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Spineology Clinical Outcomes Trial

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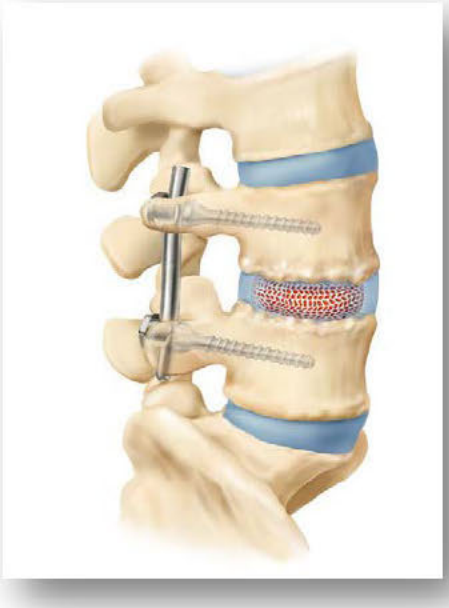

IDE G140140: Investigation Protocol

Utilization of the Spineology Interbody Fusion System

Sponsor Summary

Trial Sponsor:	Spineology, Inc.
Primary Contact:	[redacted]
Address:	7800 Third Street North Suite 600 St. Paul, MN 55128-5455
Phone:	[redacted]
Fax:	[redacted]
Email:	[redacted]
Trial Product:	Spineology Interbody Fusion System (SIFS)
IDE Number:	G140140

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1.0 INTRODUCTION AND BACKGROUND

In the process of degenerative disc disease (DDD), the intervertebral disc is often found to be the primary source of pain.[1-7] Spinal fusion procedures that stop motion at the disc are currently the preferred treatment for DDD. Posterior and posterolateral fusion procedures have been used, and fusion rates range from 46% to 100%.[8-18] Fusion with internal spinal instrumentation has been shown to yield more reliable (80% to 90%) fusion rates.[1, 19, 20]

Removal of the disc followed by an interbody fusion procedure is the most reliable procedure for treating a painful disc because it can restore tension to the annulus and further curtail motion.[4, 21-26] A successful interbody fusion is more likely to result in a successful clinical outcome (pain reduction, function improvement).[6] A bone graft placed in the intervertebral disc space has a potential mechanical advantage over posterior or posterolateral fusions by allowing restoration of disc space height, sagittal plane alignment, and weight bearing through the anterior column.[19, 21-23, 27-29] The disc space provides a large surface area for fusion, and compressive loads applied to the graft stimulate osteogenesis and fusion.

The clinical outcomes of anterior and posterior interbody fusions are similar.[19,30] An anterior interbody fusion allows a surgeon to avoid dissection of posterior paraspinal muscles and manipulation of the spinal cord and nerves. However, injury to iliac vessels and retrograde ejaculation has been reported.[19, 31-34] Also, in many cases of degenerative disc disease, a decompression of the posterior neuroforamen is warranted, which would require a separate posterior procedure.

The posterior interbody fusion approach allows the surgeon to address both anterior and posterior pathology through the same incision. Using the posterior approach, bone grafts can be placed in the disc space via a translaminar or transforaminal approach. The transforaminal approach allows the surgeon to avoid excessive nerve root and /or thecal sac retraction, which can lead to neural injury and postoperative fibrosis, and avoid excessive removal of posterior structures, which would lead to gross instability of the motion segment.[19]

In 2001, over 122,469 lumbar fusions were performed nationwide for degenerative conditions.[35] By 2005, it was estimated this number had increased to more than 300,000 lumbar spine fusion being performed in the United States annually[36]. Currently, industry research estimates that for 2014, approximately 75,000 minimally invasive posterior lumbar fusions performed domestically will utilize an interbody device with supplemental fixation.

For interbody fusion with posterior fixation, spine surgeons currently place structural intervertebral spacers into the interbody space. These spacers may be pre-shaped devices constructed of allograft (cortical bone dowels or femoral rings) or non-metallic, radiolucent materials (such as polyether ether ketone, PEEK), or metallic cage devices. Autogenous bone graft and blood components (marrow, blood) are often added.

Use of morselized bone graft in orthopedic procedures is desirable because morselized graft is more rapidly incorporated during the course of bone healing. If the morselized graft pack can be effectively contained in the interbody space, the graft material can function as a structural spacer to provide anterior column support. Contained graft material can be tightly packed within the mesh to increase the graft's compressive strength. Unlike pre-shaped cortical grafts, the morselized pack conforms intimately to the host bone at the surgical site, ensuring good vascularization potential and reducing the osteoblast jumping distance for osteogenesis. In addition, the solidly packed graft retains intra-pack porosity, ensuring an osteoconductive scaffold to facilitate vascular and bony ingrowth.

It would be desirable to minimize autograft use because of associated post-operative pain and morbidity, to optimize contact between allograft and host bone, and to permit the surgeon to place or construct an effective structural intervertebral spacer with only minimal neural retraction required.

The SIFS is intended to be used to contain the bone graft placed by spine surgeons into the interbody space to achieve spinal intervertebral body fusion. The SIFS mesh enables the use of morselized bone graft materials in spine fusion procedures instead of pre-shaped materials, such as solid allograft cortical bone dowels or femoral rings, or rigid synthetic materials such as PEEK or titanium.

In addition, the SIFS allows the surgeon to perform an interbody fusion through a small portal and to complete the entire fusion procedure from a posterior approach instead of a 360 degree anterior/posterior procedure, which is often the case with the use of cages. The minimal access portal utilized for the SIFS mesh filling allows the device to be placed via a unilateral transforaminal or translaminar approach, versus the often-used bilateral approach required for many cages and cortical spacers. This flexibility permits the surgeon to adapt the surgical approach to the local anatomy of the patient.

1.1 DEVICE DESCRIPTION

The Spineology Interbody Fusion System (SIFS) consists of two components; the SIFS mesh device and the SIFS instruments.

The Device – The SIFS mesh is a graft containment and reinforcement device. The SIFS mesh is filled *in situ* with bone graft. It is provided sterile and is a biocompatible, radiolucent, porous polyester mesh sack knitted from polyethylene terephthalate (PET) thread. PET material is widely used to make surgical sutures and meshes. The SIFS mesh device is pliable, conformable, and strong under tensile and burst forces as demonstrated through *in vitro* studies including axial compressive mechanical testing of the filled device's load-bearing capabilities and overall segmental strength. Beyond the mechanical testing, evaluation of the device was performed in an animal test model to further assess the biomechanical, radiographical and histological properties of the device. Human clinical outcomes

have also been investigated under IDE G030106. Refer to the SCOUT Investigational Plan for mechanical and biomechanical *in vitro* test protocols and results as well as *in vivo* outcomes.

