PROTOCOL TITLE:	**The MOTION™ Study**
SPONSOR:	**Vertos Medical, Inc.** **95 Enterprise, Suite 325** **Aliso Viejo, CA 92656**
SPONSOR CONTACTS:	**Karen Davis** **Vice President of Clinical Research** **Vertos Medical, Inc.**
PURPOSE:	**This study is a prospective, multicenter, randomized controlled clinical study examining functional improvement (defined by increased activity levels e.g. walking time) in lumbar spinal stenosis patients with neurogenic claudication who are treated with the MILD® procedure.**
[redacted]	[redacted]
NCT #:	**NCT03610737**
Date:	**November 18, 2020**

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1 PROTOCOL SYNOPSIS

Vertos MEDICAL — PROTOCOL SYNOPSIS	
Title: The MOTION™ Study	
Purpose: [redacted]	
Study Design: Prospective, multicenter, randomized controlled clinical study examining functional improvement in lumbar spinal stenosis (LSS) patients with neurogenic claudication who are treated with the MILD procedure plus conventional medical management (CMM), Study Group, compared to those treated with CMM alone, as the control. [redacted]	
Objective: To evaluate long-term functional improvement following treatment with MILD plus CMM, compared to CMM alone in subjects with painful LSS and neurogenic claudication.	
Number of Subjects: Approximately 150 subjects [redacted]	**Number of Study Centers:** Up to 20 centers in US
[redacted]	[redacted]
Randomization:	

Control Group: CMM alone (without MILD). [redacted]

Treatment Group: MILD plus CMM.

[redacted]

Entry Criteria

Inclusion Criteria:

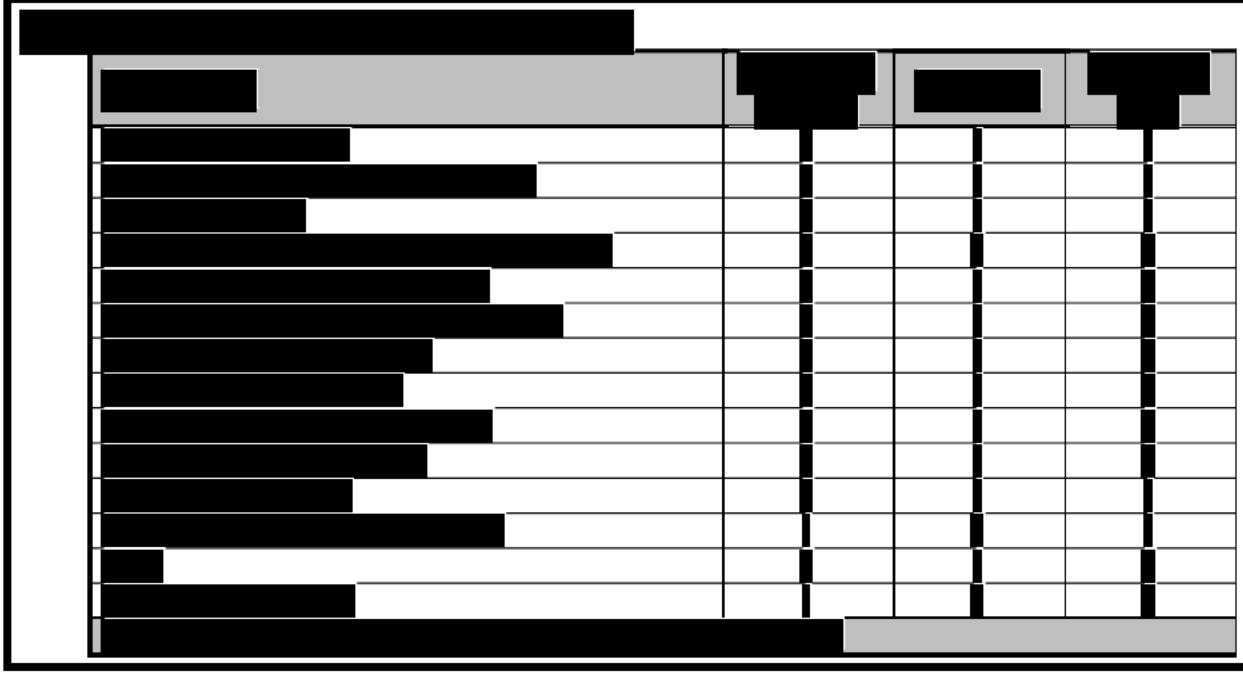
1. Age 50-80
2. Patients experiencing neurogenic claudication symptoms for at least 3 months duration.

[redacted]

   b. Radiologic evidence of LSS with unilateral or bilateral ligamentum flavum ≥ 2.5mm in thickness[2] confirmed by pre-op MRI or CT performed within 12 months of baseline visit.
3. Patients with comorbid conditions commonly associated with spinal stenosis, such as osteophytes, facet hypertrophy, minor spondylolisthesis (Grade I without instability), foraminal stenosis, and/or disk protrusion may be included unless the medical monitor and the treating physician has determined that the condition is too advanced.
4. Stable opioid intake with no change during 30 days prior to enrollment.
5. Available to complete all follow-up visits.

Exclusion Criteria:

1. ODI Score < 31 (0-100 ODI Scale).
2. NPRS Score < 5 (0-10 NPRS Scale).
3. Lumbar epidural steroid injections during eight weeks prior to study enrollment.
4. Baseline analgesic medication greater than 90 milligram morphine equivalent (MME) per day.
5. Prior surgery at the same treatment level.
6. Previously received interspinous spacer at the same treatment level.
7. Previously received intradiscal procedure at the same treatment level.
8. Previously received vertebral augmentation procedure at the same treatment level.
9. Previously received the MILD procedure at the same treatment level.
10. Received radiofrequency ablation at the same or the adjacent levels within 6 months prior to study enrollment.
11. History of spinal fractures with current related pain symptoms.
12. Grade II or higher spondylolisthesis.
13. Motor deficit or disabling back and/or leg pain from causes other than LSS neurogenic claudication (e.g. acute compression fracture, metabolic neuropathy, or vascular claudication symptoms, etc.).
14. Unable to walk ≥ 10 feet unaided before being limited by pain. In this context, 'unaided' means without the use of a cane, walker, railing, wall, another person or any other means of walking assistance.
15. Previously randomized and/or treated in a similar clinical study.
16. Epidural lipomatosis (if it is deemed to be a significant contributor of canal narrowing by the medical monitor and the treating physician).
17. On (or pending) Workman's Compensation or in active litigation or known to be considering litigation associated with back pain.



