Official Title:
A Post-Market Study of Percutaneous Peripheral Nerve Stimulation (PNS) for the Treatment of Back Pain

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A Post-Market Study of Percutaneous Peripheral Nerve Stimulation (PNS) for the Treatment of Back Pain

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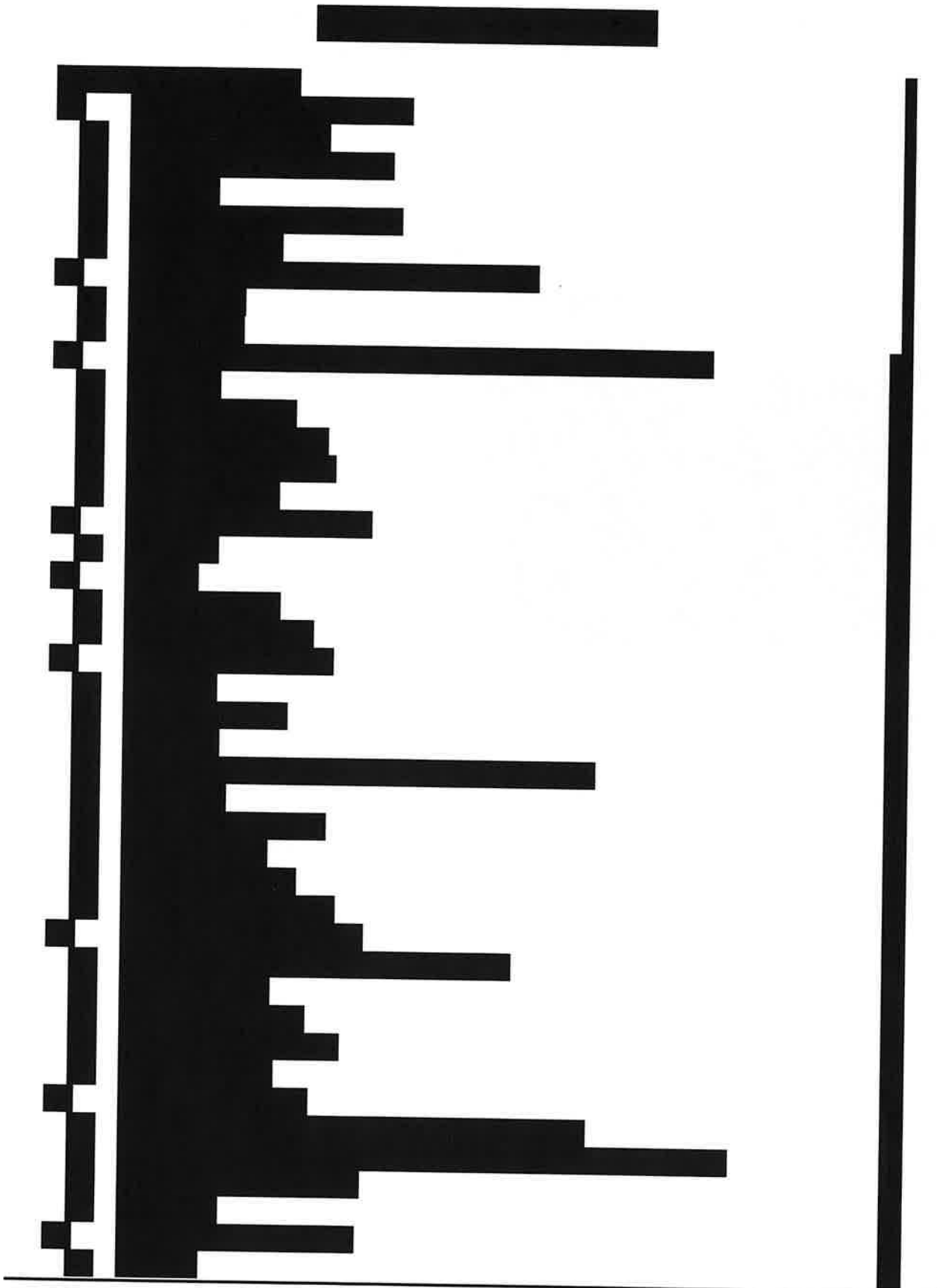
Protocol [redacted]