The Instruments – Following conventional thorough discectomy, the SIFS instruments allow the surgeon to finish the preparation of a large area of the disc space through a small portal in the annulus, introduce the SIFS mesh in its undeployed state into the prepared fusion bed cavity, and fill the mesh with bone graft. The SIFS requires only minimal vascular and neural retraction during delivery of SIFS mesh and the graft material. Utilizing the device specific instruments, the SIFS mesh is deployed and filled. During the initial stages of mesh filling, the device expands and conforms to the cavity affording intimate graft apposition against the prepared vertebral endplates. The porosity of the mesh cage permits direct contact between the graft and the bleeding host bone at the mesh pores. As the density of contained graft increases within the mesh during the filling process, the graft may then distract the spinal segment. By nature of the flexible fabric design, SIFS mesh allows complete filling of the prepared site with graft material while minimizing the risk of graft extravasation into the surrounding area. Graft containment reinforces the granular bone pack, making it capable of bearing load and increasing segmental stability.

The SIFS received market clearance (K014200) on November 26, 2003 for containment of bone graft materials within the vertebral body. In the present investigation, the SIFS mesh is considered investigational, for the current cleared labeling does not identify use of the SIFS mesh in an interbody fusion application as a cleared indication.

1.2 INTENDED USE

The Spineology Interbody Fusion System is intended for use as an adjunct to fusion in instrumented lumbar fusion procedures for the treatment of degenerative disc disease. The SIFS mesh component is intended to maintain the relative position of bone graft material. The device is limited to use by or on the order of a physician.

1.3 INDICATIONS FOR USE

The Spineology Interbody Fusion System is indicated for use in an intervertebral body fusion at one level in the lumbar spine from L2 to S1, in skeletally mature patients with degenerative disc disease (DDD) with up to a Grade I spondylolisthesis at the involved level. In this investigation, DDD is defined as discogenic back pain with degeneration of the disc confirmed by patient history, examination and radiographic studies. These patients shall have undergone six (6) months of conservative (non-operative) treatment. The Spineology Interbody Fusion System with *G2 Dry Mix* allograft is intended for use with supplemental

posterior fixation systems cleared by FDA for use in the lumbar spine. It is designed for use with autograft as an adjunct to fusion.

Note: *G2 Dry Mix* is an allograft mixture available from the Musculoskeletal Transplant Foundation (MTF), Edison, NJ. *G2 Dry Mix* contains corticocancellous bone chips and demineralized bone matrix (DBM).

1.4 INSTRUCTIONS FOR USE

Following a thorough discectomy and adequate preparation of the vertebral body endplates, the SIFS mesh is deployed within the prepared disc space, utilizing the SIFS instruments. The SIFS mesh is primarily filled with rehydrated *G2 Dry Mix* (granular human tissue allograft mixture), augmented with autograft and bone marrow aspirate. The segmental construct is further stabilized with bilateral supplemental posterior fixation. Only investigators trained in the use of the Spineology Interbody Fusion System may utilize the investigational device. Refer to the SIFS Surgical Technique Manual (**Appendix I**) for complete instructions for use and implantation of the device.

1.5 CONTRAINDICATIONS AND CAUTIONS

Use of the SIFS mesh is contraindicated in individuals with a known sensitivity to PET.

G2 Dry Mix graft: Trace amounts of Gentamicin, Primaxin and Amphotericin B antibiotics may be present. Trace amounts of Polysorobate-80, Ethanol, Methanol, Isopropanol, Polyoxyethylene (10) Phenol Ether and Hydrogen Peroxide may be present. Caution should be exercised if the patient is allergic to any of these substances.

2.0 PURPOSE AND INVESTIGATION OBJECTIVES

2.1 PURPOSE

The purpose of this investigation is to evaluate the safety and effectiveness of the Spineology Interbody Fusion System in an instrumented lumbar interbody fusion.

2.2 INVESTIGATION OBJECTIVES

The primary objective of this investigation is to demonstrate the effectiveness of the SIFS in a lumbar interbody application. Effectiveness will be determined as a composite score that represents patient success. To be considered a patient success, each of the following criteria must be met at the 24-month study interval:

- Pain – Improvement in low back pain score evidenced by a 20 mm reduction on a 100 mm Visual Analog Scale (VAS) when compared to baseline (Note: a lower VAS pain score indicates less pain),
- Function – Improvement in low back function evidenced by a 15 point decrease of the Oswestry Disability Index (ODI) score compared to baseline. (Note: a higher ODI score indicates a greater disability with respect to low back function),
- Fusion – Bridging bone demonstrated on CT Scan
- Safety – Freedom from device-related Serious Adverse Events and secondary surgical interventions at the index level through the 24-month study interval.

In additional to the above stated primary objective, this investigation will yield data on the following outcomes, subject parameters and clinical utility:

- Variable scores over time (pain, function, fusion) as individual parameters
- Adverse Event rate(s) reported by relatedness and severity
- Neurological status over time
- Quantitative/qualitative radiographic data over time specific to the index level and contiguous levels (translation, angulation, disc height, and device position)
- Demographics
- Hospitalization Utility (duration of surgery, estimated blood loss and duration of hospitalization)
- Work status over time
- Pain medication use

Data collection is not limited to the above data points. Additional parameters will be reported on as appropriate. For a more detailed list of supplemental outcomes refer to Section 3.2 Scientific Soundness and Statistical Analysis.

2.3 STUDY DURATION

This study will conclude when the final study subject has achieved their 24-month study evaluation. While the primary endpoints for this trial are defined at 24 months post-operative, this investigation will include annual subject self-assessment follow-ups at 36 months and 48 months post-operative while study enrollment is ongoing. This means that subjects enrolled into this investigation are expected to achieve a final (physical) study examination that includes imaging and neurological testing approximately 24-months after their index procedure. Following the 24-month physical evaluation and testing that supports primary endpoint analysis, subjects are expected to complete a self-assessed Patient Survey Form and a Long-Term Follow-Up Questionnaire at the 36-month and 48-month timepoint as appropriate until the final study subject has completed study participation at the 24-month timepoint. Therefore, while a subject's active participation (physical examination/testing) may conclude at 24-months post-op, their study participation may extend to include longer-term remote follow-up to a maximum of 48-months post-operative resultant of the potential for the self-administered survey/questionnaire completion.