Statistical Analysis:
Continuous data will be summarized using descriptive statistics: mean, standard deviation, median, minimum and maximum. Categorical variables will be summarized using frequency counts and percentages. For events that can occur more than once in a single subject (e.g., adverse events), the percentage will be based on subjects experiencing the event, and both patient and event counts will be reported. All hypothesis testing will be performed using a two-sided test at a 0.05 level of significance or a one-sided test at a 0.025 level of significance.

Data will be analyzed on an Intent-to-Treat basis, under which analyses will be performed according to randomized assignment irrespective of the treatment actually received. Consented patients who withdraw consent prior to randomization, or who are found not to meet the inclusion/exclusion criteria prior to randomization will not be included in the Intent-to-Treat population. The primary analysis will consist of all available data evaluated under Intent-to-Treat principles, referred to in ICH E9 ("Statistical Principles for Clinical Trials") as the *full analysis set*. An "as treated" analysis will also be performed which will report results based on treatment actually received.

[redacted]

2 STUDY DESIGN RATIONALE AND COMPLIANCE

2.1 STUDY DESIGN RATIONALE

This is a prospective, multi-center, randomized controlled clinical study examining functional improvement in lumbar spinal stenosis (LSS) patients with neurogenic claudication who are treated with the MILD procedure plus conventional medical management (CMM) compared to those treated with CMM alone, as the control. [redacted]

[redacted]

The MILD procedure provides minimally invasive lumbar decompression performed fluoroscopically through a small 6-gauge port. MILD is performed with only local anesthetic and moderate sedation, and leaves no implants behind. MILD offers an option for LSS patients experiencing symptoms refractory to more conservative therapies.

2.2 STUDY COMPLIANCE

In this study, under an IRB-approved patient informed consent, patient-reported outcomes over a 24-month study period following treatment will enable an assessment of each patient's functional status. [redacted]

In compliance with the US Federal Regulations, comments regarding product use and preference that meet the definition for product complaints should be reported to and evaluated by the sponsor. Any occurrence of at least possibly device-related adverse events

will be managed by the investigators, hospital, study principal investigator (SPI), and sponsor in accordance with the applicable reporting Regulations. Events arising from the MILD procedure meeting the definition of the MDR requirement will be reported to the FDA and the IRB where required. Documentation of significant adverse events, including unexpected and severe adverse events related to the procedures, will be in compliance with ICH guidelines for Good Clinical Practices.

3 TREATMENT DESCRIPTION

3.1 TEST DEVICE - MILD

The MILD devices, manufactured by Vertos Medical, Inc., and procedure will be used in this study. Vertos Medical has received U.S. Food and Drug Administration 510k clearance to market the MILD devices for use in lumbar decompression procedures to treat various spinal conditions.

The MILD system is designed to access the interlaminar space from the posterior lumbar spine, enabling the user to remove small portions of the lamina and preferentially resect and debulk the thickened ligamentum flavum, accomplishing a lumbar decompression. The MILD device kit is a sterile, single-use system of surgical tools consisting of the components described in Figure 1 below.

1. MILD Portal
2. MILD Trocar and Handle
3. MILD Portal Stabilizer
4. MILD Depth Guide
5. MILD Bone Sculpter Rongeur
6. MILD Tissue Sculpter
7. MILD Surgical Clamp

Figure 1: MILD Device Kit

3.1.1 MILD Procedure

The MILD procedure is performed minimally-invasively under fluoroscopic image guidance through a dorsal approach to the spine. At the beginning of the MILD procedure, patients are placed in the prone position with a slight flexion, not to exceed 20 degrees. Following epidurography, partial decompression is performed through the removal of tissue and bone at the symptomatic level confirmed with correlated MRI and clinical findings. Pre and post procedure imaging with contrast (epidurogram) will be performed with the patient in the same position for both. All procedures will be conducted in accordance with the product labeling and indications for use.

3.2 Conventional Medical Management (CMM)

CMM involves treatment with one or more conservative therapies that are commonly used for treatment of LSS with neurogenic claudication. The study investigators at each site will determine what CMM is appropriate for each patient. [redacted]

4 STUDY OBJECTIVE

The key objective of this study is to evaluate long term functional improvement following treatment with MILD plus CMM, compared to CMM alone in subjects with painful LSS and neurogenic claudication. Comprehensive safety will also be evaluated and reported.

[redacted]

[redacted]

5 STUDY DESIGN

This study is a prospective, multicenter, randomized controlled clinical study examining functional improvement (defined by improvement in ODI) in LSS patients with neurogenic claudication who are treated with MILD plus CMM compared to those treated with CMM alone, as the control. [redacted]

5.1 NUMBER OF SITES AND SUBJECTS

To ensure that the study is adequately powered, up to 150 subjects will be enrolled at approximately 20 sites. All sites will be located in the United States. Each participating investigational site will be allowed to enroll up to 20 subjects who meet all study eligibility criteria. Additional subjects may be enrolled with sponsor approval.

5.2 STUDY DURATION

Subjects who meet the inclusion / exclusion criteria may be enrolled [redacted] The screening/baseline visit and CMM procedures may take place at the investigator's medical office. MILD procedures will be performed at the treating ambulatory surgery centers or hospital. Subjects will be requested to return for follow-up at a location designated by research staff.

5.3 STUDY POPULATION

The study population will consist of subjects who are suffering from LSS with neurogenic claudication, and who meet the study selection and symptomatic diagnosis criteria.

5.4 SUBJECT INCLUSION/EXCLUSION CRITERIA

5.4.1 Inclusion Criteria

1. Age 50-80
2. Patients experiencing neurogenic claudication symptoms for at least 3 months duration.
   [redacted]
3. Patients with comorbid conditions commonly associated with spinal stenosis, such as osteophytes, facet hypertrophy, minor spondylolisthesis (Grade I without instability), foraminal stenosis, and/or disk protrusion may be included unless the medical monitor and the treating physician has determined that the condition is too advanced.
4. Stable opioid intake with no change during 30 days prior to enrollment.
5. Available to complete all follow-up visits.

5.4.2 Exclusion Criteria

1. ODI Score < 31 (0-100 ODI Scale).
2. NPRS Score < 5 (0-10 NPRS Scale).
3. Lumbar epidural steroid injections during eight weeks prior to study enrollment.
4. Baseline analgesic medication greater than 90 milligram morphine equivalent (MME) per day.
5. Prior surgery at the same treatment level.
6. Previously received interspinous spacer at the same treatment level.
7. Previously received intradiscal procedure at the same treatment level.
8. Previously received vertebral augmentation procedure at the same treatment level.

