Pilot Study to Examine the Feasibility of the DISCSS™ (Dynamic Interferential Spinal Cord Stimulation System)

Protocol Number: DISCSS 01

Sponsor: Meagan Medical

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Version 5.0: October 30, 2019

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LIST OF ABBREVIATIONS

AE	Adverse Event
CFR	Code of Federal Regulations
CMP	Clinical Monitoring Plan
CRF	Case Report Form
CRO	Contract Research Organization
DISCSS™	Dynamic Interferential Spinal Cord Stimulation System
eCRF	Electronic Case Report Form
EPG	External Pulse Generator
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
ICH E6	International Conference on Harmonization Guidance for Industry, Good Clinical Practice: Consolidated Guidance
IDE	Investigational Device Exemption
IFC	Interferential Current
IFT	Interferential stimulation therapy
IRB	Institutional Review Board
ISO	International Organization for Standardization
NRS	Numeric Rating Scale
OHRP	Office for Human Research Protections
PI	Principal Investigator
SAE	Serious Adverse Event
SCS	Spinal Cord Stimulation
SOP	Standard Operating Procedure

PROTOCOL SIGNATURE PAGE

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The above referenced trial will be carried out in accordance with Good Clinical Practice (GCP) as required by the following applicable regulations:

- United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR part 46, 21 CFR part 50, 21 CFR part 56, and 21 CFR part 812
- ICH E6

I agree to ensure that all staff members involved in the conduct of this study are informed about their obligations in meeting the above commitments.

Principal Investigator Printed Name _____

Principal Investigator Signature _____

Date of Principal Investigator Signature _____

1.0 INTRODUCTION

Chronic pain affects up to 20% of the population in developed nations. This represents a profound impact on individuals and their families as well as a burden on employers and health care providers. The management for non-cancer related chronic pain varies. The current standard of care is multidisciplinary and includes pharmacological, psychological and physical therapies, as well as surgical interventions. Opioid analgesics are often prescribed, despite long-term contraindications. For many patients the current multidisciplinary approach has not been effective or results in undesirable side effects. Neuromodulation techniques may be an option for those individuals who have not benefited from other chronic pain interventions.

The Meagan Medical, Inc., Dynamic Interferential Spinal Cord Stimulation System (DISCSS™) System is used to deliver spinal cord stimulation (SCS) via interferential stimulation therapy (IFT) for the purpose of providing pain relief. The DISCSS™ system is intended for use in an investigational device exemption (IDE) study to assess the efficacy of interferential spinal cord stimulation for treating chronic back pain.

The mechanism of action for SCS was first proposed by Melzack and Wall in 1965[1]. Dr. Norman Shealy published the first report of electrical stimulation of the spinal cord in 1967[2]. Patients in whom SCS has been commonly applied are those with chronic back and leg pain and failed back surgery syndrome. In 2010, Nevro entered the SCS market with high frequency stimulation at 10,000 pulses per second, and their studies in pain patients have demonstrated superior back pain relief with a less uncomfortable stimulation sensation than traditional low-frequency SCS[3,4] Meagan Medical has designed and developed a trial stimulator using interferential current (IFC) stimulation. IFC stimulation is a type of electrical stimulation that uses paired electrodes with two independent circuits carrying high-frequency and medium-frequency alternating currents. It is believed that IFC stimulation permeates the tissues more effectively and with less unwanted stimulation of cutaneous nerves. Meagan Medical calls their system the "Dynamic Interferential Spinal Cord Stimulation System" (DISCSS™).

The DISCSS™ device utilizes two intersecting circuits of medium frequency sine waves that are in the range of 500-20,000 Hz. The higher base frequencies reduce tissue reactance and the intersection of the two circuits produce a steerable "sweet spot" of stimulation that has a resultant beat frequency. Due to these two advantages, the DISCSS™ is anticipated to result in more effective pain relief than other commercially available SCS systems. This pilot feasibility study will explore and help determine optimal settings and configuration of the DISCSS™ System with patients that have completed a percutaneous trial with a commercially available SCS trial system.

2.0 STUDY OBJECTIVES

2.1 Primary Objectives

- Effectiveness: To assess the performance of the DISCSS™ device in achieving back pain reduction as compared to baseline by patient report using a Numeric Rating Scale (NRS) and Anatomical Pain Maps in a cohort of patients with chronic back pain during a three -four day trial of the SCS DISCSS™ system.
- Safety: To evaluate the safety of the DISCSS™ device by reviewing adverse events and serious adverse events in trial participants.

2.2 Secondary Objective

- To describe patients' experience and perceptions with the use of the DISCSS™ device for management of chronic back pain through analysis of their responses to a subjective evaluation questionnaire.

3.0 STUDY DESIGN

3.1 Description of Study Design

This investigation will be performed as a prospective, multicenter, open-label feasibility study. Thirty (30) patients with back pain greater than leg pain who were candidates for Spinal Cord Stimulation (SCS) and have successfully completed a percutaneous trial with a commercially available SCS system will be trialed with a 3-4 day exposure to the investigational DISCSS™ device. The trial will be conducted at 5-7 U.S. centers. The percutaneous trial leads from the commercial system will be connected to the External Pulse Generator of the DISCSS™ Trial System and the patients will be trialed for an additional three-four days.

The investigational product for this feasibility trial will be the DISCSS™ system, not the commercially available trial SCS system. Exposure to the commercially available trial SCS system will be considered background therapy. The purpose of the background therapy phase is to establish baseline pain levels and determine patients' eligibility to continue to the investigational phase of the trial using the DISCSS™ SCS phase of the trial. Pain assessment and complications data from the commercial spinal stimulation system will be collected during the background therapy phase. The pain and complications data from the background therapy phase will not be analyzed in terms of the study endpoints.

Commercial device selection will be left to the discretion of the Investigator. Some of the frequently used commercially available trial SCS systems include Prodigy Neurostimulation System (St. Jude Medical (ABBOTT)), Medtronic SCS, the Senza System (Nevro Corporation), and the Precision Plus (Boston

Scientific). The Sponsor will not be responsible for the cost or complications that occur during the use of the commercial trial system.