It is anticipated that the enrollment phase of this investigation shall be complete within approximately eighteen (18) to twenty-four (24) months (1.5 to 2 years) of initiation and that the overall study shall conclude in approximately 42-months (3.5 years) to 48-months (4 years) based on the following estimations:

- Although the study is approved to be conducted at a maximum of 15 investigative sites, ideally, the study shall be conducted at approximately 10 of the 15 investigative sites.
- It is anticipated that a full patient complement (enrollment) will consist of no more than 102 subjects.
- Each investigative site is expected to enroll approximately 10 subjects (.85 subjects per month/10 subjects per year yielding an anticipated total enrollment duration of 12 months per site. It is recognized that should enrollment be protracted, it may potentially require up to 18 months (1.5 years) to enroll the complete cohort.
- Allowing for staged site activation (2 - 3 sites per month x 10 sites), it is anticipated the cumulative duration of enrollment would be approximately 18 months to 24 months.
- Accounting for the 24-month follow-up, it is anticipated the total study duration will be between 42-months (3.5 years) and 48-months (4 years) from initiation to closure.

3.0 INVESTIGATION DESIGN

3.1 OVERVIEW AND GENERAL DESIGN

This is a FDA regulated, prospective, non-randomized, single treatment arm, multicenter, IRB approved performance goal investigation designed to evaluate the safety and effectiveness of the SIFS mesh device when implanted in the intervertebral body disc space with bone graft during an instrumented lumbar fusion procedure. Enrolled subjects will be evaluated for device safety and effectiveness outcomes that support primary endpoint analysis through the 24-month time point. As previously noted in the protocol, study subjects will be expected to complete a self-administered survey annually through a maximum of 48 months post-operative as necessary until the last study subject has concluded study participation. Data from this investigation will be used to support a regulatory submission (e.g., *De novo* petition).

This non-randomized investigation will examine the primary endpoint and numerous additional outcomes. A Data Monitoring Committee will be established for this trial and shall oversee trial conduct to ensure the safety and protection of study participant rights and welfare. An independent core lab will be utilized to perform fusion assessments and radiologic measurements.

3.2 SCIENTIFIC SOUNDNESS AND STATISTICAL ANALYSIS

The safety and effectiveness of the SIFS will be evaluated utilizing standard statistical practices and principles.

3.2.1 Primary Endpoint

The primary endpoint (success) is a composite endpoint of pain, function, fusion, and safety, defined as meeting each of the following criteria at the 24-month study interval:

- Pain – Improvement in low back pain score evidenced by a 20 mm reduction on a 100 mm Visual Analog Scale (VAS) when compared to baseline (Note: a lower VAS pain score indicates less pain),
- Function – Improvement in low back function evidenced by a 15 point decrease of the Oswestry Disability Index (ODI) score compared to baseline. (Note: a higher ODI score indicates a greater disability with respect to low back function),
- Fusion – Bridging bone demonstrated on CT Scan
- Safety – Freedom from investigational device-related Serious Adverse Events at the index level through the 24-month study interval.

3.2.2 Additional Outcomes

Beyond supporting the primary endpoint of this investigation, Spineology is evaluating additional outcome data. The investigation design allows for the assessment of objective and subjective findings. Descriptive data will be provided to characterize these additional effectiveness and safety measures:

- Mean low back VAS pain score over time through the 24-month interval
- Mean lower extremity (right and left leg) VAS scores over time through the 24-month interval
- Mean ODI score over time through the 24-month interval
- Fusion at the 12-month and the 24-month interval
- Occurrence of device-related Serious Adverse Events through the 24-month interval
- Occurrence of study-related Adverse Events through the 24-month interval
- Neurological status assessment (strength, sensation, and reflexes) over time through the 24-month interval (reporting categorized as improved, maintained, or reduced with new or increased neurological deficit being further categorized as transient (< 3 months/90 days) or longer term ≥ 3 months/90 days);
- Radiographic data observed over time specific to the index level (translation, angulation, disc height, and device position)
- Subject satisfaction with procedure/outcome
- Work status over time
- Pain medication use over time
- Operative time
- Estimated blood loss
- Duration of hospitalization
- Graft site pain (as applicable)
- Adjacent segment status at 24-months post-operative assessed by quantitative and qualitative radiographic data (translation, angulation, and disc height)

3.2.3 Statistical Methods

The statistical analysis of the data obtained from this study will be performed using SAS® version 9.1 or higher. All statistical tests will be performed at the 0.05 significance level, unless otherwise indicated.

Data collected in this study will be documented using summary tables and subject data listings. Continuous variables will be summarized using descriptive statistics, specifically the mean, median, standard deviation, minimum, and maximum, and a 95% confidence interval for the mean based

on the t-distribution. Categorical variables will be summarized using frequencies and percentages and 95% exact (Clopper-Pearson) confidence intervals for the true proportions.

All analyses of effectiveness and safety will be based upon the Treated Population defined to be all treated subjects.

3.2.4 Determination of Sample Size

The required sample size was calculated based on the following specifications:

1. Endpoint: success rate
2. One-sided exact binomial test for a binomial proportion
3. Alpha = 0.05
4. True percentage of successes = 68%
5. Performance Goal (null percentage of successes) = 55%
6. Power = 80%

The required sample size based upon these specifications is 87 subjects. The sample size was increased to 102 subjects to take into account an assumed 15% lost to follow-up rate.

3.2.5 Sample Size Re-Estimation

A sample size re-estimation will be performed based on 12-month interim data.

3.2.6 Analysis of Primary Endpoint

The primary endpoint for this investigation is a composite endpoint of pain, function, fusion, and safety that meets all of the following criteria at the 24-month study interval:

- Pain – Improvement in low back pain score evidenced by a 20 mm reduction on a 100 mm Visual Analog Scale (VAS) when compared to baseline (Note: a lower VAS pain score indicates less pain),
- Function – Improvement in low back function evidenced by a 15 point decrease of the Oswestry Disability Index (ODI) score compared to baseline. (Note: a higher ODI score indicates greater disability with respect to low back function),
- Fusion – Bridging bone demonstrated on CT Scan
- Safety – Freedom from investigational device-related Serious Adverse Events at the index level through the 24-month study interval.