9. Previously received the MILD procedure at the same treatment level.
10. Received radiofrequency ablation at the same or the adjacent levels within 6 months prior to study enrollment.
11. History of spinal fractures with current related pain symptoms.
12. Grade II or higher spondylolisthesis.
13. Motor deficit or disabling back and/or leg pain from causes other than LSS neurogenic claudication (e.g. acute compression fracture, metabolic neuropathy, or vascular claudication symptoms, etc.).
14. Unable to walk ≥ 10 feet unaided before being limited by pain. In this context, 'unaided' means without the use of a cane, walker, railing, wall, another person or any other means of walking assistance.
15. Previously randomized and/or treated in a similar clinical study.
16. Epidural lipomatosis (if it is deemed to be a significant contributor of canal narrowing by the medical monitor and the physician).
17. On (or pending) Workman's Compensation or in active litigation or known to be considering litigation associated with back pain.

6 STUDY PROCEDURE

6.1 PATIENT SELECTION AND BASELINE VISIT

Selection begins with a screening process when the patient is examined by their physician. Once the investigator has determined that the patient is potentially eligible for treatment in the study, the consent should be reviewed with the patient, questions answered, and the patient should be asked to sign the Informed Consent document. The eligibility of a patient for treatment in this study will be determined after all enrollment criteria have been satisfied.

[redacted] Only after these steps are

completed, all enrollment criteria are met and an informed consent signed, will the patient be officially enrolled into the study.

6.2 RANDOMIZATION

[redacted] Subjects will be randomly assigned in equal number (1:1) to one of two treatment arms: 1) MILD procedure plus CMM or 2) CMM only. [redacted] Based on the information provided, the system will automatically generate the assigned treatment.

6.3 BASELINE ASSESSMENT

The following baseline assessments for all patients should be confirmed, completed and recorded in the medical records and on the appropriate Case Report Forms (CRFs) where applicable.

[redacted]

6.4 TREATMENT

[redacted] Subjects will be treated with either MILD plus CMM or CMM alone based on randomization results.

6.4.1 MILD Procedure plus CMM

Physicians performing the MILD procedures are trained by Vertos on the proper labeling use of the MILD devices. [redacted]

6.4.2 CMM Alone

Study investigator will determine the appropriate CMM therapy or therapies during the course of the study for subjects assigned to CMM Alone. [redacted]

[redacted]

6.5 FOLLOW-UP PHASE

Subjects will complete all follow-up assessments listed below for each follow-up visit.

[redacted]

[redacted]

6.8 Pain Management

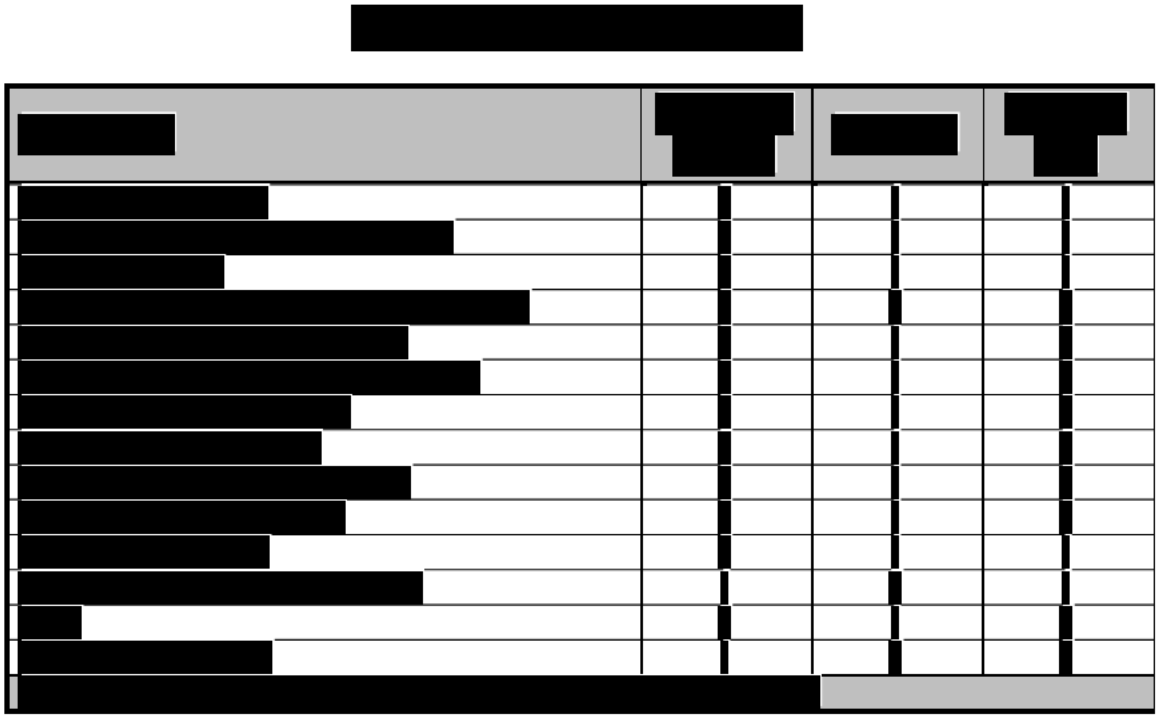
In addition to CMM therapies, investigators may use narcotic and non-narcotic analgesics as needed by subjects according to the standard of care and if used for leg/back pain, shall be recorded at baseline and follow-up visits on the appropriate CRFs/eCRFs. [redacted]

6.9 Study Schedule

[redacted]

At baseline, prior therapies will be documented, including frequency, duration, type of therapy Documentation of analgesic use for the treatment of neurogenic claudication symptoms will include frequency and dosage. [redacted]

Device/Procedure-related unexpected complications and significant adverse events will be documented throughout the study period.



7 RISKS / BENEFIT ASSESSMENT

Both the MILD and CMM treatments carry risks of complications with the procedure and recovery. This study is considered an evaluation of marketed treatments, neither of which is a 'study' or 'investigation'.

MILD offers an option for LSS patients experiencing symptoms refractory to more conservative therapies. The Vertos MILD devices were cleared by the FDA for marketing in the USA in December 2006 under a 510(k). Procedural risks are reduced by physician training and by performing the procedure under direct fluoroscopic visualization. The MILD devices are radiopaque to provide ease of x-ray imaging and placement within the body during the procedure. Conformance with the product labeling and instructions for use will minimize these risks.

Potential risks and benefits for all therapies offered in this study are listed in Table 2.