3.2 Primary Endpoints

The primary effectiveness endpoints for this study will include:

- Pain intensity ratings on a Numeric Rating Scale (NRS); and
- Anatomical Pain Maps demonstrating location of Back Pain, Leg Pain and Overall Pain

The primary safety endpoints for this study will include:

- Incidence of adverse events arising from the DISCSS™ treatment phase
- Incidence of serious adverse events arising from the DISCSS™ treatment phase

3.3 Secondary Endpoints

The secondary endpoint for this study will include:

- Patient descriptions of device efficacy and device stimulation sensation as captured on a study-specific questionnaire

4.0 STUDY ENROLLMENT AND WITHDRAWAL

4.1 Inclusion Criteria

In order to be eligible to participate in this study, an individual must meet all of the following criteria:

a) Age greater than 21 years and less than 80 years
b) Has a diagnosis of chronic neuropathic pain of trunk and limbs
c) Is eligible for a spinal cord stimulation trial of a commercially available SCS trial system. Subjects will be evaluated at the end of the background Commercial SCS Device phase for complications and appropriateness to continue to the investigational phase with the DISCSS™ system. Complications from the background phase with the commercial SCS device may include, but are not limited to unusual pain or discomfort during the trial stimulation, local skin reactions or infection at the implant site.
d) Has a Back Pain Score of minimum intensity 5.0 on a Numeric Rating Scale (NRS)
e) Has an NRS Back Pain Score that is greater than both Leg Pain Scores
f) Is not a candidate for revision surgery
g) Has completed a minimum of 6 weeks of conservative therapy (physical therapy, anti-inflammatory medications, or similar therapies) with limited or no reduction in back pain
h) Is willing to adhere to the warnings associated with the DISCSS™ system

i) Is willing to halt and/or modify the use of all prescription and over-the-counter analgesics per the Investigator's direction during study participation
j) Is capable of providing written informed consent
k) Is able to comply with the requirements of study visits, follow-up phone visits and self-assessment questionnaires
l) If existing permanent implanted leads are in place, the patient must be undergoing a paradigm shift in treatment (e.g. Conventional Sensory SCS to Sub-Perception SCS) that necessitates trialing of the new commercial SCS device.

4.2 Exclusion Criteria

An individual who meets any of the following exclusion criteria at screening will be excluded from participation:

a) Is a poor surgical candidate by determination of the Investigator
b) Is unable to operate or understand the use of the commercial or investigational Spinal Cord Stimulator systems
c) Has an active systemic infection
d) Has exposure to shortwave, microwave or ultrasound diathermy at home or at work
e) Has occupational exposure to high levels of non-ionizing radiation such as radio or cell phone transmission stations, facilities using radiofrequency heat sealers or induction heaters, or electric power infrastructure controlled environments
f) Has an implanted cardiac system (e.g. pacemakers)
g) Is currently participating in another clinical study
h) Is currently pregnant or lactating, or not using adequate birth control
i) Has any untreated major psychiatric comorbidity
j) Has serious drug-related behavioral issues per Investigator's assessment
k) Has a bleeding complication or coagulopathy
l) Requires concurrent use of anticoagulant therapy such as heparin, warfarin, rivaroxaban, dabigatran, apixaban, edoxaban, enoxaparin, fondaparinux
m) Is immunocompromised and at risk for infection
n) Has insulin-dependent diabetes not controlled through diet and/or medication
o) Has chronic pain related to malignancy
p) Has used a commercially available SCS device within the last 14 days
q) Is otherwise determined, based on the opinion of the Investigator to be an unsuitable candidate for this study

4.3 Early Discontinuation

The participant may withdraw participation in the trial for any reason. Possible reasons for early discontinuation by the participant include:

- Consent withdrawal
- Inability to tolerate the background SCS trial phase with the commercially approved device
- Occurrence of a clinical adverse event or development of a medical condition such that continued participation in the study would not be in the best interest of the participant

The Investigator may also discontinue a patient from the study in the event of:

- The participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation
- Any medical event/condition that presents a health or safety risk and prevents the participant from continuing in the study
- Participant's failure to comply with protocol requirements
- Administrative reasons (e.g. Sponsor's decision to stop the study)
- Device complication

At the time of early discontinuation, the SCS device will be removed. Percutaneous trial leads will be removed, if applicable. All end of study evaluations will be completed, and study completion source documents and case report forms will be completed. All adverse events will be followed by the Investigator until resolution.

4.4 Missed Visits

Contact information for the participant and an alternate contact (i.e. a friend, relative, etc.) will be collected at Visit 1 and documented in the records. Any participant who misses one scheduled appointment will be contacted the same day by study site personnel. Telephone contact will be repeated at least daily for 3 days. A certified letter (or its equivalent) will be sent to the participant's last known address. All attempts will be made to arrange an appointment to remove the device and leads as well as collect any end of study evaluations, as applicable. Participants who are determined to be lost to follow up after 3 phone contacts and a certified letter cannot be considered for re-enrollment.

4.5 Use of Data from Early Discontinuation Cases

Study data collected previously for patients who are discontinued from the study by the Investigator or lost to follow-up may still be included and used for the study unless the patient presents written notification of withdrawal of consent to the Investigator. In the event that a patient withdraws consent to participate in the study, data previously collected for the patient may not be included or used for the study.

4.6 Treatment for Early Discontinuation Cases

Patients who withdraw voluntarily or are discontinued by the Investigator will remain eligible for Standard of Care treatment by the Investigator and study staff.

5.0 STUDY SCHEMA

Screening	Background Phase Commerical SCS Device			Washout	Investigation Study Phase DISCSS™ SCS Device		
Day 0	Duration 3-5 days			Duration 1-2 days	Duration 3-4 days		
Visit 1	Visit 2		Visit 3		Visit 4		Visit 5

*Please note that the Screening Visit (Visit 1, Day 0) may be combined with Visit 2 (Initiation of the Background Phase with Commercial SCS Device) upon Principal Investigator discretion and participant agreement. Combining Visit 1 and Visit 2 is contingent on successful verification of eligibility, completion of all screening evaluations, including meeting informed consent requirements.