This endpoint will be summarized using the count and percentage, together with a 95% exact (Clopper-Pearson) confidence interval for the true proportion of successes. The null and alternative hypotheses for this endpoint are as follows:

H_0: $p \leq 0.55$

versus

H_1: $p > 0.55$

where p denotes the true proportion of subjects achieving success for this endpoint. The null hypothesis will be tested using a 1-sided exact binomial test for a binomial proportion conducted at the 0.05 level of significance.

Missing values for the primary endpoint at Month 24 will be imputed using the last-observation-carried-forward (LOCF) method and multiple imputation methods. For subjects who are missing at most one component of the primary endpoint at Month 24 and who have a value for the given component at Month 12, the LOCF method will be used to impute a value for that component at Month 24, so that the value of the primary endpoint at Month 24 can then be determined. Once the LOCF procedure has been performed, multiple imputation methods will be used to impute values for the remaining subjects with missing values for the primary endpoint at Month24. The imputation procedure will be based on primary endpoint data at all previous post-baseline time points.

3.2.7 Analysis of Additional Outcomes

The additional outcomes for this study are as follows:

- Mean low back VAS pain score over time through the 24-month interval
- Mean lower extremity (right and left leg) VAS scores over time through the 24-month interval
- Mean ODI score over time through the 24-month interval
- Fusion at the 12-month and the 24-month interval
- Occurrence of device-related Serious Adverse Events through the 24-month interval
- Occurrence of study-related Adverse Events through the 24-month interval
- Neurological status assessment (strength, sensation, and reflexes) over time through the 24-month interval (reporting categorized as improved, maintained, or reduced with new or increased neurological deficit being further categorized as transient (< 3 months/90 days) or longer term ≥ 3 months/90 days);

- Radiographic data observed over time specific to the index level (translation, angulation, disc height, and device position)
- Subject satisfaction with procedure/outcome
- Work status over time
- Pain medication use over time
- Operative time
- Estimated blood loss
- Duration of hospitalization
- Graft site pain (as applicable)
- Adjacent segment status at 24-months post-operative assessed by quantitative and qualitative radiographic data (translation, angulation, and disc height)

The mean low back pain score over time through the 24-month interval will be summarized using descriptive statistics and a 95% confidence interval based upon the t-distribution. The mean lower extremity (right and left leg) VAS scores over time and the mean ODI score over time will be analyzed in the same manner.

The number and percentage of subjects achieving fusion at the 12-month and 24-month intervals and the corresponding 95% exact (Clopper-Pearson) confidence intervals for the true proportion of subjects achieving fusion will be presented.

The number and percentage of subjects with any device-related serious adverse events (SAEs) and with any study-related adverse events will be presented, together with 95% exact (Clopper-Pearson) confidence intervals for the true proportions. AEs will be summarized at the subject level by type of event using frequencies and percentages. AEs will also be tabulated at the event level by severity and by relatedness.

Neurological status for strength, sensation, and reflexes will be summarized by time point using counts and percentages and 95% exact (Clopper-Pearson) confidence intervals for the true proportions.

Radiographic data for translation, angulation, and disc height specific to the index level will be summarized by time point using descriptive statistics and a 95% confidence interval based upon the t-distribution. Device position will be summarized by time point using counts and percentages and 95% exact (Clopper-Pearson) confidence intervals for the true proportions.

Subject satisfaction with the procedure/outcome will be summarized using counts and percentages and 95% exact (Clopper-Pearson) confidence intervals for the true proportions.

Operative time, estimated blood loss, and duration of hospitalization will be summarized using descriptive statistics and a 95% confidence interval based upon the t-distribution. Work status, pain medication use, and graft site pain will be summarized by time point using frequencies and percentages and 95% exact (Clopper-Pearson) confidence intervals for the true proportions.

Radiographic data at 24-months post-operative for translation, angulation, and disc height for treated and adjacent segments will be summarized using descriptive statistics and a 95% confidence interval based upon the t-distribution.

For the analyses of these additional outcomes, there will be no imputation of missing values.

3.2.8 Data Management Plan

The purpose of a Data Management Plan (DMP) is to provide guidance for all aspects of data management as it pertains to this investigation. A DMP shall be in place prior to the initiation of this clinical investigation.

3.2.9 Subject Withdrawal

An enrolled subject is considered “withdrawn” from the investigation if their participation in the study is discontinued for any reason after signing the consent form. If a subject chooses to withdraw from the investigation, a Subject Discontinuation CRF will be completed and submitted to the sponsor as soon as it is practical. Every effort will be made to complete the trial CRFs applicable up to the point of withdrawal. If a subject voluntarily withdraws from the investigation, the data generated from their participation in the study will still be used in the overall investigation data set. Approval to use the data will be documented in the consent form.

Subjects who have not voluntarily withdrawn from the investigation, but fail to return for follow-up visits, will be considered “Lost-to-Follow-Up” (LTFU). Subjects identified as LTFU will be withdrawn from the investigation through completion of a Subject Discontinuation Form. Prior to formally discontinuing a subject from the investigation for being LTFU, multiple efforts shall be made including supplemental attempts to contact the subject. As an example, supplemental efforts may include 3 attempts to reach this subject (2 by telephone and 1 by certified letter). All supplemental attempts to reach a potential LTFU subject shall be documented in writing.

3.2.10 Control Subject Population

The SCOUT IDE Investigation is a single-arm clinical trial. Accordingly, a control study population is not undertaken for this investigation as each study subject essentially functions as their own control in terms of outcome parameters over time.

3.2.11 Randomization

This is NOT a randomized investigation. All enrolled study subjects shall be treated with the investigation device (SIFS mesh).

3.2.12 Minimization of Bias

To minimize the introduction of bias into this clinical investigation, the following measures will be observed:

- All investigation participants shall be enrolled under the same inclusion/exclusion criteria,
- All investigation participants shall follow the same study protocol,
- Adverse event adjudication will be performed by an objective Data Monitoring Committee panel.

The study entrance criteria for this investigation are designed to accommodate enrollment of a study population that would closely match the intended patient population for the device. Following determination that a subject is eligible for study participation and the approved Informed Consent Form (ICF) for the investigative site is signed, a subject is considered enrolled into the SCOUT clinical investigation. All study subjects will receive the investigational treatment device (SIFS mesh).

4.0 SELECTION OF SUBJECTS

To participate in this clinical investigation, a subject shall meet the study entrance criteria. This means that at the time of screening, a subject shall meet all of the inclusion criteria and none of the exclusion criteria.