Table 2: Procedure Risks and Benefits

Therapy	Benefits	Risks/Side Effects

Physical Therapy (PT): Passive PT includes heat and cold therapy, Iontophoresis, tens, and ultrasound. Active PT includes exercise and stretching.[13]	• Non-surgical therapy that may provide relief of lower back and limb symptoms in patients with neurogenic claudication • Muscle strengthening • Correction of posture • Reduction of inflammation • Reduction of muscle spams	• Fatigue • Muscle ache • Increase lower back • Soreness • Swelling • Increase in localized pain • Decrease in immunity due of the suppressive effect of the steroid
Nerve Blocks: • **Epidural steroid injection:** Minimally invasive procedure that delivers steroids into the epidural space around spinal nerve roots to relieve pain.[20] • **Facet joint injection:** Minimally invasive procedure using fluoroscopy for guidance and delivery of medication to relieve pain.[14] • **Trigger point injection:** Minimally invasive procedure used to treat painful areas of muscle that contain trigger points, or knots of muscle that form when muscles do not relax.[15] • **Medial branch injection:** Minimally invasive procedure in which an anesthetic is injected near small medial nerves connected to a specific facet joint.[16] • **Sacroiliac joint injection:** Minimally invasive procedure used either to diagnose or treat low back pain and/or sciatica symptoms associated with sacroiliac joint dysfunction.[17]	• Potential relief of lower limb symptoms in patients with neurogenic claudication • Shorter procedure time versus more invasive open or endoscopic surgical decompression • Quick recovery following treatment, which may allow patients to return home same day as procedure • No requirement for general anesthesia • Less likelihood of significant complications versus open surgical procedures. • No requirement for sutures	• Increase in localized pain • Headaches or fever • High blood sugar • Decrease in immunity due to the suppressive effect of the steroid • Increased intraocular pressure or cataracts • Anxiety/sleeplessness • Increased risks of osteoporosis • Increased risk of avascular necrosis • Exacerbation of diabetes • Exacerbation of hypertension • Numbness or slight weakness • Allergic reaction, rash, itching • Weight gain • Increase in energy • Soreness at injection site • Bleeding • Infection • Worsening of pain symptoms • Nerve or spinal cord damage or paralysis • Shrinkage of fat under skin • Death (in rare cases)
Radiofrequency ablation: Minimally invasive procedure that uses electrical current to heat a small area of nerve tissue for the purpose of	• Potential relief of lower limb symptoms in patients with low back pain	• Transient sunburn type pain • Pain or discomfort around the area treated • Numbness of skin covering the area treated

decreasing pain signals from that specific area.[18,19]	• Shorter procedure time versus more invasive open or endoscopic surgical decompression • Quick recovery following treatment, which may allow patients to return home same day as procedure • No requirement for general anesthesia • Less likelihood of significant complications versus open surgical procedures • No requirement for sutures	• Worsened pain due to muscle spasm in the area treated • Permanent nerve pain • Allergies or reactions to medications used • Infection
MILD Procedure: Minimally invasive procedure that provides partial decompression through the removal of tissue and bone at the symptomatic level[20]	• Potential relief of lower limb symptoms in patients with neurogenic claudication • Shorter procedure time versus more invasive open or endoscopic surgical decompression • Quick recovery following treatment, which may allow patients to return home same day as procedure • No requirement for general anesthesia • Less likelihood of significant complications versus open surgical procedures • No requirement for sutures	• Soreness at surgical site • Nerve injury (e.g., partial or complete paralysis, paresthesia, radiculopathy) • Injury to adjacent bony or soft tissue structures • Infection requiring surgical intervention • Inadequate pain relief • Allergic reaction and/or side effects from medications (e.g., constipation, gastrointestinal distress) • Dural tear or puncture • Bleeding (e.g. epidural hematoma)

7.1 Risks to Confidentiality of Study Subjects

Patient confidentiality will be maintained under HIPAA Privacy Rules by de-identifying personal subject information and following the applicable Good Clinical Practice guidelines for clinical research.

8 ADVERSE EVENTS

Subject safety is of the utmost importance. Each investigator has the responsibility for the safety of the subjects under his/her care. Throughout the course of the study, all significant study related adverse events will be documented and monitored on an adverse event CRF/eCRF, including seriousness, severity, treatment, and relationship to the study device/procedure.

8.1 ADVERSE EVENT

An adverse event (AE) is any undesirable experience (sign, symptom, illness, abnormal laboratory value, or other medical event) occurring to a patient, whether or not considered related to the study product(s) prescribed as part of the protocol, that is identified or worsens during a clinical study. Any current condition that is recorded as a pre-existing condition, unless there is a change in nature, severity, or degree of incidence, is not an AE.

[redacted]

8.2 SERIOUS ADVERSE EVENT

A serious adverse event (SAE) is an AE that:

- Led to death,
- Led to serious deterioration in the health of the subject, that resulted in
    1) a life-threatening illness or injury, or
    2) a permanent impairment of a body structure or a body function, or
    3) in-patient or prolonged hospitalization, or
    4) medical or surgical intervention to prevent permanent life-threatening illness or injury or permanent impairment to a body structure or a body function.
- Led to fetal distress, fetal death or a congenital anomaly or birth defect

The investigator must determine whether each event meets the definition of a "serious" adverse event. All SAEs must be reported on the CRFs/eCRFs, regardless of relationship, or lack thereof, to the device/procedure.

All other events that are considered medically serious by the investigator should be reported immediately to the study sponsor.

Planned hospitalization for a pre-existing condition, or a procedure required by the protocol, without serious deterioration in health, is not considered an SAE.

8.2.1 Serious Adverse Device Effect

A serious adverse device effect (SADE) is an adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event. An anticipated serious adverse

device effect (ASADE) is an effect which by its nature, incidence, severity or outcome has been identified in the risk analysis report.

8.2.2 Unanticipated Adverse Device Effect

An unanticipated adverse device effect (UADE) means any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the study protocol or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects. (21 CFR 812.3 (s)).

8.3 Severity of Adverse Events

The severity of an AE is a qualitative judgment of the degree of intensity, as determined by the Investigator or as reported by the subject. The severity of the AE should be evaluated according to the following scale:

- **Mild:** No limitation of usual activities, no therapy or only symptomatic therapy required to treat the injury or illness.
- **Moderate:** Some limitation of usual activities or specific therapy is required.
- **Severe:** Inability to carry out usual activities, hospitalization, emergency treatment, life threatening events, or death.

The assessment of severity should be made independent of the relationship to the investigational device and therapy or the seriousness of the event.

