standard of care.
This study may or may not benefit the subjects involved, but may help future subjects by increasing current knowledge and understanding of treatment options for subjects who are indicated for the trial neuromodulation system for SCS.
Lead placement for BurstDR™ has proceeded to use temporary tonic stimulation such that the sensory qualities of tonic programming (paresthesias) can be used to elicit feedback from patients and ensure the leads are properly placed and programmed. Because BurstDR™ results in sensation-free therapy for most patients, it has been proposed that anatomic placement of the leads could result in effective therapy while reducing procedure times during both the trial evaluation and permanent system implants. This benefit may be applicable for subjects randomized to Group 1 (AB).

7.1 Risks Associated with the Device Under Investigation

There are no additional risks to the study subjects beyond those associated with the implant and use of the approved trial neuromodulation systems. Please refer to section 7.1.1 for the list of anticipated adverse events.

7.1.1 Anticipated Adverse Device Effects

The implantation of a SCS trial system is an invasive procedure and therefore carries certain risks. In addition to those risks commonly associated with surgery, the following anticipated adverse device effects are associated with implanting or using the trial neuromodulation system for SCS:

- Unpleasant sensations or motor disturbances, including involuntary movement, caused by stimulation at high outputs (If either occurs, turn off the EPG immediately.)
- 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
- Stimulation in unwanted places
- Lead migration, causing changes in stimulation or reduced pain relief
- Epidural hemorrhage
- Hematoma
- Infection

- Spinal cord compression
- 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
- Allergic or rejection response to implant materials
- Seroma (mass or swelling) at the implant site
- Local skin erosion
- Persistent pain at lead site

7.1.2 Risks Associated with Clinical Investigation Assessments

The risks involved with this clinical investigation are comparable to those associated with the implant of any other commercially available neuromodulation system.

7.2 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
- Training of Investigators both on the CIP, lead placement procedure, anchoring technique and imaging guidelines.

7.3 Possible interactions with concomitant treatments

There are no known interactions of the neuromodulation trial system with concomitant medical treatment or with any previously implanted active devices. Please refer to the Clinician's Manual for the SJM™ External Pulse Generator and leads for information related to MRI compatibility.

7.4 Risk-to-Benefit Rationale

Any undesirable side effects, under normal conditions of use, are considered to be acceptable risks when weighed against the performance of the device and benefits to the subject.

8 Requirements for Investigator Records and Reports

8.1 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.

8.2 Safety Reporting

Safety surveillance and safety reporting by the investigator starts as soon as the subject is enrolled in this clinical investigation (date of signature of informed consent).

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.

Per this CIP, the applicable reportable adverse events data including deaths will be collected throughout the clinical investigation and will be reported to the Sponsor through the EDC system. The Sponsor will ensure that all applicable events are reported to the relevant authorities as per regulations. The investigators must notify the IRB/EC, if appropriate, in accordance with their institutional requirements, national and local laws and regulations, of the AEs reported to the Sponsor.

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

Descriptive endpoints for the safety datapoints are as follows:

1. Rate of serious adverse device effects (SADE) in each group.
2. Number and proportion of meaningful lead migrations* during the initial trial evaluation periods by treatment group
3. Number and proportion of meaningful lead migrations* during the initial trial evaluation periods in subjects who have a temporary trial lead implant compared to subjects who have a permanent trial lead implant.

*A meaningful lead migration is defined as a lead migration resulting in the inability to program for therapeutic response

For the purposes of this clinical investigation, the following events will be reported:

- All Adverse Device Effects (non-serious device/procedure related)
- All Serious Adverse Events (whether or not the event is considered device/procedure related)

Reportable adverse events shall be submitted to the Sponsor as soon as possible after becoming aware of the event. The sites should notify the Sponsor of reportable adverse events by creating and saving the applicable CRF within the electronic data capture (EDC) system. Additional information may be requested by the Sponsor in order to support the reporting of AEs to regulatory authorities. All adverse events will be reported as per applicable regulatory requirements.

Subject Death:

Subject deaths will be documented and reported to the Sponsor on the applicable CRF as soon as possible after becoming aware of the event. It is the investigator's responsibility to notify the IRB/EC of the death reported to Sponsor in accordance with national and local laws and regulations. .