4.1 INVESTIGATION POPULATION

Candidates for this investigation shall be skeletally mature, presenting with painful lumbar degenerative disc disease at a single level from L2 to S1. Subjects may have up to a Grade I spondylolisthesis at the index (involved) level. For this investigation, DDD is defined as discogenic back pain with degeneration of the disc confirmed by patient history, examination and radiographic studies. Study subjects shall present with low back pain. These subjects are to have been treated with conservative (non-surgical) measures for a minimum of six (6) months without achieving sufficient relief from their symptoms. The investigator is responsible for determining subject eligibility per the defined investigation inclusion and exclusion criteria.

4.2 INCLUSION CRITERIA

To participate in this investigation, a study subject shall meet all of the following inclusion criteria:

- Minimum age of twenty-one (21) years but not greater than eighty (80) years;
- Skeletally mature;
- Have a confirmed diagnosis of lumbar degenerative disc disease requiring single-level fusion between L2 and S1. Lumbar DDD diagnosis confirmation shall be determined by subject history, physical examination, and radiographic studies with one or more of the following factors:
  - Instability as defined by >3mm translation or ≥ 5° angulation;
  - Osteophyte formation of facet joints or vertebral endplates;
  - Decreased disc height, on average by > 2mm, but dependent upon the spinal level;
  - Scarring/thickening of the ligamentum flavum, annulus fibrosis, or facet joint capsule;
  - Herniated nucleus pulposus;
  - Facet joint degeneration/changes; and/or
  - Vacuum phenomenon;
- Report pre-operative low back pain score of ≥ 40mm on a 100mm Visual Analog Scale (VAS) correlating with involved level;
- Report pre-operative Oswestry Disability Index (ODI) score of ≥ 40;
- Received at least 6 months of conservative (non-surgical) treatment without sufficient relief from symptoms;
- Willing and able to comply with follow-up evaluations per protocol, including completion of self-assessment survey questionnaire(s), and has read,

understood and signed the sponsor and IRB approved site-specific informed consent form.

4.3 EXCLUSION CRITERIA

In the event a subject meets one or more of the following exclusion criteria, they shall be excluded from study participation:

- Previous implant surgery (i.e., fusion procedure or total disc replacement) at the index level (Note: Previous less invasive procedures such as laminectomy, discectomy, etc., at the index level are not considered exclusionary);
- Greater than Grade I spondylolisthesis;
- Presents with a diagnosis of symptomatic non-index level lumbar degenerative disc disease between L2 and S1. Non-index level lumbar DDD diagnosis confirmation shall be determined by subject history, physical examination, and radiographic studies with one or more of the following factors:
  - Instability as defined by >3mm translation or ≥ 5° angulation;
  - Osteophyte formation of facet joints or vertebral endplates;
  - Decreased disc height, on average by > 2mm, but dependent upon the spinal level;
  - Scarring/thickening of the ligamentum flavum, annulus fibrosis, or facet joint capsule;
  - Herniated nucleus pulposus;
  - Facet joint degeneration/changes; and/or
  - Vacuum phenomenon;
- Active systemic infection or infection local to the surgical site;
- Active or suspected malignancy;
- Body Mass Index (BMI) of ≥ 40;
- Significant metabolic bone disease (e.g., osteoporosis or osteomalacia) to a degree that would contraindicate spinal instrumentation. Osteoporosis is defined as a T-score of < -2.5 on a DEXA scan. A screening questionnaire for osteoporosis, SCORE (Simple Calculated Osteoporosis Risk Estimate), will be administered to identify those patients that require a DEXA scan (a score greater than or equal to 6 requires DEXA scan);
- Taking medications that are known to potentially interfere with bone or soft tissues healing (e.g., chronic systemic steroids);
- Has a current diagnosis of substance related disorder, as defined per the Diagnostic and Statistical Manual of Mental Disorders 5th Edition, May 2013 (DSM – V);
- Has a diagnosis of somatoform, dissociative, eating or psychotic disorder per DSM – V;
- Waddell Signs of inorganic behavior (3 or more signs);

- Is a current tobacco user (current use defined as tobacco use ≤ 30 days prior to surgery);
- Is a prisoner at the time of enrollment;
- If female: pregnant/contemplating pregnancy during the follow-up period;
- Enrolled in a concurrent clinical investigation that may confound the findings of the present investigation.

Waddell Signs constitute a test methodology that evaluates for inorganic problems. Waddell Signs are findings that deviate from the usual presentation of a disease. Waddell identified five (5) types of signs: Tenderness, Simulation, Distraction, Regional Disturbance and Overreaction. During the subject evaluation, the Investigator should note any observed signs of inorganic behaviors displayed by the subject. If a subject has three (3) or more inorganic behaviors, they do not meet the study entrance criteria and should be excluded from clinical trial participation. A description of Waddell Signs is provided as **Appendix II**.

5.0 TREATMENT

5.1 INVESTIGATIONAL PRODUCT

Each SIFS mesh device package is labeled in accordance with federal regulation (21 CFR §812.5(a)) "Caution – Investigational device. Limited by United States law to investigational use". Beyond the cautionary labeling, each device package is labeled with a lot number. The lot number, along with the date of use, disposition, etc., will be captured on the appropriate study-related case report form. The SIFS investigational device package labeling is provided as **Appendix III**. Investigational product will be provided only to investigation sites determined qualified and approved by Spineology Clinical Affairs to receive the device. To qualify for investigational product receipt, a site must have obtained IRB approval, have a fully executed clinical trial agreement, meet all administrative requirements, and be trained in the investigation protocol and study conduct.

5.2 DESCRIPTION OF PROCEDURE

Standard posterior techniques for exposure of spinal elements will be employed. The surgical approach to the intervertebral disc space may be open or minimally invasive, translaminar (midline to mid-pedicular line; PLIF), or transforaminal (lateral to mid-pedicular line; TLIF). Following completion of a thorough discectomy and sufficient decortication/denuding of the vertebral endplates to expose bleeding bone, the SIFS mesh is deployed using a minimally invasive surgical access. A working cannula is guided into the intervertebral disc space. The cannula provides an access pathway for use of the remaining surgical instruments. To ensure proper disc space preparation, four Spineology discectomy tools must also be utilized prior to implantation of the SIFS mesh device. The compulsory tools are:

- Shaper – shaves through the central endplate cartilage, to expose bleeding bone;
- BackHoe – loosens disc material, curettes off endplate cartilage;
- Disc Brush – removes any remnants of disc left behind by curettes and other tools; and
- Verify – confirms depth and breadth of discectomy.