[redacted]

Only those possibly related or definitely related will be reported in EDC for this study unless the AE is determined to be an SAE. All SAEs will be reported in EDC regardless of relationship, or lack thereof, to the study devices/procedures.

8.5 Reporting of Adverse Events

Subjects will be carefully monitored during the study for possible AEs. Any AE observed should be fully evaluated by the investigator. Collection of related AEs and all SAEs will

commence from the time the patient has the study procedure. Routine collection of AEs will continue until Study Completion or Termination visit.

At each study visit, the investigator will assess whether any device/procedure related AEs or SAEs have occurred. Subjects may report AEs occurring at any other time during the study.

All subjects experiencing AEs, whether considered associated with the device and/or procedure or not, must be monitored until the symptoms subside and have returned to baseline or until there is a satisfactory explanation for the changes observed. All AEs will be documented on the Adverse Event CRF, when the investigator concludes the event to be either possibly or definitely related to the study device/procedure, and/or the AE is serious. The event term, start and stop date and severity will be documented, along with the investigator's opinion of the nature of the causal relationship between the event and the device/procedure.

UADEs have special reporting requirements. investigator and sponsor will follow adverse device effects reporting requirements per CFR Title 21 Part 803:

Investigator Report: If a subject experiences an UADE, the investigator must notify sponsor within 24-hours of receiving knowledge of the event, and the IRB/EC as soon as possible, but no later than the deadline specified by IRB/Ethics Committee (EC) reporting policy.

Sponsor Report: UADEs will be reported to FDA, all reviewing IRB/ECs, and participating investigators as soon as possible, but no later than 10 working days, after receiving notice of the UADE(s).

As with any AE outside of the study, all AEs should be followed up until resolution or until the investigator judges that further follow-up is not necessary.

The investigator must follow their local IRB policy for AE reporting. Such events may be reportable to the FDA under the Medical Device Reporting Regulation. Product complaints related to the MILD devices will be documented and investigated per Vertos quality policy.

9 GENERAL STATISTICAL METHODOLOGY

All subjects who are treated will be evaluated for safety regardless of whether or not the procedure is aborted or the patient withdraws prior to the completion of all post-treatment evaluations.

Continuous data will be summarized using descriptive statistics: mean, standard deviation, median, minimum and maximum. Categorical variables will be summarized using frequency counts and percentages. For events which can occur more than once in a single subject (e.g., adverse events), the percentage will be based on subjects experiencing the event, and both patient and event counts will be reported. All hypothesis testing will be performed using a two-sided test at a 0.05 level of significance or a one-sided test at a 0.025 level of significance.

Data will be analyzed on an intent-to-treat (ITT) basis, under which analyses will be performed according to randomized assignment irrespective of the treatment actually received. Consented patients who withdraw consent prior to randomization, or who are found not to meet the inclusion/exclusion criteria prior to randomization will not be included in the ITT population. The primary analysis will consist of all available data evaluated under ITT principles, referred to in ICH E9 ("Statistical Principles for Clinical Trials") as the full analysis set. An as-treated analysis will also be performed for the primary efficacy endpoint which will report results based on treatment actually received irrespective of randomization.

9.1 Primary Efficacy Endpoint

The study will test the hypothesis that the primary endpoint among subjects randomized to the MILD arm will have superior (that is, more favorable changes on the ODI) outcomes compared to those randomized to CMM. Rejection of the below null hypothesis is consistent with the superiority of the MILD treatment:

$$H_0: \mu_{MILD} - \mu_{CMM} \leq 0$$

$$H_A: \mu_{MILD} - \mu_{CMM} > 0$$

where μ_{MILD} and μ_{CMM} are the mean values of the primary endpoint as defined above, for subjects in the MILD and CMM groups, respectively. Since lower scores represent favorable outcomes in the ODI scoring system, the endpoint is defined using baseline score minus follow-up score, so that positive values indicate improvement from baseline.

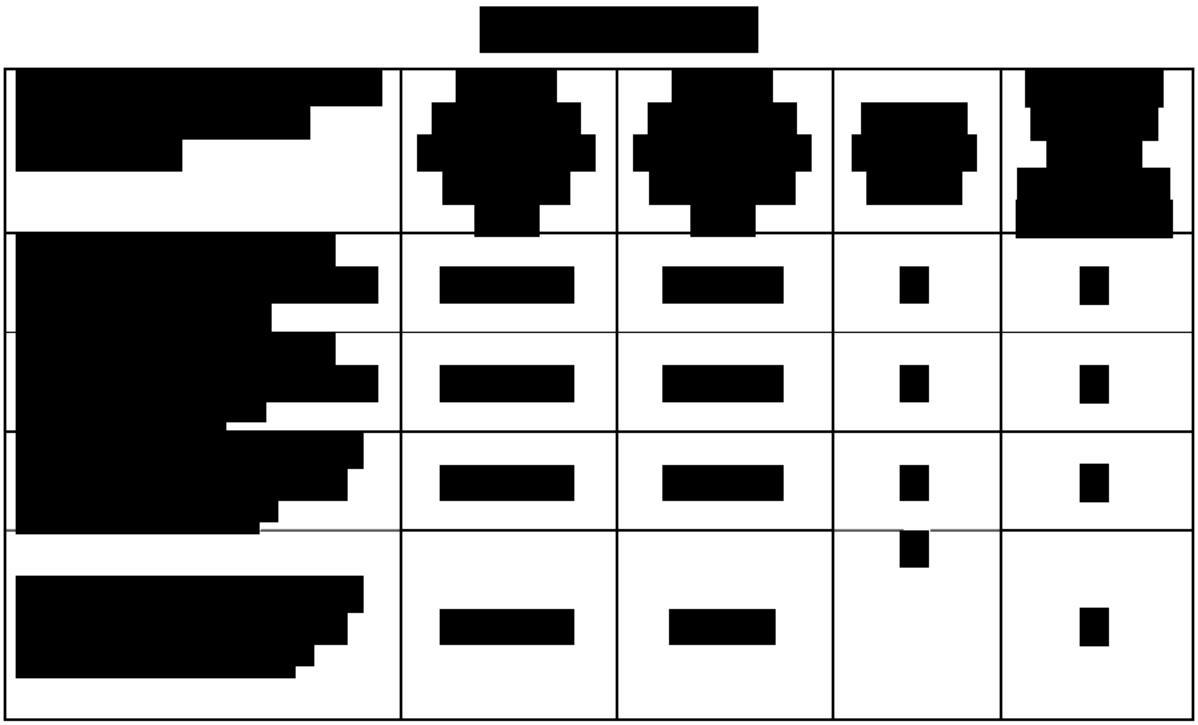
[redacted]