6.0 STUDY PROCEDURES

6.1 Screening (Visit 1)

Potential participants will be identified from the patient population at the investigative sites. The following procedures will be conducted at Screening:

- Informed Consent: Only patients who sign the IRB-approved informed consent form will be permitted to participate in the clinical study. Participants who do not speak English must be provided a copy of an IRB-approved informed consent form in their native language. The original signed copy of the informed consent will be retained in each participant's study file and a copy will be given to the patient to take home for their records. No study-specific procedures will be done prior to the patient providing informed consent.
- Physical Exam
- Medical History
- Conservative Therapy History
- Medication History
- Urine Pregnancy Test (for female participants only)
- NRS Pain Assessments (back, bilateral lower extremities, and overall pain)
- Anatomical Pain Maps (back, bilateral lower extremities, and overall pain)
- Inclusion and Exclusion Criteria Evaluation

At the completion of the screening exam, the Investigator will evaluate the patient for eligibility. If eligible, the patient can be enrolled. Please note that Visit 1 and Visit 2 may be combined if eligibility is verified and all screening evaluations are completed prior to initiating Visit 2 activities.

6.2 Initiation of Background Commercial Trial SCS Device Phase (Visit 2)

During this visit, the following will occur:

- NRS Pain Assessments (back, bilateral lower extremities, and overall pain)
- Anatomical Pain Maps (back, bilateral lower extremities, and overall pain)
- Concomitant Medication Review
- Percutaneous lead implantation under fluoroscopic guidance, per Manufacturer instructions, if applicable. Note: If the subject has existing permanent implanted leads in place, the permanent leads may be used if the subject is undergoing a paradigm shift in treatment that necessitates trialing of the commercial SCS device. In this case the trial leads will not be used.
- Radiographic Imaging of implanted percutaneous trial leads as described in Section 16.4.
- Connection of the external trial leads to the commercial External Pulse Generator (EPG) system per Manufacturer instructions.
- Programming and adjustment of settings for the commercially available trial SCS system per Manufacturer instructions.
- Assessment of Complications, including but not limited to unusual pain or discomfort during the trial stimulation, local skin reactions at the implant site, and complications related to implantation of percutaneous trial leads
- Review of device use instructions during patient's home use, including all pertinent warnings

The duration of the Background Commercial Trial SCS Device Phase is 3-5 days. At the end of the visit they will be scheduled for Visit 3, the planned termination of the Background Commercial Trial SCS Device Phase.

6.3 Completion of Background Trial Commercial SCS Device Phase (Visit 3)

During this visit, the following will occur:

- NRS Pain Assessments (back, bilateral lower extremities, and overall pain)
- Anatomical Pain Maps (back, bilateral lower extremities, and overall pain)
- Assessment of Complications, including but not limited to unusual pain or discomfort during the trial stimulation, local skin reactions or infection at the implant site
- Concomitant Medication Review
- Disconnection of commercial External Pulse Generator (EPG) (note: the percutaneous trial leads are to remain for the DISCSS™ treatment phase).

Participants who are determined by the Investigator to have successfully completed the background therapy with the commercially available SCS and are willing to participate in the investigational trial phase will return to the clinic after a 24-48 hour washout period to receive the investigational DISCSS™ SCS device and begin the Investigational Study Phase.

6.4 Washout Period

Participants will spend 24-48 hours undergoing a "washout period" between study phases.

During this period, they will be reminded not to increase the usual dosages of any of their prescribed medications, including pain medications. However, they may decrease their pain medications, if desired. All other prescribed medications (i.e., antihypertensives, hypoglycemics, cardiovascular medications, cardiopulmonary medications, membrane stabilizers, etc.) are to continue as usual.

6.5 Initiation of Investigational Study Phase with DISCSS™ SCS Device (Visit 4)

Participants will return to the clinic at Visit 4 for initiation of a 3-4 day trial period with the investigational DISCSS™ device. During this visit, the following will occur:

- Investigator confirmation of patient eligibility to start the Investigational Study Phase with the DISCSS™ SCS Device
- NRS Pain Assessments (back, bilateral lower extremities, and overall pain)
- Anatomical Pain Maps (back, bilateral lower extremities, and overall pain)
- Concomitant Medication Review
- Assessment of adverse events
- Radiographic Imaging of implanted percutaneous trial leads.
    - If migration of implanted percutaneous leads has occurred, modification of placement by guided fluoroscopy is performed, followed by radiographic confirmation of location of trial implanted leads
    - Note: Percutaneous lead modification of placement is conducted per the package instructions of the percutaneous trial leads in use.
- Connection of the DISCSS External Pulse Generator (EPG) to the percutaneous trial leads following the instructions in Appendix III: DISCSS™ Stimulator System Clinician Use Guide
- Investigator programming of settings for the investigational DISCSS™ SCS device per the instructions provided in Appendix III: DISCSS™ Stimulator System Clinician Use Guide

The subject will be instructed to contact the Investigator in the event of any adverse events with the DISCSS™ SCS device and/or the percutaneous trial leads. The subject will be trained on the information included in Appendix II:

DISCSS™ Patient User Manual and provided a copy of this document. If device complications occur between Visit 4 and Visit 5, the Investigator will follow the instructions provided in Section 8.9. The subject will return to the clinic for an unscheduled visit as described in Section 6.7, and the device complications and/or adverse events will be addressed clinically and per the procedures outlined in the protocol and the DISCSS™ Stimulator System Clinician Use Guide. If indicated, the Investigator will adjust the settings on the DISCSS™ Stimulator System or, if necessary replace the DISCSS™ Stimulator System Clinician Use Guide as outlined in Section 8.9. If the complication cannot be resolved, the subject will be discontinued from the study as described in Section 4.6.

At the end of the visit they will be scheduled for Visit 5, the completion of the Investigational Study Phase and reminded to return to the clinic at this time to complete the trial.