The prepared disc space cavity is cleared with suction and the SIFS mesh device is introduced through the cannula. The implant is filled within the disc space with the G2 Dry Mix graft mixture freshly inserted into the placement tube. Utilizing a rotational deployment technique for the introduction of the graft, the SIFS mesh device is evenly packed until sufficient height and disc space conformance is achieved. No additional bone graft (i.e., "sentinel graft") is placed within the disc space.

Supplemental fixation is placed to stabilize the intervertebral construct utilizing the recommended manufacturer's technique. No posterolateral (dorsal) grafting may be

applied. This protocol allows for utilization of the following commercially available supplemental rigid posterior fixation instrumentation systems:

- Expedium® and Viper® Systems, DePuy Synthes, (multiple clearances, including K110216), or
- Fortress™ Pedicle Screw System, Spineology, Inc. (K140010).

A complete description of the surgical procedure for device implantation is provided in the SIFS Surgical Technique Manual as **Appendix I**.

5.3 ASSESSMENTS AND PATIENT CARE

5.3.1 Screening and Enrollment

Prior to enrollment into this investigation, subjects shall be screened for potential inclusion. Subjects who undergo screening but do not meet the study entrance criteria are considered screen failures. Screen failures are documented on the Screening Log. Subjects meeting all study entrance criteria may be enrolled and treated. Enrolled subjects are to be followed in accordance with the study protocol through a maximum of 48-months postoperative (active visits through the 24 months postoperative; remote longer-term follow-up self-administered questionnaires at 36 months and 48 months post-op as necessary and appropriate until the last subject enrolled has achieved their final exam at 24-months postoperative). Once a subject has achieved their final assessment based on the above parameters, the subject's participation in this trial is complete.

5.3.2 Study Interval Evaluations

Intervals – Following enrollment into this investigation, subjects are followed periodically over time with pre-specified data being obtained at designated intervals. Subjects are actively assessed (i.e., includes physical examination and testing) prior to receiving the study treatment (baseline), through the surgical procedure and discharge from the hospital, at 6-weeks post-operative and at 3-, 6-, 12-, and 24-months post-operative. Beyond the above active assessment intervals performed in the health practitioner's setting, subjects shall undergo longer-term remote assessment in the form of completion of self-administered surveys/questionnaires. The longer-term patient survey/questionnaire forms shall be completed at the 36- and 48-month interval until the final study subject has achieved their 24-month study evaluation. **Table 1** indicates the subject evaluation time points and the correlating assessments to be performed at each study interval.

X-rays – Study radiographs shall be performed weightbearing (WB) and utilizing a magnification marker, allowing core lab assessments to adjust for magnification discrepancies and ensuring measurement accuracy over time.

The study specific magnification marker shall be provided by the sponsor to investigation sites. X-rays are performed at each active study visit through the 24-month interval.

Adverse Event Assessment – Beginning with the surgery/hospital interval and for each subsequent post-operative interval through study conclusion, subjects shall be assessed for adverse event (AE) occurrence, resolution, or status update.

Post-Operative Instruction – It is acknowledged that individual post-operative care plans are tailored to the specific subject by the treating investigator, however the following post-operative care plan is provided to assist in the standardization of care provided across investigative sites:

- Avoid driving for a minimum of 1 week following discharge.
- Avoid driving while on pain medication.
- Ambulate as soon as it is comfortable.
- Observe the following lifting restrictions:
  - Less than 10 pounds for 2 to 4 weeks post-op.
  - Less than 20 pounds through 12 weeks post-op.
- Limit bending and twisting for a minimum of 4 weeks post-op.
- Use of a lumbar support brace is optional.

Table 1: Study Intervals and Data Collection Requirements

Assessment	Baseline	Surgery & Hosp.	6-Week 42 days (± 7 days)	3-Month 90 days (± 14 days)	6-Month 180 days (± 30 days)	12-Month 365 days (± 45 days)	24-Month 730 days (± 60 days)	36-Month & 48-Month as applicable (1095 & 1460 days ± 60 days each)
Inclusion/Exclusion	X	-	-	-	-	-	-	-
Informed Consent	X	-	-	-	-	-	-	-
Pain Medication Use	X	-	X	X	X	X	X	-
Neurological Examination	X	X	X	X	X	X	X	-
Surgery/Hospitalization	-	X	-	-	-	-	-	-
Patient Survey[ι]	X	-	X	X	X	X	X	X
Work Status	X	-	X	X	X	X	X	-
MRI or other imaging study[‡]	X	-	-	-	-	-	-	-
Weightbearing AP X-ray	X	X	X	X	X	X	X	-
Weightbearing NL X-ray	X	X	X	X	X	X	X	-
Weightbearing Flex/Ext X-rays	X	-	-	-	X	X	X	-
CT scan	-	-	-	-	-	X	X*	-
Adverse Event Assessment	-	X	X	X	X	X	X	-
Patient Questionnaire	-	-	-	-	-	-	-	X

[ι]Patient Survey consists of VAS (low back, lower extremities, and iliac crest as applicable), ODI, SF-36 Health Survey and subject satisfaction.

[‡]As defined per protocol.

*Performed only if determined to be not fused per CT scan at the 12-month interval

5.3.3 Baseline / Pre-Procedure Study Interval – Active Assessment (≤ 3 months of investigational treatment date)

The following forms/assessments are required to be completed at this interval:

- Screening Log (enrolled subjects and screen failures)
- Informed Consent
- Patient Survey
- Pre-Operative Evaluation
- Neurological Assessment
- Pain Medication Log
- Radiographs: Weightbearing AP, neutral lateral, flexion and extension views
- MRI or other appropriate imaging per protocol

5.3.4 Surgery / Hospitalization Study Interval – Active Assessment

The following forms/assessments are required to be completed at this interval:

- Surgery/Hospitalization
- Neurological Assessment
- Radiographs: Weightbearing AP and neutral lateral, at discharge

5.3.5 Six (6) Week Study Interval – Active Assessment **(42 days ± 7 days)**

The following forms/assessments are required to be completed at this interval:

- Patient Survey
- Follow-Up Evaluation
- Neurological Assessment
- Pain Medication Log
- Radiographs: Weightbearing AP and neutral lateral

5.3.6 Three (3) Month Study Interval – Active Assessment (90 days ± 14 days)

The following forms/assessments are required to be completed at this interval:

- Patient Survey
- Follow-Up Evaluation
- Neurological Assessment
- Pain Medication Log
- Radiographs: Weightbearing AP and neutral lateral