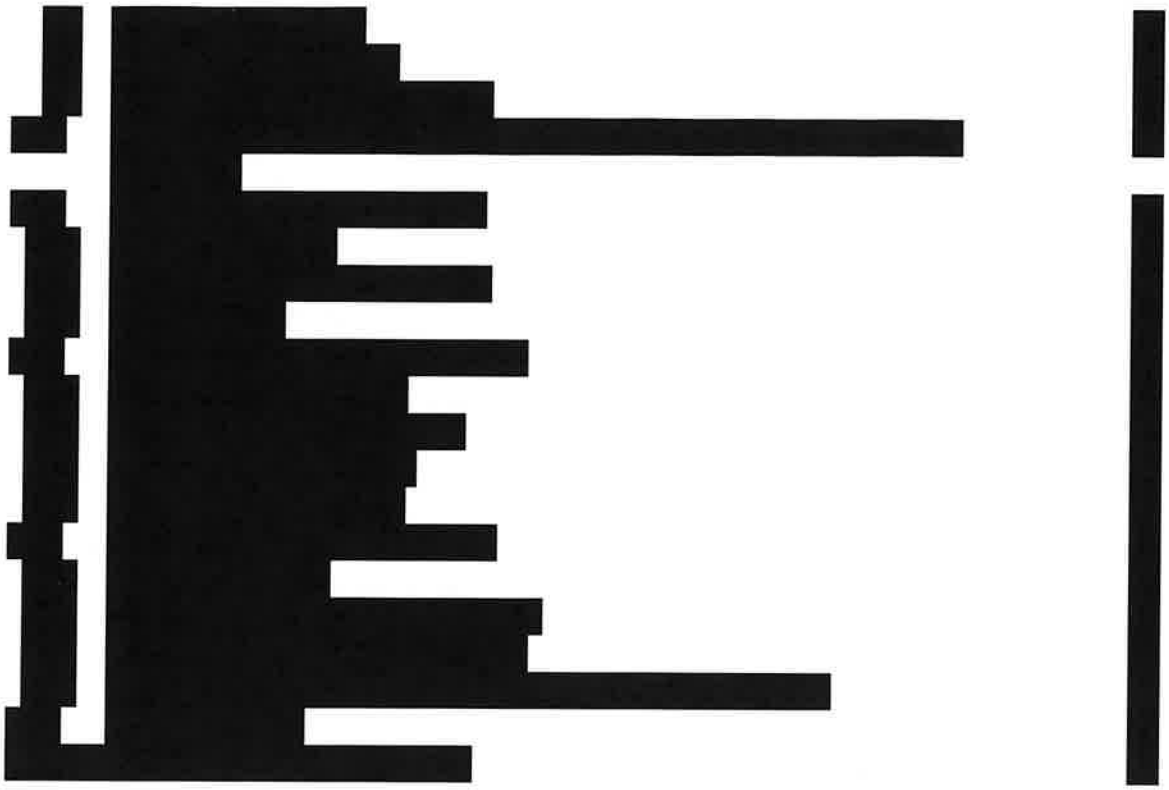
Amendment Date(s): [redacted]

April 29, 2019

FDA Clearance for SPRINT® PNS System: K181422.

CONFIDENTIAL INFORMATION
This protocol contains confidential information for use by the Investigator and his designated representatives participating in this clinical investigation. It should be held confidential and maintained in a secure location. Do not copy or distribute without permission.



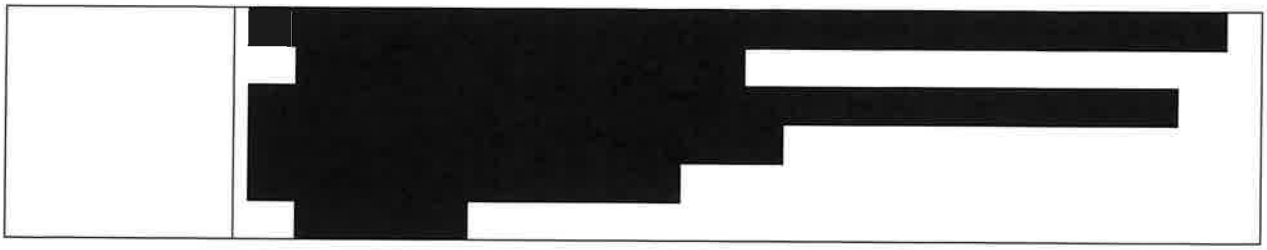


Protocol Synopsis

Title	A Post-Market Study of Percutaneous Peripheral Nerve Stimulation (PNS) for the Treatment of Back Pain
Device (510k Cleared)	The SPRINT Peripheral Nerve Stimulation (PNS) System
Study Design	Post-Market, On Label Prospective Case Series Study
Primary Study Objective	The study objective is to gather post-market data on the safety and clinical effectiveness of the PNS System for the treatment of chronic low back pain.
Study Plan	**Individuals must have an average pain intensity score of ≥ 4 out of 10 to qualify** Individuals who report chronic low back pain (pain isolated to the lower back lasting for more than 12 weeks) will be considered for enrollment into the study. After obtaining informed consent, potential subjects will be evaluated for general eligibility. To qualify for enrollment in the study, individuals must report average pain intensity in the previous week of ≥ 4 out of 10 (Brief Pain Inventory-Short Form, Question #5). Subjects must have previously used at least two categories of conservative therapies for low back pain (*e.g.,* medications, physical therapy, or injections) and/or must have been recommended for surgery or another interventional pain procedure (*e.g.,* radiofrequency ablation, spinal cord stimulation). After qualifying for participation, subjects will undergo a diagnostic medial branch block (MBB), a standard diagnostic procedure for patients with chronic low back pain. If a subject has previously undergone a diagnostic lumbar MBB within 3 months of the baseline visit, and results and medical records are available from that block, a subject may skip the MBB. Subjects will proceed to lead placement at the next study visit, regardless of the outcome of the MBB. **Percutaneous leads will be placed to stimulate nerves innervating muscles in the lower back** [redacted] Following programming of stimulation parameters, subjects will undergo [redacted] stimulation [redacted] **Average pain intensity will be measured during treatment period and 12 months following lead removal** Subjects will be permitted to use medications at baseline levels and daily doses will be recorded. Subjects will use numerical rating scales to record average pain intensity (BPI-5) and worst pain intensity (BPI-3) in the past 24 hours during the treatment period. Outcomes will be assessed at baseline, each day during treatment, at the end of treatment (EOT) visit, and at follow-up visits up to 12 months after lead placement.