6.6 Completion of Experimental Study Phase with DISCSS™ SCS Device (Visit 5)

Participants will return to the clinic 3-4 days later for Visit 5. During this visit, the following will occur:

- NRS Pain Assessments (back, bilateral lower extremities, and overall pain)
- Anatomical Pain Maps (back, bilateral lower extremities, and overall pain)
- Patient Subjective Evaluation Questionnaire
- Concomitant Medication Review
- Radiographic documentation and archiving of location of implanted percutaneous leads as described in Section 16.4
- Disconnection of investigational DISCSS™ External Pulse Generator (EPG) SCS device as described in Appendix III: DISCSS™ Stimulator System Clinician Use Guide
- Percutaneous lead removal per Manufacturer instructions, if applicable. Note: If the subject has existing permanent implanted leads in place, the permanent leads may remain in place.
- Assessment of adverse events
- Return of device as described in Section 9.0

6.7 Unscheduled Visits

Participants may be seen for unscheduled visits as needed. Any adverse events, device complications and concomitant medication changes that are reported at unscheduled visits should be documented in the study records and entered in the EDC. Adverse event follow up should be completed per Section 10.0 (Safety Reporting).

6.8 Study Completion

The final study visit occurs at Visit 5 of the Investigational Study Phase with DISCSS™ SCS Device. Participants who undergo early discontinuation from the study will have final data collection on the date of withdrawal.

7.0 SCHEDULE OF EVALUATIONS

	Screening	Background Phase with Commercial SCS Device Duration: 3-5 days		Washout 24-48 hours	Investigational Phase with DISCSS™ Duration: 3-4 Days	
	Day 0	Start of Commercial SCS Device Phase	End of Commercial SCS Device Phase		Start of DISCSS™ Device Phase	End of DISCSS™ Device Phase
	Visit 1[a]	Visit 2[a]	Visit 3		Visit 4	Visit 5
Informed Consent	X					
Inclusion/Exclusion Criteria	X[b]					
Eligibility Re-assessment					X[b]	
Demographics	X					
Physical Exam, Medical History and Conservative Therapy History	X					
Urine Pregnancy Test (females only)	X					
NRS Pain Assessment	X	X	X		X	X
Anatomical Pain Maps	X	X	X		X	X
Concomitant Medication Review	X	X	X		X	X
Patient Subjective Evaluation Questionnaire						X
Percutaneous Trial Lead Implantation[e], Adjustment & Removal (under guided fluoroscopy)		X[c, e]			X[c, e]	X[c, e]
Radiographic Imaging of Implanted Percutaneous Trial Leads		X[d]			X[d]	X[d]

	Screening	Background Phase with Commercial SCS Device Duration: 3-5 days		Washout 24-48 hours	Investigational Phase with DISCSS™ Duration: 3-4 Days	
	Day 0	Start of Commercial SCS Device Phase	End of Commercial SCS Device Phase		Start of DISCSS™ Device Phase	End of DISCSS™ Device Phase
	Visit 1[a]	Visit 2[a]	Visit 3		Visit 4	Visit 5
Device Use Initiation & Programming, and adjustment of External Pulse Generator (EPG) Settings		X			X	
EPG Removal[e]			X			X
Commercial Device Complications Evaluation		X	X		X	
Adverse Event Review					X	X
Study Completion and Device Return						X

[a] Visit 1 and Visit 2 may be combined if eligibility is verified and all screening evaluations are completed prior to initiating Visit 2 activities.

[b] Eligibility criteria will be reviewed by the PI during Screening at Visit 1. PI will re-assess eligibility to continue participation in the Investigational Phase with the DISCSS™ SCS device at the start of Visit 4.

[c] Leads will be implanted percutaneously at Visit 2. At Visit 4 their positioning may be modified, if required. At Visit 5 they will be removed after the DISCSS™ EPG device is disconnected. Removal of percutaneous trial leads is not done under guided fluoroscopy.

[d] Radiographic imaging will be performed to document lead positions at Visit 2 once the leads have been implanted. At Visit 4 & 5 radiographic imaging will be performed to confirm that migration has not occurred.

[e] If applicable. Note: If the subject has existing permanent implanted leads in place, the permanent leads will be used, and the trial leads will not be implanted or removed.

8.0 INVESTIGATIONAL PRODUCT

8.1 Description of Investigational Product

The Meagan Medical, Inc. DISCSS™ System is comprised of the following components:

- Clinician programmer (Programmer)
- Patient remote (Remote)
- External feasibility neurostimulator (Stimulator)
- Patch cable

The stimulator applies electrical stimulation to the patient via a patch cable to implanted leads. The clinician programmer connects wirelessly to the stimulator to configure stimulation settings and provide stimulation to the patient. The patient remote connects wirelessly to the stimulator to activate stimulation, using only settings previously configured by the clinician programmer.

Stimulation consists of multiple sinusoidal waveforms driven to trial implanted lead electrodes positioned around the spinal column. Programmed stimulation parameters define the amplitude, frequency, phase, and duty cycle of the waveforms generated by the stimulator. Stimulation parameters also define the mapping of the generated waveforms to the lead set contacts.

A single sinusoidal waveform is referred to as a channel, which consists of both a positive and negative output. Channels are configured and activated in pairs,

referred to as clusters. The first channel of a cluster is driven at a base frequency and the second channel at a beat frequency.

8.2 Risk Analysis

Based on pre-clinical testing, Adverse Events that may be associated with the investigational DISCSS™ device include the following:

- Skin infection
- Spinal infection
- Allergic reaction
- Nerve damage
- Tissue inflammation
- Patient discomfort
- Electric shock
- Major tissue damage

Risks associated with the use of the investigational device and commercial device are expected to be comparable.

8.3 Methods to Minimize Risk

Adequate measures have been taken to minimize all of the above risks prior to initiation of a U.S. feasibility clinical study, including proper design specification and review, and preclinical testing.

The study Sponsor will provide appropriate training to each Investigator prior to each site's respective study initiation. Medical professionals will be trained on the selection criteria and protocol for the clinical study prior to their first use of the investigational device. The training will address topics such as the indications and contraindications for the use of the device, management of adverse events, and follow-up care.

Investigators will assess the possible presence of the risks associated with each device during the study treatment and at each follow-up visit by physical examination and participant interview as applicable.