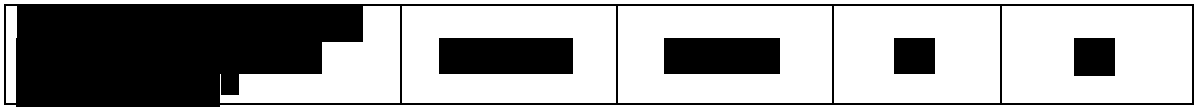
9.2 SECONDARY ENDPOINTS

Secondary endpoints will be compared between randomized groups in an analogous fashion to the primary efficacy endpoint [redacted]

Safety will be reported as the incidence of all serious device/procedure related AEs, as adjudicated by an independent clinical events adjudicator. The adjudicated events will be coded using the Medical Dictionary for Regulatory Activities (MedDRA). This endpoint will be tabulated and reported by randomized group. A summary of all reported AEs will also be provided.

[redacted]





10 STUDY GOVERNANCE

10.1 STUDY PRINCIPAL INVESTIGATOR (SPI)

During the course of the study, the SPI will:

- Oversee clinical trial activities including protocol development, and any changes that may be desired or required during conduct of the study.
- Assist in obtaining evaluation and feedback from peers throughout the course of the study.
- Review and approve protocol and site selection.
- Register the study protocol on ClinicalTrials.gov prior to enrollment of first patient.
- Direct and support site investigators.
- Perform comprehensive periodic review and assessment of patient enrollment, study data and protocol compliance.
- Oversee safety of adverse event reporting.
- Report study results on ClinicalTrials.gov within 1 year of study completion.
- Support publication of study results in peer-reviewed journal within 1 year of study completion.

10.2 MEDICAL MONITOR (MM)

The MM will be an Individual who is knowledgeable in the appropriate disciplines and medical specialties pertinent to the disease state being evaluated in this clinical Study. The MM will be a qualified medical practitioner who has experience and training in the MILD device and procedure. During the course of the study, the MM will:

- Review all subject medical records, baseline imaging to confirm the diagnosis and the appropriate level(s), Measure the thickness of ligamentum flavum at the treatment level(s). Also, ensure that eligibility criteria are met prior to randomization.
- Monitor overall study safety.
- Approve patient enrollment including review of MRIs.
- Respond to patient safety related inquiries from members of the Clinical Team including, but not limited to: patient eligibility, prohibited medications or procedures, exclusionary medical history, adverse events, and protocol deviations that impact patient safety.
- Participate in protocol development and amendment review.

- Perform comprehensive periodic review and assessment of patient enrollment, study data and protocol compliance.
- Prepare and/or review SAE narratives if applicable.
- Ensure adequate documentation of safety decisions.
- Escalate safety events as necessary.
- Consult with other study advisors as needed for safety issues requiring additional input.
- Support publication of study results in peer-reviewed journal within 1 year of study completion.

10.3 Clinical Events Adjudicator (CEA)

The CEA will be an individual who is independent of the Investigational Sites. The CEA will be responsible for the review and validation of all complications that occur over the course of the Study and the subsequent classification of these complications as related to the device or procedure. The CEA will review all complications and adjudicate them as defined in Section 8: Adverse Events. The CEA can request additional source documentation and any available imaging to assist with adjudication.

11 STUDY MANAGEMENT

11.1 Source Documentation

All required data for this study is to be recorded in the subject's medical chart for source documentation and data verification. Clinical research coordinators (CRC) at each site will perform primary data collection from source documents (reviews prior to transcribing onto Case Report Forms (CRFs), or eCRFs. Source data includes original records of clinical findings, observations, or other activities in a clinical trial. Examples of these original documents and data records include: hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate and complete, microfiches, photographic negatives, x-rays, and subject files.

The investigator is ultimately responsible for the integrity of the data recorded and submitted on the CRFs/eCRFs; therefore, each CRF/eCRF must be reviewed and signed by the investigator. To protect subject confidentiality, the subject's name must not appear anywhere on the CRF/eCRF, and must be removed or redacted from any supporting documentation. Each page should be identified with the subject's study ID number and initials only. All other subject identifiers (e.g. medical record number, social security number) are to be obscured. CRFs/eCRFs will be completed in a timely fashion.

Regulations require that investigators maintain information for every subject participating in the clinical study, in the study subject's medical records that corroborate data collected on the CRFs/eCRFs. In order to comply with these regulatory requirements, the following information will be maintained and made available as required to monitors and/or regulatory inspectors:

- Medical history and physical condition of the study subject before involvement in the study sufficient to verify protocol entry criteria (if not already present).
- Dated and signed notes in the subject's medical record on the day of entry into the study that identify: signed study Informed Consent, the participant's date of entry into the study, the study sponsor, the clinical site, the subject number assigned and a statement that informed consent was obtained. It must be possible for the investigator and the hospital personnel to identify each patient by using this participant's file. If the participant's data is recorded electronically, the investigator should assure hard-copies are filed on a regular basis.
- Dated and signed notes from each study participant visit with reference to the CRFs/eCRFs for further information, if appropriate (for specific results of procedures and exams).
- Completed study questionnaire surveys.
- Notes regarding narcotic and non-narcotic analgesics taken during the study.
- Documentation of co-interventions used during the study.
- Study participant's condition upon completion of or withdrawal from the study.
- Documentation is required to show reasons patients failed screening, along with their signed informed consent form.

11.2 Data Maintenance and Collection

The applicable data recorded in this study shall be documented on CRFs/eCRFs that have been specifically designed for this study. The CRFs/eCRFs will then be recorded, evaluated, and stored in accordance with data protection regulations. The CRFs/eCRFs are documents that must be suitable for submission to regulatory authorities should this become necessary to support changes to the product labeling in future regulatory agency submissions.

11.3 Study Discontinuation

The clinical study can be discontinued prematurely at the discretion of the IRB or sponsor. Subjects may withdraw from the study at any time upon request, or they may be withdrawn at any time at the discretion of the PI or sponsor for safety, or administrative reasons.

11.3.1 Study Discontinuation by IRB

The IRB may choose to discontinue the study at any center(s) for which they granted approval if:

- The research study is not conducted in accordance with the IRB's requirements
- The research study indicates unexpected serious harm to subjects

11.3.2 Study Discontinuation by Sponsor

The sponsor may choose to discontinue the study if the sponsor discovers additional information during the study that may cause harm to subject safety. If the study is terminated prematurely or suspended, the sponsor will promptly inform all clinical investigators of the termination or suspension and the reason(s) for this action. The IRB/EC will also be informed, either by the sponsor or investigator if a local IRB/EC is utilized, promptly and provided with the reason(s) for the termination. If applicable, regulatory authorities will be informed.