Sites (N)	Up to 15 investigational sites
Subjects (N)	Up to 200 subjects
Inclusion Criteria	• At least 21 years of age • Able to understand and comply with study requirements and provide written informed consent • [redacted] Chronic low back pain [redacted] • Reports an average low back pain score ≥ 4 on a scale of 0-10 (BPI-5) • [redacted] stable pain treatment or medication as indicated by subject reported medication history [redacted] and willingness to continue at baseline rates or lower for duration of treatment period • Previous use of at least two categories of conservative therapies (e.g., medications, physical therapy, or injections) and/or prescribed treatment of surgery or other interventional procedure (e.g., radiofrequency ablation, spinal cord stimulation)
Exclusion Criteria	• [redacted] Signs of infection on or around the low back near the anticipated region of lead insertion, or other conditions that increase risk to the subject in the opinion of the Investigator [redacted] • Signs of serious underlying cause of low back pain [redacted] as determined by the Investigator • Implanted cardiac pacemaker/defibrillator, Deep Brain Stimulator, Spinal Cord Stimulator, or any other implantable neurostimulator (implantable pulse generator) located in the abdomen or lower back • Anesthetic or corticosteroid injections in the low back [redacted] or botulinum toxin (Botox) injection in the low back [redacted] • Current participation, or less than 30 days since participation, in any drug or device trial • [redacted] Condition that would alter sensations and muscle movements, [redacted] • Clinically relevant stenosis of the central canal or foramina as determined by the Investigator • Radicular leg pain, or back pain that spreads to the lower extremities (e.g., pain that is worse in the lower extremities, or pain that radiates below the buttocks) • Lumbar Scoliosis • History of significant trauma to the lumbar spine or paraspinal musculature [redacted]

	• Score of > 20 on the Beck Depression Inventory (BDI-II) • Obese with a body mass index (BMI) > 40 • Current illicit substance abuse or opioid dependence in the opinion of the Investigator [redacted] • Pending litigation, workers compensation or other secondary gain issues • Allergy to skin surface electrodes and/or medical-grade adhesive tapes • Allergy to all local anesthetic agents (*e.g.,* lidocaine) [redacted] Any other medical condition that may interfere with ability to participate in a clinical trial as determined by the Investigator [redacted] • Vulnerable populations (*e.g.,* prisoners, investigational site employees) • Bleeding disorder (e.g., hemophilia)
Sub-Study Criteria	Up to [redacted] subjects [redacted] will participate in the sub-study (counted within the overall subject limit). This includes [redacted] subjects who have undergone previous lumbar surgery and [redacted] subjects who have undergone previous RFA (the RFA must have been at least 6 months prior to Visit 1).
Additional Exclusion Criteria *(assessed before MBB or lead placement)*	• Average pain intensity score of < 4 [redacted] • INR ≥ 1.5 for those on warfarin • Pregnancy
Primary Safety Endpoint	Study-related adverse event rates. Adverse device effects will be assessed at all visits.
Primary Clinical Endpoint	• Clinically significant reduction in chronic low back pain as evidenced by ≥30% reduction in "average pain intensity" (BPI-5) at the end of therapy (*i.e.,* average across last week of stimulation) compared to baseline (*i.e.,* average across week prior to stimulation).
Secondary Endpoints	• Change in "worst pain" as measured using Question #3 of the BPI-SF (BPI-3) at EOT compared to baseline • Change in disability as measured using the Oswestry Disability Index (ODI) at EOT compared to baseline • Change in health-related quality of life (RAND 36-Item Health Survey) • Change in emotional state as measured by Beck Depression Inventory (BDI-II) at EOT compared to baseline • Patient Global Impression of Change (PGIC) • Change in pain interference as measured using Question #9 of the BPI-SF (BPI-9) at EOT compared to baseline
[redacted]	[redacted]



1.0 GENERAL INFORMATION

1.1 Title of Investigation
A Post-Market Study of Percutaneous Peripheral Nerve Stimulation (PNS) for the Treatment of Back Pain

1.2 Sponsor Name and Address
SPR Therapeutics
22901 Millcreek Boulevard, Suite 110
Cleveland, OH 44122
Phone: 216-378-9108
Fax: 216-378-9116

1.3 Materials
The SPRINT® Peripheral Nerve Stimulation (PNS) System

1.4 Approved Indication for Use
The PNS System is 510(k) cleared with the following Indication for Use.

The SPRINT® Peripheral Nerve Stimulation (PNS) System is indicated for up to 60 days in the back and/or extremities for:

- Symptomatic relief of chronic, intractable pain, post-surgical and post-traumatic acute pain;
- Symptomatic relief of post-traumatic pain;
- Symptomatic relief of post-operative pain.

The SPRINT® PNS System is not intended to treat pain in the craniofacial region.

1.5 Study Objective
The study objective is to gather post-market data on the safety and clinical effectiveness of the PNS System for the treatment of chronic low back pain.

2.0 INTRODUCTION AND BACKGROUND

2.1 Introduction
[redacted]

[redacted]

[redacted]

The objective of the proposed study is to collect post-market data on percutaneous PNS for the treatment of chronic low back pain (LBP). Secondary objectives include determining if PNS can relieve pain and improve function and quality of life. Subjects with chronic LBP lasting for more than 12 weeks will enroll. Fine-wire leads will be placed [redacted]

Subjects will receive stimulation at home [redacted] During the treatment period, subjects will be queried on a daily basis for pain intensity and medication usage, and weekly for adverse device effects. The leads will be removed at eight weeks (+2 day window) for a maximal lead indwelling time of 60 days. Primary and secondary outcome measures will be assessed at baseline, during treatment, at end-of-treatment, and at follow up visits at 1-month, 3-months, 6-months, 9-months, and 12-months post-treatment. [redacted]

2.2 Background

Chronic LBP is a substantial medical problem

[redacted]

[redacted]

[redacted]

Present treatments for chronic low back pain are ineffective, not well tolerated or associated with side effects and complications

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

The proposed therapy may provide long-lasting relief of low back pain

[redacted]

Summary

Chronic low back pain is a substantial problem and current therapies for treatment are ineffective

[redacted]

or associated with side effects and complications. Percutaneous peripheral nerve stimulation (PNS) to produce muscle contractions may relieve chronic LBP and improve function and quality of life. The proposed study will gather post-market data on this therapy.