8.4 Rationale for the Investigation

Although many of these risks are significant in nature, they are infrequent. The probability of incidence for any given event is extremely rare. Moreover, if use of the DISCSS™ system produces a successful result, it may reduce the participant's symptoms of pain and dysfunction. Based on these potential benefits, and the anticipated risks, Meagan Medical believes this study is justified.

8.5 Instructions for Use and Administration

Instructions for use of the DISCSS™ System are provided in the DISCSS™ Clinician Use Manual, which will be provided to each Principal Investigator during device use training, and retained in the site's regulatory files for reference during the study.

8.6 Packaging and Labeling

In accordance with federal regulations set forth in 21 CFR 812.5, the DISCSS™ System and User Manual will be labeled with the following statement:

'CAUTION – Investigational Device. Limited by Federal (or United States) law to investigational use.'

8.7 Investigational Product Accountability

The investigational device may only be used in the treatment of participants enrolled in the study. Investigators are responsible for the documented accountability for every investigational device. This includes maintaining the security of device inventory and keeping accurate records of device receipt, usage, and disposition. Each Investigator must adhere to the following:

- Each DISCSS™ trial system will be identified with a unique serial number and assigned to one patient on the trial. Following completion of Visit 5, each device will be returned to Meagan Medical.
- The investigational device may be only administered to patients under the Investigator's personal supervision and treatment, or under the supervision of an authorized sub-Investigator as designated in the Investigator's Agreement and the Delegation of Authority Log.
- The receipt, use, and disposition of the investigational device must be recorded in the Device Accountability Log.
- Complete and accurate accountability records must be kept, which document the receipt and transfer or return of all investigational devices for this study, including number of devices, catalogue part numbers, lot numbers, and names of all site personnel who received, used, transferred or returned the device(s) and associated dates.

  The DISCSS™ trial system serial number will be linked to each patient's Subject ID in the EDC. The Subject Identification Number is the only Subject information entered into the DISCSS™ System during device calibration at Visit 4. Each DISCSS™ System used in this trial is designed to be used with one subject and returned to Meagan Medical upon study completion, unless the system is replaced for any reason during use as described in Section 8.9 Device Complications. In the event of device replacement, the serial number of the replacement device will be recorded on CRFs and entered into the EDC.

8.8 Return of Investigational DISCSS™ Device

As described above, the DISCSS™ System will be returned to Meagan Medical after study completion for each subject for download of the device use log output as described in Appendix III: DISCSS™ Stimulator System Clinician Use Guide "Download Logs." An electronic copy of the device use log output identified by device serial number and subject identification number will be transmitted to the Investigator site for storage with the Subject's records. The device use logs will be uploaded to the database at Meagan Medical for analysis and storage.

8.9 Device Complications

In the event of a device malfunction or complication, subjects will be advised to return to the clinic for evaluation as described in Section 6.7 Unscheduled Visits. The device complications and/or adverse events will be addressed clinically and per the procedures outlined in the protocol Study Procedures Section 6.0, Safety Reporting Section 10.0 and the DISCSS™ Stimulator System Clinician Use Guide. If indicated, the Investigator will adjust the settings on the DISCSS™ Stimulator System or, if necessary replace the DISCSS™ Stimulator System according to the Clinician Use Guide as outlined in Section 8.9. If the complication cannot be resolved, the subject will be discontinued from the study as described in Section 4.6.

All information regarding the adverse event, device malfunction or complication and replacement, as applicable will be captured in the medical records, Case Report Forms and entered into the clinical database. The malfunctioning device will be returned to Meagan Medical where the device use logs will be downloaded and analyzed.

9.0 CONCOMITANT MEDICATIONS/THERAPIES

Study participants will be counseled to stop the use of the following medications throughout the duration of their study participation: warfarin, rivaroxaban, dabigatran, apixaban, edoxaban, enoxaparin, fondaparinux, and aspirin.

10.0 SAFETY REPORTING

10.1 Overview and Definitions

All adverse events associated with the DISCSS™ will be recorded and analyzed. Regulations contained in the FDA and ICH Guidelines will be followed in the identification, reporting and analysis of adverse events.

Adverse Event: An adverse event (AE) is any untoward medical occurrence, disease, injury, or untoward clinical signs (including abnormal laboratory findings, surgical complications, etc.), whether related or unrelated to the investigational device or its use.

Anticipated Adverse Device Effect: Any adverse effect related to the device, which is identified in the protocol prior to study commencement.

Serious Adverse Event (SAE): A Serious Adverse Event is an adverse event which:

- Led to a death,
- Resulted in life threatening illness or injury*
- Resulted in patient hospitalization or prolongation of existing hospitalization,
- Resulted in patient disability or permanent damage or required intervention to prevent permanent impairment/damage
- Led to a congenital abnormality or birth defect

* NOTE: the term "life-threatening" refers to an event in which the patient was at a risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.

Unanticipated Adverse Device Effects (UADE): An Unanticipated Adverse Device Effect is:

1. 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 is not identified in nature, severity, or degree of incidence in this protocol; or
2. Any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of the patients.

10.2 Safety Monitoring

The Sponsor/designee will monitor all adverse event reports to identify and trend all events that would require temporary discontinuation of study enrollment, to fully characterize device safety, to modify the study protocol, or to terminate the study.

10.3 Reporting Procedures for All Adverse Events

All adverse events occurring during the study, whether or not attributed to the DISCSS™ treatment, observed by the Investigator or reported by the participant, will be recorded on the Adverse Event CRF. After review with the participant by the study site personnel, all adverse events will be documented in the participant's source document and on the appropriate CRF pages. The following information must be collected:

- Description of event
- Date of onset
- Date of resolution
- Duration
- Severity
- Relationship to the study device
- Action(s) taken
- Outcome(s)

The Sponsor will make the determination of whether event is anticipated or unanticipated.

The participant should be given appropriate care under medical supervision until symptoms resolve. If the adverse event is of such severity in the Investigator's judgment that it warrants withdrawal from the study, the participant should be withdrawn from treatment and the end of study evaluations should be completed and recorded on Case Report Forms.