11.3.3 Subject Discontinuation by Investigator

An investigator may discontinue a subject from the study, with or without the subject's consent, for any reason that may, in the investigator's opinion, negatively affect the wellbeing of the subject. Reasons to discontinue may include, but are not limited to the following:

- Poor compliance
- Occurrence of an adverse experience that is unacceptable to the subject
- Investigator determination that it is in the subject's best interest due to health issues unrelated to LSS

If a subject is withdrawn from the study, the investigator will promptly inform the subject and sponsor.

11.3.4 Withdrawal by Subject

If a subject chooses to withdraw from the study, and also withdraws consent for disclosure of future information, no further evaluation(s) should be performed, and no additional data will be collected. The sponsor may retain and continue to use any data collected prior to the withdrawal of consent, unless specified by the subject.

If early termination is due to death or injury from a device or procedural-related AE, the investigator will evaluate it as a potential medical device event. If it is determined to be a device-related failure, the investigator and sponsor will report it per the regulations (21 CFR 803).

11.4 Missed Surveys and Visits

For compliance, each subject is instructed on the importance of complying with the directions for treatment and medication, pain and function questionnaires, and the follow-up office visit schedule. Any subject who does not complete their surveys and/or return for a scheduled follow-up visit should be contacted by the site study personnel to determine the reason. An assessment of whether the missed visit was associated with a device/procedure related problem, an unrelated medical problem, or a non-medical problem will be made. Written documentation of the study site's efforts to locate and/or gain compliance from a "lost to follow-up" subject must be maintained.

11.5 Center Discontinuation

Study center participation can be discontinued and the study closed in case of insufficient recruitment of patients, recall of any MILD device, continuous non-compliance with the protocol, or continuous non-compliance with IRB requirements.

11.6 Quality Control/Assurance Procedures

The investigator and identified personnel are expected to ensure that all aspects of the protocol are followed, results are accurately recorded, all device/procedure related AEs are reported, and appropriate record keeping is performed. They will also verify that the CRFs/eCRFs are in agreement with the applicable patient medical records.

When subjects are enrolled who fail to meet the inclusion/exclusion criteria or who have not signed an informed consent, the site will notify the IRB, as well as the sponsor, and the SPI. Continued enrollment of subjects who do not meet the inclusion/exclusion criteria or who are not properly consented, may result in the investigator being suspended from further participation in the trial; however, compliance with clinical follow-up on subjects previously enrolled will still be required.

11.7 On-Site Audits

Representatives of the IRB or the sponsor (or designee) may visit the study site to carry out an audit of the study in compliance with regulatory guidelines and company policy. Such audits will require access to all study records including source documents, CRFs/eCRFs, and other study documents. Direct access to these study records must be guaranteed by the investigator, who must provide support for these activities at all times.

Similar auditing procedures may also be conducted by agents of any Regulatory Authority reviewing the results of this study. The investigator/institution should immediately notify the sponsor if they have been contacted by a Regulatory Authority concerning an upcoming inspection.

12 CLINICAL MONITORING

A designated CRC will be assigned by the investigator. Good Clinical Practices will be implemented for this study. The sponsor or designee will review the CRFs/eCRFs for completeness and assess them for any product complaints, potential adverse events, and/or medical device reports per the FDA regulations. Any missing entries in the CRFs/eCRFs, or protocol compliance issues will be brought to the investigator's or CRC's attention for correction.

The sponsor or its designee will conduct ongoing monitoring of each site to assess enrollment commitments and the accurate and timely submission of data forms. As the study proceeds, the investigators will closely monitor compliance with the protocol.

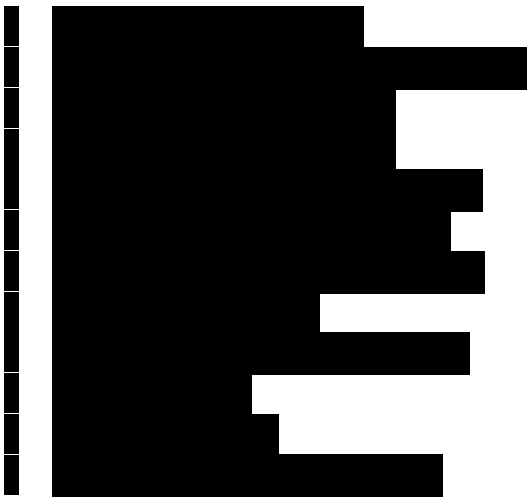
[redacted] The investigator will accommodate adequate time for such monitoring activities. The investigator will also ensure that the monitor or other compliance or quality assurance reviewer is given access to all of the above-noted study-related documents and study related facilities, and has adequate space to conduct the monitoring visit.

12.1 Study Manual Training

The training of appropriate clinical site personnel in CRFs/eCRFs completion will be the responsibility of the sponsor. To insure uniform data collection, the sponsor or its designee will review the Study Binder with the CRC. All CRCs will undergo adequate training to become thoroughly familiar with the following items:

12.2 Study Regulatory Binder

The CRC at each site will be trained on the proper maintenance of the Study Regulatory Binder. All correspondence, agreements, and logs are to be kept up to date and should be forwarded to the sponsor in a timely fashion. The contents of the Study Regulatory Binder may include:



12.3 Confidentiality and Protection of Study Files and Data

The sponsor is dedicated to maintaining the confidentiality and privacy of subjects who volunteer to participate in the study; therefore, HIPAA Privacy Rules will be adopted and adhered to throughout the study. Passwords are issued to appropriate personnel to insure

confidentiality and protection of the database by allowing variable levels of access to the computer system. The hard copies of the CRFs/eCRFs and source documentation are to be maintained in a secure area with limited access. All patient identifiers will be redacted from all photocopies of source documents removed from the site. Patient identifiers include, but are not limited to: subject's name, social security number, and medical number. All study documents will identify the subject by a subject ID# assigned by the sponsor and by the subject's initials (first, middle, last).

12.4 Site Initiation, Monitoring and Close-Out of Clinical Sites

The monitor for this study is the sponsor or its designee. The study will be monitored to ensure that applicable FDA regulations are followed. This includes, but is not limited to, the following sections of the Code of Federal Regulations: 21 CFR Part 812, Investigational Device Exemption; 21 CFR Part 50, Protection of Human Subjects, 21 CFR Part 54, Financial Disclosure by Clinical Investigators and 21 CFR Part 56, Institutional Review Boards.