3.0 STUDY OUTCOMES [redacted]

3.1 Overview

Outcomes [redacted] will be collected before, during, and after the stimulation treatment period (see Appendix A for schedule) and include:

[redacted] Numerical rating scales for pain intensity: Average Pain [redacted]

[redacted] Numerical rating scales for pain intensity: Worst Pain [redacted]

[redacted] Change in disability [redacted]

4. Change in health-related quality of life [redacted]

[redacted] Change in emotional state [redacted]

[redacted] Change in pain interference [redacted]

8. Patient Global Impression of Change during the treatment period [redacted]

3.2 Primary Outcome

The primary outcome of this study will be calculated as the mean score of average daily pain intensity calculated over the last week of stimulation compared to baseline. This will be recorded using Question 5 of the Brief Pain Inventory Short Form (BPI-5; details of BPI below), which assesses "average pain" on an 11 point numerical rating scale, with one end representing "no pain" (0) and the other end representing "pain as bad as you can imagine" (10). Subjects will record BPI-5 scores daily in a diary, and the mean score for each week will be calculated for each subject. The primary endpoint will be a clinically significant reduction in pain evidenced by $\geq$ 30% reduction in mean "average pain" (BPI-5) over the last week of stimulation compared to baseline.

3.3 Secondary Outcomes

Secondary outcome measures will provide additional information on pain and function, which will be used to aid in the design of future clinical studies.

Brief Pain Inventory-Short Form (BPI)

The BPI is a widely used assessment designed to measure pain intensity and the interference of pain on daily activities and moods (Cleeland and Ryan 1994). The BPI is recommended by the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) panel and has demonstrated validity and reliability across many cultures and languages (Tan et al. 2004, Dworkin et al. 2005). The IMMPACT panel was assembled to develop consensus recommendations to improve and standardize the design and conduct of clinical trials involving treatments for pain. Invited participants included academic centers, regulatory agencies, the National Institutes of Health, the US Veterans Administration, and industry representatives. Individual questions of the BPI (e.g., "average pain" (BPI-5), "worst pain" (BPI-3), and pain interference (BPI-9)) may be assessed during visits at various time points, including: baseline and lead-placement visits, treatment or follow-up visits and take-home diaries. When answering BPI questions, subjects will be asked to focus on their back pain. The site may call to remind the subjects to complete or turn in their diary, and/or ask questions from the BPI verbally if subjects fail to submit their responses.

Oswestry Disability Index (ODI)

The ODI is a short, widely used assessment designed to measure the degree of disability in patients with low back pain. This validated questionnaire includes topics concerning the intensity of pain, the subject's ability to perform normal daily activities such as personal care, walking, sitting, or standing, and how pain affects the subject's sex life, social life, and travel (Roland and Fairbank 2000). The ODI will be administered at baseline during Visit 1, treatment, and follow up visits, and may be assessed at any other time during subject participation. This assessment will provide important information on how disability caused by pain changes during and after treatment with stimulation.

Health-related quality of life (RAND 36-Item Health Survey)

It is important to measure the health-related quality of life (HRQOL) in chronic pain studies, as pain is known to impact daily activities (Dworkin et al. 2005). The RAND 36-Item Health Survey asks questions about the subject's general health and activities and assesses physical and emotional problems associated with pain during the past 4 weeks. This is a widely accepted form that has been used in a number of studies and shown acceptable reliability and validity to quantify quality of life (Patrick et al. 1995, Ferrari 2007, Tavafian et al. 2007, Bentsen et al. 2008). The RAND 36-Item Health Survey will be administered at baseline, 4-weeks treatment visit, end of treatment visit, and follow up visits.

Beck Depression Inventory (BDI-II)

The Beck Depression Inventory (BDI-II) assesses the severity of symptoms of depressive disorders and has been validated for its reliability and responsiveness to change (Dworkin et al. 2008). Total scores range from 0 to 63, with scores < 13 and scores < 20 reflecting minimal or no depression and mild to moderate depression, respectively (Beck et al. 1988, Beck et al. 1993), while a score of 21 distinguishes patients with major depressive disorder (Geisser et al. 1997). The BDI-II will be administered at Visit 1, 4-weeks treatment visit, end of treatment visit, and follow up visits.

Patient Global Impression of Change (PGIC)

Participant ratings of global improvement are one of the core outcome domains in chronic pain studies (Dworkin et al. 2005). The Patient Global Impression of Change (PGIC) Scale will be administered at end of treatment and 6- and 12-month follow-up to assess subject perception of overall improvement. The PGIC Scale asks subjects to rate their improvement with treatment on a 7-point scale that ranges from "very much worse" to "very much improved". The scale provides subjects the opportunity to combine all of the components of their experience into one overall measure and allows clinicians to assess the clinical significance of each subject's improvement or worsening over the course of the study.