Should a death occur, the investigator is requested to record death information in the hospital records and immediately document the information on the Death CRF and submit to Sponsor through the electronic data capture (EDC) system deployed by Abbott.

- All efforts to obtain the details about the circumstances surrounding the patient death should be made by the Investigator.
- If a death event is an outcome of an adverse event, an AE CRF must be completed in addition to the Death CRF.

The subject's death is an early conclusion of the subject's participation in the clinical investigation. Therefore, the Investigator is requested to complete the Withdrawal form

8.2.1 Complaints/Device Deficiencies

During the study, the investigator will be responsible for reporting all complaints/device deficiencies.
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.

A device deficiency (DD) is defined as an inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance.

If the complaint/DD does not involve an AE, the investigator must notify the Abbott Post Market Surveillance Department by submitting the complaint information via email to [redacted] as soon as possible after becoming aware of the complaint.
Complaints/DDs information will not be collected on a CRF for the study.

If the complaint/DD involves an AE, the investigator must complete an AE through the EDC system, including the information on the complaint and submit to Abbott as soon as possible.

8.3 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.

8.4 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.

9 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.

9.1 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.

9.2 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.

Only authorized site personnel will be permitted to enter the CRF data through the EDC system deployed by Abbott. An electronic audit trail will be used to track any subsequent changes of the entered data.

9.3 Document and Data Control

9.3.1 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.

9.3.2 Recording Data

The CRF will be reviewed by the authorized site personnel. An appropriate comment will be provided to explain changes to data reported on the CRF.

10 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.

Monitoring will be conducted according to Abbott's Clinical Monitoring work instruction.
Prior to beginning the clinical investigation, the Sponsor will contact the investigator or designee to discuss the clinical investigation and data requirements. A designated monitor will periodically review the subject records and associated source documents. The investigator shall make subject and clinical investigation records available to the clinical monitor for monitoring.

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.

11 Compliance Statement

11.1 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 patients or requesting informed consent from any patient 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.

11.2 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.

11.3 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.

12 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.

13 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.

14 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.
Publication planning and authorship determinations will be overseen by the Steering Committee or Publications Committee, and investigators will be notified via email about the dissemination of study data and opportunities for involvement as authors on publications/presentations.

15 Reporting Results on ClincalTrials.gov Website

This clinical investigation will be registered on ClinicalTrials.gov. A full report of the pre-specified outcomes, regardless of the results, will be made public through the ClinicalTrials.gov website.

16 Appendix A: CIP Revisions

17 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 medical device under clinical investigation.

This definition includes events related to the 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
  - A malignant tumor (only for specific countries)
- 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 a 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 medical device.