5.3.7 Six (6) Month Study Interval – Active Assessment (180 days ± 30 days)

The following forms/assessments are required to be completed at this interval:

- Patient Survey
- Follow-Up Evaluation
- Neurological Assessment
- Pain Medication Log
- Radiographs: Weightbearing AP and neutral lateral

5.3.8 Twelve (12) Month Study Interval – Active Assessment (365 days ± 60 days)

The following forms/assessments are required to be completed at this interval:

- Patient Survey
- Follow-Up Evaluation
- Neurological Assessment
- Pain Medication Log
- Radiographs: Weightbearing AP, neutral lateral, flexion and extension views
- CT scan

5.3.9 Twenty-four (24) Month Study Interval – Final Active Assessment (730 days ± 60 days)

The following forms/assessments are required to be completed at this interval:

- Patient Survey
- Follow-Up Evaluation
- Neurological Assessment
- Pain Medication Log
- Radiographs: Weightbearing AP, neutral lateral, flexion and extension views
- CT scan (performed only if determined not fused per CT scan at the 12-month interval)

5.3.10 Thirty-Six (36) Month Study Interval – Remote Assessment (1095 days ± 60 days)

The following forms/assessment are required to be completed at this interval until the last subject enrolled in the trial has completed their 24-month exam:

- Patient Survey
- Long-Term Follow-Up Questionnaire

5.3.11 Forty-Eight (48) Month Study Interval – Remote Assessment (1460 days ± 60 days)

The following forms/assessment are required to be completed at this interval until the last subject enrolled in the trial has completed their 24-month exam:

- Patient Survey
- Long-Term Follow-Up Questionnaire

6.0 RADIOGRAPHIC EVALUATIONS

Radiographic evaluations (x-rays) are to be performed in accordance with the study protocol. All x-rays are to be performed weightbearing (standing). Anterior/Posterior (AP) and Neutral Lateral (NL) X-rays are taken preoperatively and are repeated prior-to-discharge from the hospital and at the 6-week, 3-, 6-, 12-, and 24-month post-operative visits. The prior-to-discharge weight-bearing AP and neutral lateral X-ray will serve as the baseline postoperative assessment of disc space height. Lateral Flexion/Extension X-rays are taken preoperatively and repeated at the 6-, 12- and 24-month post-operative visits to document the preoperative condition of the involved disc space and to evaluate stability and fusion of the operative level during follow-up. X-rays shall be obtained with a study-specific magnification marker in place. The marker allows the core lab to adjust for magnification discrepancies and ensure measurement accuracy. ***Further, to help assure accurate reporting of quantitative sagittal alignment by lumbar segment in this investigation, neutral lateral radiographs shall adequately display the vertebral bodies from T-12 through S1.***

A CT scan will be performed at the 12-month study interval. In the event a subject is determined "not fused" at the 12-month timepoint per the CT scan assessment, a second CT scan would be performed at the 24-month post-op interval. **Table 2** below indicates the per protocol radiographic schedule.

Table 2: Radiographic Assessment Schedule

	Pre operative	Post operative	6 week	3 month	6 month	12 month	24 month
MRI (T2 weighted image)[ŧ]	X						
Standing AP X-rays	X	X	X	X	X	X	X
Standing NL X-rays	X	X	X	X	X	X	X
Lateral flexion-extension films	X				X	X	X
CT Scan						X	X*

[ŧ]Or other appropriate radiologic study as defined per protocol.

*Performed only if determined to be not fused per CT scan at the 12-month interval

The following radiographic analyses are planned:

Radiographic assessment for bridging bone will be completed by two board-certified radiologists. A third radiologist will provide a “tie-breaker” reading if needed. Radiologist evaluations will be centralized for films from all investigational sites.

Fine-cut CT images with sagittal and coronal reconstructions will be used as the primary determinant of fusion status. X-ray images will also be subjected to a qualitative assessment to evaluate for the presence of bridging bone.

Follow-up x-rays will be evaluated by an independent radiographic core laboratory. For this trial, the core lab will measure relative angulation and translation of the vertebral bodies at the involved motion segment during flexion/extension motion, and will also measure both anterior and posterior disc space height. The core lab will further evaluate for device condition/configuration and position changes over time.

Imaging will be reviewed by the radiologist/core lab for the presence of any of the following negative conditions:

- Expulsion: Implant moved outside of disc space
- Migration: > 5 mm migration of implant from original position
- Subsidence: > 5 mm loss of disc height
- Significant Radiolucency: > 50% of implant/endplate interface shows true lucency (true lucency is black, not gray)
- Adjacent level disc degeneration, defined as:
  - > 5mm loss of disc height
  - > 3mm translation on flexion/extension
- Loosening and/or breakage of pedicle screws

The radiographic assessment protocol, film labeling instructions, and other radiographic reference material are included in **Appendix IV**.

7.0 BENEFIT / RISK ANALYSIS

7.1 BENEFITS

In this investigation there may or may not be a direct benefit to the subject for study participation. Potential direct benefits may include but are not limited to:

- Stabilization of the spine as an adjunct to bony fusion
- Restoration of the disc space which may lead to immediate symptom relief
- Reduction of low back and/or leg pain and other associated symptoms
- Improved function of the low back

An indirect benefit to subject participation in this investigation is that it may lead to future improvements in the treatment of lumbar degenerative disc disease and help to relieve lumbar DDD associated symptoms in other patients suffering from this condition.

7.2 RISKS

7.2.1 SIFS Mesh Risks

The potential risks associated with the study device include but are not limited to:

- Mesh disruption (tear)
- Device migration
- Allergic reaction to PET

7.2.2 MTF G2 Dry Mix Graft Risks

The potential risks associated with the Graft Mix include but are not limited to:

- Disease or infection from use of human tissue, and allergic reaction to trace substances including Gentamicin, Primaxin and Amphotericin B antibiotics and Polysorobate-80, Ethanol, Methanol, Isopropanol, Polyoxyethylene (10) Phenol Ether and Hydrogen Peroxide.