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

3.5 Safety Endpoint

The primary safety endpoint is the occurrence of study-related adverse events, also known as adverse device effects (ADEs). All ADEs that occur during the study will be documented and analyzed. [redacted]

4.0 DEVICE DESCRIPTION

4.1 Overview

This study utilizes the commercially available SPRINT® PNS System [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

5.0 SCOPE

5.1 NUMBER OF SITES
Up to 15 investigational sites.

5.2 NUMBER OF SUBJECTS
Up to 200 subjects will be consented for the study. Up to [redacted] will participate in the sub-study described in Section 8.4 (counted within the 200 subject limit). [redacted] Screened and consented consecutive subjects will be given a unique Subject ID number.

6.0 STUDY PROTOCOL

6.1 Overview
This study is a post-market prospective case series study to gather post-market data on the clinical effectiveness of percutaneous Peripheral Nerve Stimulation (PNS) therapy for the treatment of chronic low back pain.

6.2 Study Population
Prospective subjects will be screened for eligibility into the study using the Eligibility criteria listed in section 6.3. Recruitment materials will be provided to aid in subject enrollment. All recruitment materials will be IRB approved prior to their use.

6.3 Eligibility
6.3.1 Inclusion Criteria

1. At least 21 years of age
2. Able to understand and comply with study requirements and provide written informed consent
3. [redacted]Chronic low back pain [redacted]

[redacted]

4. Reports an average low back pain score ≥ 4 on a scale of 0-10 (BPI-5)
5. [redacted] stable pain treatment or medication [redacted] and willingness to continue at baseline rates or lower for duration of treatment period
6. Previous use of at least two categories of conservative therapies (e.g., medications, physical therapy, or injections) and/or prescribed treatment of surgery or other interventional procedure (e.g., radiofrequency ablation, spinal cord stimulation)

6.3.2 Exclusion Criteria

1. Signs of infection on or around the low back near the anticipated region of lead insertion, or other conditions that increase risk to the subject in the opinion of the Investigator [redacted]
2. Signs of serious underlying cause of low back [redacted] determined by the Investigator
3. Implanted cardiac pacemaker/defibrillator, Deep Brain Stimulator, Spinal Cord Stimulator, or any other implantable neurostimulator (implantable pulse generator) located in the abdomen or lower back
4. Anesthetic or corticosteroid injections in the low back [redacted] or botulinum toxin (Botox) injection in the low back
5. Current participation, or less than 30 days since participation, in any drug or device trial [redacted] Condition that would alter sensations and muscle movements [redacted]
7. Clinically relevant stenosis of the central canal or foramina as determined by the Investigator
8. Radicular pain, or back pain that spreads to the extremities (e.g., pain that is worse in the lower extremities, or pain that radiates below the buttocks)
9. Lumbar Scoliosis
10. History of significant trauma to the lumbar spine or paraspinal musculature [redacted]
11. Score of > 20 on the Beck Depression Inventory (BDI-II)
12. Obese with a body mass index (BMI) > 40
13. Current illicit substance abuse or opioid dependence in the opinion of the Investigator [redacted]
14. Pending litigation, workers compensation or other secondary gain issues
15. Allergy to skin surface electrodes and/or medical-grade adhesive tapes
16. Allergy to all local anesthetic agents (*e.g.,* lidocaine)
17. Any other medical condition that may interfere with ability to participate in a clinical trial as determined by the Investigator [redacted]
18. Vulnerable populations (*e.g.,* prisoners, investigational site employees)
19. Bleeding disorder (*e.g.,* hemophilia)

6.3.3 Additional Exclusion Criteria (assessed before lead placement)

1. Average pain intensity score of <
2. INR ≥ 1.5 for those on warfarin
3. Pregnancy

6.4 Concurrent Medications and Non-Drug Therapies

Subjects will be permitted to use analgesic medications (opioid or non-opioid) as prescribed/recommended by their physician and analgesic usage will be recorded. However, to qualify for enrollment, their current medication or therapy must have been stable for at least 4 weeks.

Subjects will not be allowed to start any new medications or therapies for the duration of the therapy. Subjects will also not be allowed to use other electrical stimulation therapies for back pain for the duration of the therapy. All interventions targeting pain control will be recorded on the appropriate pages of the diaries or source documents.

6.5 Study Plan

The study procedures for this protocol are classified according to the following time periods: Consent; Lead Placement and Stimulation Programming; Treatment; and Follow up. Appendix A provides a schedule of the study procedures.

6.5.1 Visit 1 - Consent

Potential subjects will receive a detailed explanation of study specific procedures as well as the risks and benefits of participating in the study. The subject will be asked to sign the approved study consent form during this visit if he/she would like to participate. If the subject agrees to participate by signing the consent form, all inclusion/exclusion criteria will be verified by completing the eligibility form and then all baseline information will be collected and recorded on the appropriate forms.

The following measures may be assessed:

[redacted]Selected questions from Brief Pain Inventory (BPI) [redacted]
Low back pain treatment and diagnostic testing history [redacted]

- Oswestry Disability Index (ODI)
- Health-related quality of life [redacted]
- Beck Depression Inventory (BDI-II)
- Pain drawing
- Key demographic information

A weekly diary will be distributed at this visit [redacted] Individuals may be contacted to be reminded of the upcoming Visit 2 date, and to review the baseline diary for contents and completion.