10.4 Adverse Event Severity Assessment

Adverse events are described as mild, moderate or severe. The severity of adverse events will be assessed on the following severity index scale:

***Mild*:** The adverse event is transient, requires no treatment, and does not interfere with the participant's daily activity.

***Moderate*:** The adverse event introduces a low level of inconvenience or concern to the participant and may interfere with daily activities, but is usually ameliorated by simple therapeutic measures.

***Severe*:** The adverse event interrupts the participant's usual daily activity and requires systematic therapy or other treatment.

10.5 Relationship to Device or Procedure

The relationship of an adverse event to the study will be graded as follows:

***None*:** The adverse event is not associated with the study device use.

***Remote*:** The temporal association is such that the study device is not likely to have had an association with the observed adverse event.

***Possible*:** This causal relationship is assigned when the adverse event:

a) Follows a reasonable temporal sequence from device use, but
b) Could have been produced by the study participant's clinical state or other modes of therapy administered to the study participant.

***Probable*:** This causal relationship is assigned when the adverse event:

a) Follows a reasonable temporal sequence from device use;
b) Abates upon discontinuation of the treatment;
c) Cannot be reasonably explained by known characteristics of the participant's clinical state.

***Definite*:** This causal relationship is assigned when the adverse event:

a) Follows a reasonable temporal sequence from device use;
b) Abates upon discontinuation of the treatment; and
c) Is confirmed by the reappearance of the adverse event on repeat exposure.

10.6 Timelines for Adverse Event Reporting

Adverse events shall be recorded in the patient's study records and in the EDC on the Adverse Event eCRF within 72 hours of the site becoming aware of the event. The study database will be configured to notify the Sponsor of all adverse events that are indicated to be 'serious'. Serious adverse events (SAEs) will trigger the database to send an email notification to the Sponsor using the contact information provided below.

Sponsor Contact: Bill Carroll
E-mail: BCarroll@RSMedical.com
E-mail: tyearwood@nopaindr.com

The Investigator should provide additional information on the SAE by updating the information on the Adverse Event eCRF as updates become available. The Sponsor may also ask for additional clinical reports including redacted source documents to be provided by the Investigator to assist in the assessment of the event. Significant new information and updates should continue to be submitted promptly to the Sponsor and entered on the Adverse Event eCRF as they become available, and the Investigator should follow the SAE until it is resolved or no further improvement is expected.

The Sponsor shall ensure that the Investigator submits safety event notifications to the governing Investigational Review Board (IRB) within the timeframe specified by the IRB, when applicable. Acceptable means of confirming that the IRB requirements have been met include forwarding a copy of the written, signed report that was sent to the IRB to the Sponsor. Copies of this report should be filed in the Investigator's site files and the Sponsor's clinical investigation files.

10.7 Determination and Reporting of Unanticipated Adverse Device Effects

The Sponsor shall review all reported SAEs to evaluate whether they meet the criteria for an Unanticipated Adverse Device Effect. For adverse events that are determined to be UADEs, the Sponsor will submit an expedited safety report to the FDA's Center for Devices and Radiological Health (CDRH). The expedited safety report will consist of a completed Form FDA 3500A and a cover letter analyzing the significance of the event. The expedited safety report will be submitted to the FDA as soon as possible and, in no event, later than 10 working days after the Sponsor first receives notice of the UADE. A copy of this safety report will be provided to all participating study Investigators.

If, following receipt and investigation of follow-up information regarding an adverse event that was previously determined not to be a UADE, the Sponsor determines that the event does meet the requirements for expedited reporting, the Sponsor will submit a completed Form FDA 3500A and cover letter as soon as possible, but in no event later than 10 working days after this is determined.

10.8 Study Termination

The Sponsor, in consultation with the Investigators, shall determine if the reported event presents an unreasonable risk to study patients. If the event is determined to pose an unreasonable risk, the Sponsor shall develop procedures to terminate the study within 5 working days.

10.9 Treatment of Adverse Events

Adverse events that occur during the study shall be handled by established standards of care to protect the health and safety of the patient. Necessary care shall be provided by the Investigator or designee.

11.0 Protocol Deviations

A protocol deviation is any noncompliance with the clinical protocol or Good Clinical Practice Guidelines. The noncompliance may be either on the part of the participant, the Investigator, or the study site staff. The site must record all protocol deviations with an explanation for the deviation on the appropriate study forms. If required, deviations will be reported to the IRB per the IRB's guidelines.

Minor Deviations: A minor deviation does not impact the participants' rights, safety, or well-being, or the completeness, accuracy or reliability of the study data. Minor deviations shall be documented in the study database along with a full description of the event and outcome. The Sponsor will analyze these deviations and assess their significance. Minor deviations should be reported to the reviewing IRB if required by the IRB's deviation reporting guidelines.

Major deviations: A major deviation is a deviation from the protocol that may impact the participants' rights, safety, or well-being, or the completeness, accuracy or reliability of the study data, or a deviation from FDA regulations or IRB guidelines. Major deviations should be reported to the Sponsor within 24 hours of site awareness of the event and must be documented in the study database along with a full description of the event and outcome. The Sponsor will analyze these deviations and assess their significance. Major deviations should be reported to the reviewing IRB per the IRB's deviation reporting guidelines.

12.0 STATISTICAL CONSIDERATIONS

For this feasibility study, descriptive statistics will be utilized to describe the data for each endpoint. For continuous variables, this include the mean value, change from baseline, standard deviation, and 95% confidence interval. For categorical variables, the rate and a 95% confidence interval will be presented. As there is no comparator group for this clinical study, no hypothesis-based statistical testing is planned. For adverse event information, the

number of events, the number of subjects experiencing events, and the rate of subjects experiencing an event will be presented.