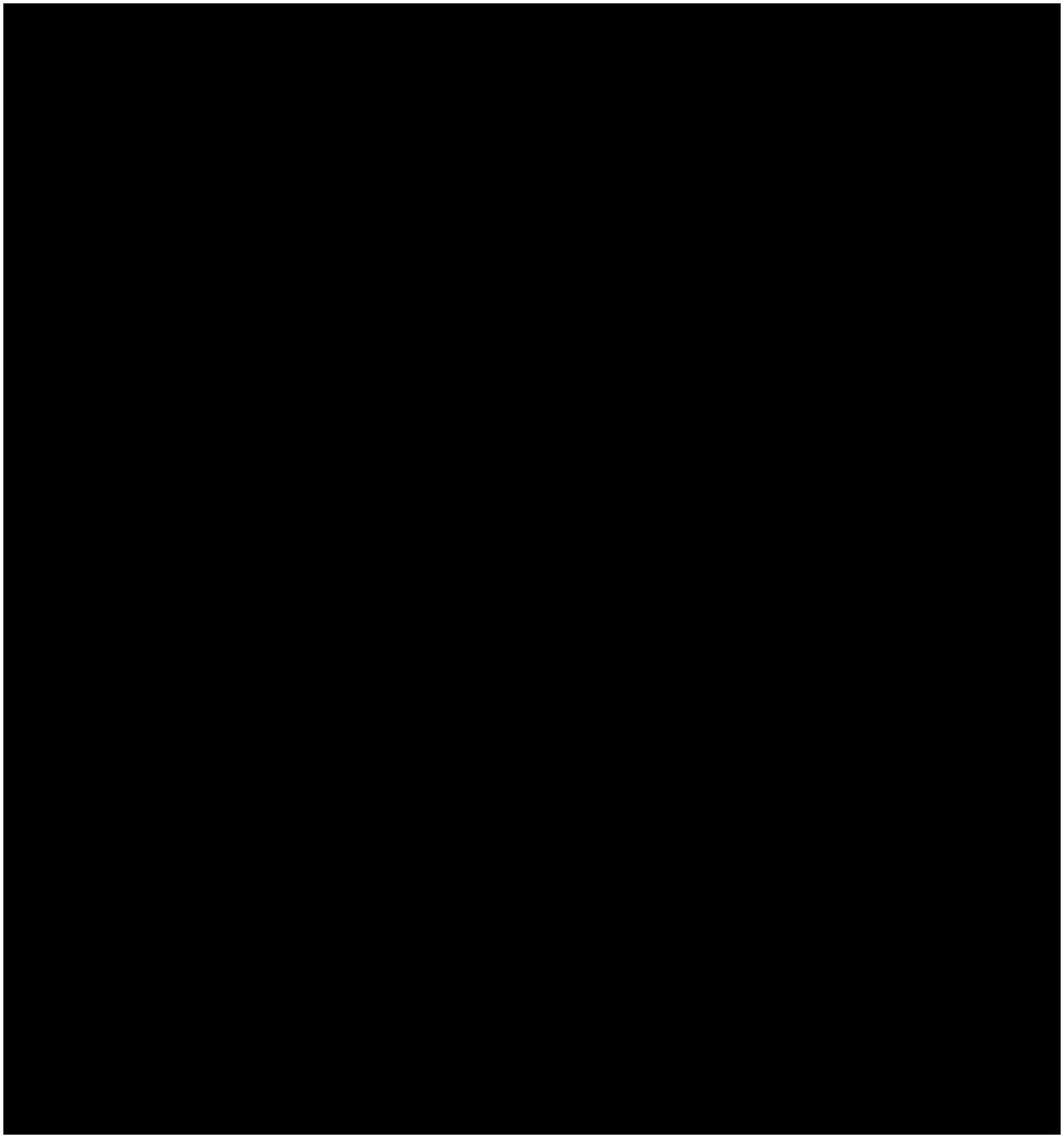
This definition includes any event resulting from the use error or from intentional misuse of the medical device.

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

18 Appendix C: BurstDR Programming Guidelines

[redacted]

19 Appendix D: Imaging Guidelines



20 Appendix E: Bibliography

1. Taylor RS. Spinal cord stimulation in complex regional pain syndrome and refractory neuropathic back and leg pain/failed back surgery syndrome: Results of a systematic review and meta-analysis. J Pain Symp Mgmt, 2006; 31(4S):S13-S19.

2. Deyo RA, Dworkin SF, Amtmann D, Andersson G, Borenstein D, Carragee E, Carrino J, Chou R, Cook K, DeLitto A, Goertz C, Khalsa P, Loeser J, Mackey S, Panagis J, Rainville J, Tosteson T, Turk D, Von Korff M, Weiner DK. Report of the NIH Task Force on research standards for chronic low back pain. J Pain. 2014 Jun;15(6):569-85.

3. Huang KT, et.al. A national survey of spinal cord stimulation trial-to-permanent conversion rates. Neuromodulation, 2014; Neuromodulation, 2015;18(2):133-9.

4. Deyo RA, Ramsay K, Buckley DI, Michales L, Kobus A, Eckstorm E, Forro V, Morris C. Performance of a patient reported outcomes measurement information system (promis) short form in older adults with chronic musculoskeletal pain. Pain Medicine 2016; 17: 314–324.

5. Rosenberg J, et. al. Spinal cord stimulation provides pain relief with improved psychosocial function: results from EMP3OWER. Pain Medicine, 2016; 17: 2311–2325.

21 Appendix F: Case Report Form

[redacted]

22 Appendix G: Informed Consent Form

[redacted]