6.5.2 Visit 2 – Medial Branch Block (MBB)

Screening

To increase the likelihood of enrolling subjects who are able to comply with the study requirements for data collection, subjects must complete the 7 day baseline diary to be eligible to participate in the study. [redacted]

Diagnostic Medial Branch Block (MBB)
Subjects will undergo a standard diagnostic medial branch block (MBB) targeting the area where they have chronic low back pain. [redacted]

The diagnostic medial branch block (MBB) will be performed according to standard practice [redacted]

If a subject has previously undergone a diagnostic lumbar medial branch block (MBB) within 3 months of the baseline visit, and results and medical records are available from that block, a subject may skip the second part of Visit 2 [redacted]

6.5.3 Visit 3 – Lead Placement and Stimulation Programming

Women of childbearing age and reproductive potential will have a pregnancy test completed as part of eligibility confirmation before or at Visit 3.

As a safety precaution to prevent potential excessive bleeding, subjects on warfarin will have blood drawn to confirm an INR of < 1.5. If the INR is not below 1.5, subjects will be given the opportunity to have their warfarin dosage adjusted and the INR will be retested up to two additional times. The INR must be collected within 48 hours prior to Lead Placement.

Lead Placement

Following the consent visit, participants who meet all Eligibility criteria will undergo placement of the percutaneous leads.

[redacted]

[redacted]

[redacted]

[redacted]

[redacted] at the conclusion of this Visit a subject will

a. Proceed to treatment phase:
Subjects with acceptable lead placement and stimulation parameters will be prepared to proceed to the treatment phase. The subject will be instructed to use the Stimulator [redacted]
Subjects will be provided with detailed instructions on the use and care of the System, and full details are also supplied the Patient Manual. Subjects will complete the daily diary on each day stimulation is received. OR

b. Return for another Visit 3:
If there is not sufficient time to complete lead placement or the testing, or if the subject does not respond to stimulation, the investigator may present the subject with the option to return for a repeat or additional lead placement visit. If it is determined that additional leads may be needed, the subject may return for placement of additional leads [redacted] anytime until Visit 12. OR

c. Terminate from the Study:
If the subject does not wish to continue with further lead placement, they will be terminated from the study if no adverse device effects (ADE) are noted at a 24-48 hour telephone follow-up. If an ADE is noted, the subject will be followed until the ADE resolves.

[redacted]

6.5.4 Telephone Follow-Up (Visit 4)

[redacted]

[redacted]

6.5.5 Treatment: Weeks 1 through 7 after Lead Placement (Visits 5-11)

During the treatment phase after lead placement, follow-up visits will take place weekly [redacted]

[redacted]

6.5.6 End of Treatment: 8 weeks after Lead Placement (Visit 12)

The End of Treatment will occur 8 weeks after Lead Placement. Each lead must be removed within 60 days of lead placement. [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

6.5.7 Follow up Visits: Visits 13 (1 month), Visit 14 (3 months), Visit 15 (6 months), Visit 16 (9 months), and Visit 17 (12 months).

Visits will occur at 1, 3, 6, 9, and 12 months (Visits 13-17) after Lead removal (See Schedule of Visits in Appendix A).

[redacted]

[redacted]

6.6 Study Visit Windows

The acceptable windows for each visit are listed below in **Table 1.**

Table 1 Study Visit Windows

Visit Number	Visit Name	Window
1	Baseline	[redacted]
2	Medial Branch Block (MBB)	
3	Lead placement and Stimulation Programming	
4	Follow up phone call	
5	Treatment – 1 week interim	
6	Treatment – 2 week interim	
7	Treatment – 3 week interim phone call	
8	Treatment – 4 week interim	
9	Treatment – 5 week interim phone call	
10	Treatment – 6 week interim	
11	Treatment – 7 week interim phone call	
12	End of Treatment (Lead Removal)	
13	1 month Follow up	
14	3 month Follow up	
15	6 month Follow up	
16	9 month Follow up	
17	12 month Follow up	

6.7 Study Duration

The duration of this study is expected to be approximately [redacted]

6.8 Early Termination

[redacted]

6.9 Subject Compensation

Subjects will receive [redacted] compensation for taking part in all study visits. Compensation will be based on the subject completing milestones within the study. The disbursement schedule will be as follows:

[redacted] after the completion of Visit 1 – Consent and baseline
after the completion of Visit 2 Screening
after the completion of Visit 2 Medial Branch Block
after the completion of Visit 3 – Lead placement and stimulation programming
after the completion of each in person treatment visit (Visits 5, 6, 8, 10, and 12)
after the completion of each telephone treatment visit (Visits 7, 9, and 11)
after the completion of each follow-up visit (Visits 13, 14, 15, 16, and 17)

If a subject volunteers to participate in an additional Visit 3 (returns for another session of stimulation testing or for a lead replacement), the subject will receive [redacted] compensation at the completion of that visit. All requirements for Visit 3 will be repeated.

[redacted]

7.0 DATA MANAGEMENT

7.1 Subject Screening and Identification Log

A subject screening log will be completed at the investigational site for all subjects who were considered for the study. Those individuals who are excluded will be listed along with the reason for exclusion. [redacted] The Subject identification log will be completed for subjects enrolled in the study.

7.2 Data Collection

For this study, an Electronic Data Capture (EDC) system which utilizes electronic CRFs (eCRFs) will be used. A 21 CFR Part 11 compliant system will be selected for use which enables entry of study data into an Electronic Data Capture system by each participating clinical site.

Source documents will be completed and maintained in a fashion that is consistent with accepted Good Clinical Practices. If necessary, corrections will be made by using a single line strikeout with the initials and date of the person making the correction. The corrections will be made so as not to obscure the original data. Correction fluid or correction tape may not be used.