13.0 ETHICS & PROTECTION OF HUMAN SUBJECTS

13.1 Ethical Review

Prior to the start of the study the Investigator will provide the Sponsor or its designee with documentation that the IRB/EC has reviewed and approved the protocol and the Informed Consent Form. Additional documentation may be submitted pending applicable local requirements. Each Investigator must provide at least the following documentation:

- The IRB/EC approval of the protocol.
- The IRB/EC approval of the Informed Consent Form.
- The IRB/EC annual (or any other frequency when applicable – i.e. quarterly, semiannually according to the local IRB standard operating procedure) renewed approval of the protocol.
- The IRB/EC approval of any revisions to the Informed Consent Form or amendments to the protocol.

13.2 Regulatory Considerations

This study will be conducted in accordance with the Good Clinical Practice (GCP) guidelines and applicable regulatory requirements (FR, ICH, E3-E6 ISO14155) including but not limited to:

- The Food and Drug Administration (FDA) Regulations on Investigational Device Exemption (21 CFR 812),
- The FDA Regulations on research with human beings (21 CFR 50 and 56),
- The Health and Human Services (DHHS) Regulations on research with human beings (45 CFR 46 Subparts A, B, C, and D) and
- The International Conference on Harmonization (ICH) "Guidance for Industry-E6 Good Clinical Practice: Consolidated Guideline."

13.3 Informed Consent

The Informed Consent Form (ICF) for this study will be prepared in accordance with FDA 21 CFR Part 50. The ICF will be used to explain the possible risks and benefits to the patient in simple terms before the patient is entered into the study. The ICF will contain a statement that the consent is freely given, that the patient is aware of the risks and benefits of entering the study, and that the patient is free to withdraw from the study at any time. The ICF will need to be reviewed and approved by the Sponsor or its designee prior to the IRB/EC submission. All appropriate bills/ legislative actions are to be considered and the ICF amended, as appropriate (e.g. California Bill of Rights is to be on the forefront of the ICF if study conducted in California).

Prior to a patient's participation in the study, the written ICF will be signed and personally dated by the patient or by the patient's legally acceptable representative, and witnessed by the person who conducted the informed consent discussion. If a patient is unable to read or if a legally acceptable representative is unable to read, an impartial

witness will be present during the entire consent discussion. After the written ICF and any other written information to be provided to the patient is read and explained to the patient or legal representative, and oral consent to the patient's participation in the study has been given by the patient, the witness will sign and date the ICF.

The Investigator must document acquisition of patient consent in the patient's medical records, and the patient or legal representative must be given a copy of the ICF document prior to enrollment into the study.

The Investigator is required to report any failure to obtain patient consent to the IRB/EC and the Sponsor or its designee, within 24 hours of learning of such an event.

13.4 Participant and Data Confidentiality

The study will be conducted in accordance with the Privacy Rule (45 CFR Parts 160 and 164) of the Health Insurance Portability and Accountability Act of 1996 (HIPAA).

Participating Investigators, their staff, the sponsor(s) and their agents will extend all efforts to maintain participant confidentiality. The study protocol, documentation, data, and all other information generated for the study will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party without prior written approval of the Sponsor. The study monitor, other authorized representatives of the sponsor, representatives of the IRB may inspect all documents and records required to be maintained by the Investigator, including but not limited to medical records and study documentation for the participants in this study. The clinical study site will permit access to such records.

The study participant's contact information will be securely stored at each clinical site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long as dictated by the IRB and for at 2 years following the date a marketing application is approved for the device for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until 2 years after the investigation is discontinued and FDA is notified.

All participant data will be identified by Participant Identification Numbers. Participant Identification Numbers will be assigned in a XX-YYY format, where XX = a unique site identification number and YYY = a unique patient identification number.

The only information entered into the DISCSS™system is the Subject Identification Number, which is linked to the serial number of the device by a Study-specific log and entered into the EDC.

14.0 CLINICAL MONITORING

The Sponsor's Clinical designee (the CRO) will perform the clinical study monitoring. The CRO's staff will be trained and have the scientific and clinical knowledge needed to monitor the study appropriately.

Monitoring will include pre-investigational site Visits (Site Qualification Visit and Site Initiation Visit), Interim Monitoring Visits and a Close-out Visit. Monitoring will occur as frequently as needed to assure proper conduct of the protocol.

Interim Monitoring visits will be performed as frequently as needed in order to assure appropriate study implementation. Monitoring visits will be documented on monitoring visit reports, and will aim to verify that:

- Compliance with the clinical protocol and applicable regulations is being maintained
- Only authorized site individuals are participating in study activities
- The investigational device is being used according to the protocol and instructions for use
- Adequacy of staffing and facilities
- Adequate access of site to eligible patients
- Signed and dated informed consent forms have been obtained from each patient
- eCRFs and queries are complete
- Source data is verified and signed-off upon as accurate
- Patient files are accurate and complete
- All adverse events are reported to the Sponsor
- All serious and unanticipated adverse device events are reported to the Sponsor and the IRB/EC
- All other required reports, notifications, applications, submissions, and correspondence are maintained in the Investigator's files and are accurate
- Maintenance and calibration of equipment relevant to clinical assessments is appropriately performed and documented
- Patient withdrawal has been documented (if applicable)
- Patient non-compliance has been documented (if applicable)
- The Investigator and site staff are informed and knowledgeable of all relevant document updates concerning the clinical investigation
- Corrective and preventive actions have been implemented (if applicable)

Each site's Investigator will allocate adequate time for monitoring activities. The Investigator will also ensure that the monitor or other compliance or quality assurance reviewer is given access to the study-related documents and study related facilities, and has adequate space to conduct the monitoring visit.

15.0 STUDY TRAINING

Training of study site personnel will be initiated prior to the protocol being implemented. All participating Investigators and coordinators will under a comprehensive training with the DISCSS™ device and trained on its components. Training will consist of both lecture and practicum. Application of DISCSS™ procedure will be performed only by PI or

his/her designee following formal device training by the Sponsor or the Sponsor's designee. Training materials for the Clinician and for the Subject will be provided by Meagan Medical.

16.0 DATA HANDLING AND RECORDKEEPING

16.1 Source Documents

Each participating site will maintain appropriate medical and research records for this trial, in compliance with ICH E6 and regulatory and institutional requirements for the protection of confidentiality of participants.