Prior to subject enrollment, a study initiation visit, web-conferencing training, and/or telephone call (if appropriate), will be completed at each clinical site to ensure the following: IRB approval has been obtained and documented; the investigators and study personnel are appropriately trained and clearly understand the study, the investigators and study personnel accept the obligations incurred in undertaking this clinical investigation.

Periodic monitoring visits will be made at all active study sites throughout the study to assure that the investigator obligations are fulfilled and all applicable regulations and guidelines are being followed. These visits will assure that the facilities remain acceptable; the protocol is being followed, the IRB has been notified of approved protocol changes as required, complete records are being maintained, appropriate and timely reports have been made to the sponsor and the IRB, and the investigator is carrying out all agreed activities.

13 INVESTIGATOR RESPONSIBILITIES

The investigator shall be responsible for ensuring that the study is performed in accordance with the protocol, the practice of medicine, the medical device laws, patient data and/or privacy protection regulations and applicable country and local regulatory requirements.

13.1 Required Documents from the Investigators

All investigators must be approved in advance by the SPI and trained by the sponsor. Each site investigator must provide the following documents prior to the start of the study:

[redacted]

13.2 Training of Study Center Staff

It is the investigator's responsibility to ensure that all Sub-investigators and other staff assisting with the study have appropriate qualifications and are fully instructed on the study procedures. investigator shall ensure that there is an experienced CRC for the study, and that the investigator and staff have adequate time to conduct the study.

13.3 Data Recording

The CRFs/eCRFs should be a complete and accurate record of the patient's data collected during the study according to Good Clinical Practice recommendations. The investigator is responsible for the quality of the data collected, corrected, and recorded.

13.4 Adverse Event Reporting

It is the investigator's responsibility to promptly report all device/procedure related AEs and/or SAEs occurring during the study to the SPI and to inform their IRB as required.

13.5 Protocol Adherence / Deviations

The protocol, as written, must be followed. If the medical condition of a patient necessitates a major deviation from the protocol, the protocol deviation must be approved by the SPI and clearly documented.

13.6 Amendments / Changes to the Protocol or Treatment Procedure

During the course of the study, an amendment to the protocol may be necessary. Only the sponsor is allowed to amend this protocol. Any amendments or modifications must be approved by the research site's IRB/EC prior to research-study staff implementation, unless the modifications increase subject safety. The research sites will receive the following for their regulatory file, and if applicable, IRB/EC submission:

[redacted]

[redacted]

Any amendment(s) that affect the informed consent require a revised, sponsor and IRB/EC-approved informed consent, before changes in study procedures are implemented. These requirements should in no way prevent any immediate action from being taken by the investigator or by the sponsor to preserve the safety of any subjects included in the study, as necessary. If an immediate change to the protocol is felt to be necessary by the investigator and is implemented by him/her for safety reasons, the sponsor should be immediately notified.

13.7 Informing Patient's Primary Care Physician

It is the investigator's responsibility to notify the primary care or referring physician of the patient's participation in the study.

13.8 Record Retention

It is the investigator's responsibility to ensure that the data sources, CRFs/eCRFs, and study patient files are stored securely during and after the study termination for a minimum 2-year period, or longer, if designated by the IRB. Such materials must be accessible for auditing by regulatory authorities. They may be discarded only upon notification from sponsor. To avoid error, the investigator should contact sponsor before the destruction of any records and reports pertaining to the trial to ensure they no longer need to be retained. In addition, sponsor should be contacted if the investigator plans to leave the clinical site so that arrangements can be made for transfer of records.

14 ETHICAL AND REGULATORY CONSIDERATIONS

14.1 Role of Study Sponsor

As the study sponsor of this clinical study, sponsor has the overall responsibility for the conduct of the study, including assurance that the study meets the regulatory requirements of the Food and Drug Administration. In this study, sponsor and/or its designee will have certain direct responsibilities and will delegate other responsibilities as applicable. Sponsor and/or its designee will ensure adherence to the sponsor general duties (21 CFR Part 812.40), selection of investigators (21 CFR Part 812.43), monitoring (21 CFR Part 812.46), and maintaining records [21 CFR Part 812.140 (b)].

14.2 INFORMED CONSENT & IRBS (21 CFR PARTS 50 AND 56)

All subjects must provide written informed consent in accordance with the local clinical site's IRB. A copy of the consent form from each center must be forwarded to sponsor for review and approval prior to submitting it to the IRB. Each site must provide the sponsor with a copy of the clinical site's IRB approval letter (stating the study name, protocol revision being approved and an approval date) and the informed consent. Yearly approvals for the continuation of the trial at each clinical site must also be forwarded to the sponsor.

An unconditional prerequisite for participation of a patient in the clinical study is his/her consent after having been informed about the following basic elements of Informed Consent in accordance with the Declaration of Helsinki, with reference to the USA Code of Federal Regulations 21CFR50.25.a.:

1. A statement that the study involves research, an explanation of the purposes of the research, and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental.
2. A description of any reasonably foreseeable risks or discomforts to subjects.
3. A description of any benefits to the subject or to others which may reasonably be expected from the research.
4. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.
5. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained and that notes the possibility that the regulatory authorities and study sponsor may inspect the records.
6. For research involving more than minimal risk, an explanation as to whether any compensation is available and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of or where further information may be obtained.
7. An explanation of who to contact for answers to pertinent questions about the research and research subjects' rights, and who to contact in the event of a research-related injury to the subject.
8. A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the

subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

The following statement shall be provided to each clinical trial subject in informed consent documents and processes. This will notify the clinical trial subject that clinical trial information has been or will be submitted for inclusion in the clinical trial registry databank under paragraph (j) of section 402 of the Public Health Service Act. The statement is: "A description of this clinical trial will be available on *http://www.ClinicalTrials.gov,* as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time."

The investigators must inform the patient both verbally and in writing. The wording must be chosen so that lay persons may fully and readily understand the content.

It is the responsibility of the investigators to give to each patient, prior to inclusion in the study, full and adequate information regarding the objectives and the procedures of the study and the possible risks and benefits involved. Furthermore, it is the responsibility of the investigators to obtain a signed informed consent from all patients prior to inclusion in the study. Sponsor and the IRB must approve any modification to the sample Patient Informed Consent made by the study site. The study center must provide sponsor with a copy of the IRB approved informed consent and renewed approvals and consents as appropriate for the duration of the study.

The original informed consent should be retained in the patient's study records, and a signed/dated copy provided to the patient.

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