All source documentation will be stored in a locked storage facility (either a locked office or a locked cabinet).

7.3 Subject Numbering

Screened and consented consecutive subjects will be given a unique Subject ID number [redacted]

7.4 Confidentiality of Data

Every effort will be made to protect subject confidentiality. Subject names and personal identifiers will not appear in any publications resulting from this work. [redacted]

[redacted]

[redacted]

8.0 DATA ANALYSIS

All primary and secondary outcome data will be analyzed and reported. [redacted]

8.1 Analysis of Outcomes

A table of outcomes [redacted] to be collected during the study can be found in Appendix A.

Primary Outcome

Question 5 of the Brief Pain Inventory-Short Form (BPI-5) is an 11-point numerical rating scale rating "average pain". The BPI-5 will be measured in a daily diary prior to Lead Placement to establish a baseline score, as well as daily in diaries during treatment and follow-up. For each subject, the mean BPI-5 will be calculated for each diary (7 days). The mean BPI-5 for the last week of treatment (End of Treatment, EOT) will be compared to mean BPI-5 from the baseline diary. The overall mean across all subjects may also be calculated and compared to baseline levels.

Secondary Outcomes

Additional sub-analyses may be performed to determine the mean "average pain" at different treatment intervals or calculate the mean for each subject and across subjects up to End of Treatment (week 8). The mean "worst pain" for the last week of treatment will be compared to baseline.

At the weekly visits during stimulation, subjects may also be asked to recall their "average pain" or "worst pain" over the past week. The mean over different intervals (e.g., weeks 1-4 or weeks 5-8) will be calculated. Changes in "average" or "worst pain" may also be assessed between baseline and other study time points, e.g., follow up visits, to further explore pain relief with this therapy.

Other Outcome Surveys

Surveys performed during the study will include the Oswestry Disability Index (ODI), Beck Depression Inventory (BDI), RAND 36-Item Health Survey, Patient Global Impression of Change (PGIC), selected questions from the Brief Pain Inventory (e.g., BPI-9), [redacted] The ODI, BDI, BPI, and RAND 36-Item Health Survey will each be used to calculate a mean total score across all subjects, means score of specific subsections or individual questions, and to calculate differences in scores at EOT and follow up compared to baseline. A mean PGIC score may be calculated across all subjects. [redacted]

[redacted]

8.2 Plan to maximize subject retention and minimize loss of data

Significant efforts will be made to maintain maximum subject retention and follow up data and minimize the percentage of missing data.

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

8.3 Safety Endpoint Analysis

All adverse device effects will be documented, reported, and categorized so that the safety profile of this approach may be further understood. Knowledge gained from this study will further refine consent forms and the risk benefit profile for future studies.

8.4 Sub-Study

A sub-study will be performed for subjects who have previously undergone either lumbar surgery or radiofrequency ablation (RFA). [redacted]

[redacted]

[redacted] Data from the sub-study of subjects may be analyzed, published, and/or presented separately from the primary group of subjects.

9.0 STUDY MONITORING

9.1 Training

SPR Therapeutics or their designee will conduct a Site Initiation and Training Visit prior to initiation of the study. The purpose of this visit will be to develop a common understanding of the clinical protocol, Case Report Forms (CRFs), study specific procedures, Investigator Responsibilities, and Good Clinical Practices (GCPs) among the clinical research monitors and the Investigational Site team.

9.2 Routine Monitoring

Monitoring visits to the Investigational Site will be conducted periodically, as determined by the rate of subject enrollment, during the study to ensure that the most currently approved version of the Investigational Plan is being followed and that the site is in adherence with all Good Clinical Practices and any specific study Data Monitoring Plan that is in place. In addition, source documents will be reviewed for accuracy against data found on the electronic Case Report Forms

[redacted]

9.4 Designation of Study Monitor

SPR Therapeutics or a designated qualified study monitor will monitor this study.

SPR Therapeutics, Inc.

22901 Millcreek Boulevard, Suite 110
Cleveland, OH 44122
Phone: 216-378-9108
Fax: 216-378-9116

Other appropriately qualified clinical monitors may also be involved in the monitoring of study investigational sites.

10.0 ADVERSE EVENTS AND UNANTICIPATED ADVERSE DEVICE EFFECTS

An Adverse Event (AE) is defined as any untoward medical occurrence in a patient whether or not related to the medical device or procedure. Adverse Events will not be captured unless they are study related or the relationship is unable to be determined.

An Adverse Device Effect (ADE) is a study-related Adverse Event. Adverse Device Effects (ADEs) that occur during the study will be captured on an Adverse Event Form and reported to the Sponsor. If the relationship of the adverse event to the System is not able to be determined, it will be captured on an Adverse Event Form and reported to the Sponsor. Specific details regarding the ADE, including the event category, severity of event, and seriousness will be collected. Any necessary treatment or intervention required and the resolution status of the ADE will also be documented. ADEs will be followed to resolution. Any ADEs that meet the requirements for Medical Device Reporting (MDR) will be entered into SPR's complaint system.

All ADE's are further categorized as anticipated or unanticipated. Any ADE's specified in the Risk Analysis of this Investigational Plan will be considered "anticipated". All other ADE's are considered "unanticipated". Anticipated events that occur with a greater frequency than expected are also considered unanticipated.

An Unanticipated Adverse Device Effect (UADE) is 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 this Investigational Plan or application or any other unanticipated serious problem associated with a device that relates to the rights, safety or welfare of subjects.