Source data include all information, original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Examples of these original documents and data records include, but are not limited to hospital records, clinical and office charts, device logs, memoranda, recorded data from automated instruments, study-specific source worksheets, and copies or transcriptions certified after verification as being accurate and complete.

16.2 Data Collection and Management Responsibilities

Source documents and electronic Case Report Forms (eCRFs) will be completed in a 21 CFR Part 11 compliant electronic data capture (EDC) system for each patient enrolled into the clinical study. The Study Coordinator will review and sign off on completed eCRFs to attest that all data entered on the eCRFs are complete and accurate after the monitor finishes the source document verification process. The Investigator will sign off on the Eligibility Criteria, all Adverse Event, and Protocol Deviation and Study Completion eCRFs and will sign each patient's casebook once the patient completes the study to attest that all data entered on the eCRFs are complete and accurate. All of the above signatures will be completed digitally within the EDC system using the system's Part 11 compliant digital signature system function.

Any required data clarifications will be handled within the EDC system's query management system. The EDC will be programmed to automatically issue data clarification queries on missing values and values out of acceptable ranges. Study monitors and data managers will also be able to add data clarification queries to data points within the system. Study coordinators will have the opportunity to correct data and/or respond to the query for review by monitors and data managers.

16.3 Study Records Retention

The Investigator and Sponsor will maintain records in accordance with 21 CFR 812, Subpart G, to include:

- Current and past versions of the IRB-approved clinical protocol and corresponding IRB-approved consent form(s) and, if applicable, patient recruitment advertisements

- FDA correspondence related to the IDE application; including supplemental IDE applications, current Investigator lists, progress reports
- IRB correspondence (including approval notifications)including safety and protocol deviation reports, and annual or interim reports
- Signed Investigator Agreements and financial disclosure forms for participating Investigators
- Curriculum vitae (Investigator and Sub-Investigators)
- Certificates of required training for Investigators and Sub-Investigators, including human subject protection and Good Clinical Practice
- Instructions for handling the investigational device and other study-related materials
- Signed Informed Consent Forms
- Source Documents
- Monitoring visit reports
- Copies of relevant Sponsor-Investigator correspondence, including notifications of adverse event information
- Screening and Enrollment Log
- Final clinical study report

The sponsor and study Investigators will retain all study records and reports for up to two years after the marketing application is approved for the investigational device; or, if a marketing application is not submitted or approved for the investigational device, until two years after investigations under the IDE have been discontinued and the FDA so notified.

16.4 Collection, Transfer and Archiving of Radiographic Imaging Data

Radiographic imaging will be taken to confirm the location of implanted percutaneous trial leads during Visit 2 when the percutaneous trial leads are implanted, Visit 4 at the initiation of the investigational study phase with the DISCSS™ device, and Visit 5 to confirm lead placement and successful percutaneous trial lead removal. A radiograph of the marked insertion point will be taken. Documentation of the lead placement will be generated and maintained with the subject's records on site. At Visit 4, any lead migration or abnormalities will be noted on the radiology report. The de-identified image will be saved electronically (via DICOM files or equivalent) for transfer to Meagan Medical at the conclusion of the study. All imaging data will also be maintained at the clinical site.

16.5 Transfer and Storage of Device Use Log

The Investigator will return each device to Meagan Medical after study completion for each subject. Only one device will be used per subject per site. The devices are uniquely identified by serial number. Both Subject ID and Serial Number will be recorded on Case Report Forms and entered into the clinical database. Meagan Medical will download a copy of the Device Use Log and upload the logs into the clinical database.

An electronic copy identified by Subject Identification Number and Device Serial Number will be provided to the investigative site for their records.

16.6 Publication and Data Sharing Policy

Any Investigator involved with this study is obligated to provide the Sponsor with complete test results and all data derived from the study. Investigators are not permitted to publish or share the results or any part of the results of this study, nor any of the information provided by the Sponsor for the purposes of performing the study, to any third party without the consent of Meagan Medical, Inc.

17.0 AUDITS AND INSPECTIONS

Sites may be audited by the Sponsor or Sponsor designee, by IRBs, the Office of Human Research Protection or FDA during this trial. The investigational site will provide direct access to all trial related files, source documents, and reports for the purpose of monitoring and auditing by the sponsor and inspection by local and regulatory authorities.

18.0 PUBLICATION PLAN

The study will be registered on Clinicaltrials.gov in compliance with 42 CFR Part 11. Results of the study, including negative outcomes or an unanticipated early termination of the trial, will be posted to the Clinicaltrials.gov database at the conclusion of the study. In the event that the study is terminated early, the posting of these results will be completed within 30 days of completion of data analysis.

19.0 LITERATURE REFERENCES

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3. Kapural L, Yearwood TL, et al. Novel 10-kHz High-frequency Therapy (HF10 Therapy) Is Superior to Traditional Low-frequency Spinal Cord Stimulation for the Treatment of Chronic Back and Leg Pain. Anesthesiology. 2015; 123: 851-860.
4. Kapural L, Yearwood TL, et al. Comparison of 10-kHz High-Frequency and Traditional Low-Frequency Spinal Cord Stimulation for the Treatment of Chronic Back and Leg Pain: 24-Month Results From a Multicenter, Randomized, Controlled Pivotal Trial. Neurosurgery. 2016; 79: 667-677.
5. North RB, Wetzel FT. Spinal Cord Stimulation for Chronic Pain of Spinal Origin: A Valuable Long-Term Solution. Spine. 2002; 27: 2584-2591.
6. Taylor RS, Van Buyten JP, Buchser E. Spinal cord stimulation for chronic back and leg pain and failed back surgery syndrome: a systematic review and analysis of prognostic factors. Spine. 2005; 30: 152-160.
7. Kumar K, Taylor R, Jacques L, et al. Spinal cord stimulation versus conventional medical management for neuropathic pain: a multicenter randomized controlled trial in patients with failed back surgery syndrome. Pain 2007; 132: 179-188.

20.0 APPENDICES

Appendix I: Informed Consent Form

Appendix II: DISCSS™ Stimulator System User Guide

Appendix III: DISCSS™ Stimulator System Clinician Use Guide