[redacted]

Table 2: Unanticipated Adverse Device Event Sponsor Contact Information

UNANTICIPATED ADVERSE DEVICE EVENT SPONSOR CONTACT INFORMATION			
Name/Title	**Email address**	**Telephone Number**	**Fax Number**
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]

It is the responsibility of the investigator to inform his/her Institutional Review Board (IRB) of any ADEs and UADEs as required by the IRB. In addition, some IRBs will require that AEs that are serious in nature, even if not study related, will be reported as well. SPR Therapeutics is responsible for furnishing the required information to the appropriate regulatory authorities.

Deficiencies related to the identity, quality, durability, reliability, usability, safety or performance of a device should be reported to SPR promptly. Sites will be provided with instructions for the reporting of device complaints in accordance with SPR's standard operating procedures.

11.0 RISK BENEFIT ANALYSIS

The potential risks and benefits to study subjects participating in this study are listed below.

11.1 Potential Benefits

Subjects in this study may not receive any direct benefit by participating in this study.

If the treatment is successful, subjects may experience some or all of the following benefits during and/or after stimulation:

A reduction in the degree of pain [redacted]

This research may benefit future patients with chronic low back pain.

11.2 Known and Anticipated Risks

The risks listed below are described as common [redacted], uncommon [redacted], or rare [redacted]

[redacted]

[redacted]

[redacted]

Risk of skin irritation, infection, or inflammation at the lead exit sites

[redacted]

[redacted]

[redacted]

[redacted]

Risk of the percutaneous lead breaking beneath the skin

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted] **Risk of skin irritation under the pad, lead connector tape, or bandages**

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

Risk of discomfort or increased pain

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

11.3 Risk Analysis

As described above, all efforts will be made to mitigate each potential risk associated with the use of the system [redacted] The potential risks of participation in this study have been minimized such that they are unlikely to occur and/or have non-serious consequences. [redacted]

[redacted]

12.0 ETHICAL CONSIDERATIONS

12.1 Declaration of Helsinki

The study will be performed in accordance with the relevant parts of the ICH Guidelines for Good Clinical Practices (GCPs), the Declaration of Helsinki, and the FDA regulations.

12.2 Institutional Review Boards

It is the responsibility of the Principal Investigator to obtain and maintain written approval of the study protocol and the informed consent from the appropriate Institutional Review Board (IRB). It is further the Principal Investigator's responsibility to notify the IRB regarding any amendments/supplements to either the study protocol or the consent form. A copy of the written IRB approval, along with the approved versions of the consent and protocol, will be maintained in the study regulatory file. Written approvals will identify the study name and document the date of review.

12.3 Informed Consent Form

In accordance with 21 CFR 50, it is the responsibility of the Principal Investigator to give each participant (or the participant's legally authorized representative) full and adequate verbal and written information about the objectives of the study, the study procedures, and the potential risks of participating in the study prior to inclusion in the study. Potential study participants will be informed that their participation is voluntary and that they may withdraw their consent at any time and for any reason without sanction, penalty, or loss of benefits to which they are otherwise entitled. Potential participants will also be informed that withdrawal from the study will not jeopardize their future medical care. It is the Principal Investigator's responsibility to obtain a signed Informed Consent Form from each potential study participant prior to performing any study-related procedures and to document the informed consent process in the subject record.

The Informed Consent Form will be amended whenever new information becomes available that may be relevant to the subjects continued participation. Modifications to the Consent Form must be approved by SPR Therapeutics prior to submission to the IRB. The investigator must also inform SPR Therapeutics of any IRB mandated revisions to the study protocol.

12.4 Amending the Protocol

This study will be carried out in accordance with this Study Protocol/Investigational Plan. SPR Therapeutics will prepare written amendments to revise the protocol, if necessary. Changes that are deemed administrative in nature, which do not require IRB approval (such as editorial changes for clarity or changes to contact information) may be made without any further approvals. Documentation of the approval of the amendment will be maintained in the study regulatory files.

13.0 STUDY ADMINISTRATION

13.1 Record Retention

By signing the Investigator Agreement, the Investigator agrees to retain study-related documents in a secure location to which access can only be gained if required. Following study completion, the following documents will be archived: the study regulatory files containing all Good Clinical Practice (GCP) documents, including signed Informed Consent forms, patient-related materials, and CRFs. The Investigator will be required to retain all records required by this study during the investigation and for a period of 2 years after the later of the following two dates: The date of which the investigation is terminated or completed or, the date that the records are no longer

required for purposes of supporting a pre-market approval application or a notice of completion of a product development protocol. The investigator must inform SPR Therapeutics if the location of the records changes or if there are any plans to destroy the records.

13.2 Criteria for Terminating the Study

SPR Therapeutics reserves the right to terminate the study at any time. SPR Therapeutics only intends to exercise this right for valid scientific or administrative reasons, and reasons related to the protection of Human Subjects participating in this study. Principal Investigators and IRBs will be notified in writing in the event of a study termination.

13.3 Criteria for Terminating a Center

SPR Therapeutics reserves the right to suspend or stop the enrollment of subjects at a study center at any time after the study initiation if no subjects have been enrolled or if enrollment numbers are well below anticipated enrollment expectations. [redacted]

13.4 Investigator Qualifications/Responsibilities and Investigator Training

To participate in this study, the Investigator must sign the Investigator Agreement which documents his responsibilities in the study. The Investigator will require training on this study plan and the device. [redacted]

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Appendix A: Schedule of Visits