7.2.3 Surgery Risks

Recognized risks associated with lumbar fusion surgery and surgery in general, are well documented in literature and include but are not limited to:

- *Hardware related* conditions such as malposition of the pedicle screws, pedicle wall perforation, hardware breakage/fracture or loosening, hardware disassembly, soft tissue irritation, and penetration of the endplate/disc, and other potential events related to the commercial hardware

- *Incisional related* including infection (local or deep tissue), Seroma/hematoma, hemorrhage, bone graft harvest site pain, and other potential incisional related events
- *Spine-related neurological* conditions such as spinal cord compression, paraplegia, paraparesis, transient radiculopathy, reflex sympathetic dystrophy, dural teal, nerve injury, foot drop, and other potential neurological conditions
- *Spine-related musculoskeletal* conditions such as sacroiliac joint instability or pain, symptomatic disc degeneration at other lumbar levels, muscle spasm or strain, vertebral body or facet fracture, bone infection, or other musculoskeletal conditions
- *General surgery related* conditions including but not limited to events related to the respiratory (e.g., pneumonia, pulmonary embolism, pulmonary edema, atelectasis, anesthesia complications, etc.), cardiovascular (e.g., cardiac arrhythmia, myocardial infarction, stroke, coagulopathy, deep vein thrombosis, thrombophlebitis, transient drop in blood pressure, vascular injury, false aneurysm, etc.), endocrine/immune (e.g., adrenal insufficiency, adrenal hormone excess, diabetes mellitus, hypoglycemia, thyroid disorders, osteoporosis, pituitary disorder, amenorrhea, Graves' disease, multiple sclerosis, myasthenia gravis, rheumatoid arthritis, lupus, etc.), gastrointestinal, urinary and reproductive symptoms (e.g., ileus, bowel incontinence, urinary tract infection, sexual dysfunction, etc.)
- *New, or increase in, pain experienced* such as in the low back, leg(s), graft harvest site or other type of pain.
- *Exposure to radiation* from medical imaging including x-rays to diagnose the condition and monitor recovery, and fluoroscopic imaging used during any treatment procedure; because ionizing radiation can cause damage to DNA, exposure can increase a person's lifetime risk of developing cancer
- *Death*

7.3 RISK MINIMIZATION

In this investigation, risks will be minimized through the following measures:

- Formal surgeon training in the proper use of the Spineology Interbody Fusion System,
- Investigation site training on the study protocol and trial conduct,
- Close subject assessment during the treatment and clinical follow-up period, and
- Risk assessment based monitoring practices and trial oversight.

8.0 SAFETY EVALUATION

Safety of the Spineology Interbody Fusion System will be determined through the reporting process for Adverse Events. All adverse events, whether felt to be device-related or not, are to be reported and followed at each study interval to resolution, or for events that remain unresolved, until the subject concludes study participation. Information captured will include the type and description of the event, date of onset, treatment required and resolution status. The investigator shall additionally provide any supplemental information pertinent to the overall evaluation of the event. All reported events will be reviewed and adjudicated by an independent Data Monitoring Committee (DMC)/Clinical Events Committee (CEC).

For this investigation, an adverse event is defined as a secondary disease or condition that develops in addition to, or at an increased rate or severity from, the expected response to treatment, necessitating further evaluation and treatment by a physician. An adverse event may be an undesirable clinical occurrence, subject complaint, change in health status, or product issue. A clinical event will not be reported if it existed at the time of enrollment and continued unchanged thereafter, unless the event worsened considerably requiring additional medical or pharmacological treatment. Adverse Event reporting begins during the study treatment surgical procedure.

8.1 Adjudication Procedure

Each AE will be reviewed individually by a DMC/CEC. The DMC Charter is provided as **Appendix V.** Each event is initially classified as an adverse event or a non-event. A non-event is an event that does not require treatment. An event captured and determined to be a non-event will be reported as an observation. Following this determination, an adverse event is assessed for relatedness to the trial and may be classified as a study-related adverse event or a not-study-related adverse event. A not-study-related adverse event is an adverse event determined to not have a causal relationship with either the device or the procedure. All study-related adverse events are further adjudicated for severity and relatedness to the procedure/device as defined below.

Event severity refers to the degree of seriousness of the AE. The categories of event severity are: Serious Adverse Event (SAE) and a rating of mild, moderate or severe. Event relatedness refers to the association to the investigational device, fixation hardware or the surgical procedure. Event relatedness is categorized by the following associations: device related, hardware related, procedure related, other related, or unknown (undeterminable) relatedness.

For clarification, the following “relatedness” definitions will be applied in this investigation:

- Device Related: An adverse event that results from the presence or performance of the SIFS mesh device.
- Hardware Related: An adverse event that results from the presence or performance of any of the supplemental fixation device components.
- Procedure Related: A procedure related adverse event shall be evaluated and adjudicated in accordance with the below sub-classifications. A procedure related AE may occur as a result of one or more of the following and shall be specified as such for analysis and reporting purposes:
  - *Procedure – Device:* Occurs due to the implantation procedure for the investigational mesh device
  - *Procedure – Hardware:* Occurs due to the implantation procedure for the supplemental fixation
  - *Procedure – General Surgery:* Occurs as a result of the general surgical procedure and is not related to any of the above defined definitions or any of the below definitions.
- Other Related: An adverse event that occurs and is determined to have a relatedness that is not device, hardware, procedure, general surgery, or unknown relatedness.
- Unknown: An adverse event that cannot be determined to have a causal relationship with either the device or procedure will be classified as unknown.

It is anticipated that resultant of the defined criteria for each relatedness determination, few adverse events will be categorized as "Other". The severity of events will be classified by the DMC as described in the following two sections.

8.2 Serious Adverse Event

The DMC will first determine whether an AE is serious. A Serious Adverse Event, corresponding to FDA's definition, is an adverse event that results in one of the following outcomes:

- requires hospitalization,
- prolongs hospitalization,
- is life-threatening,
- results in a congenital anomaly/birth defect, or
- results in death.

8.3 Event Severity

The DMC will adjudicate the severity of each AE. Severity is categorized as follows:

- **Severe Adverse Event**: Significant impairment of functioning; subject is unable to carry out usual activities. A severe AE requires treatment or intervention.
- **Moderate Adverse Event**: Subject experiences sufficient discomfort to interfere with or reduce their usual level of activity. A moderate AE requires treatment.

- **Mild Adverse Event**: Subject is aware of event or symptom, but event/symptom is easily tolerated. A mild AE may not require treatment.

The Clinical Event Committee shall be convened on a quarterly basis through the duration of the investigation to formally review and adjudicate study events. The DMC Chairperson shall perform an interim (continuous) review of adverse events prior to conducting the quarterly committee review(s). The Chairperson may convene a Committee meeting at his/her discretion at any time to ensure subject safety is adequately protected.

9.0 ETHICS

This investigation will be conducted in accordance with ethical principles having their origins in the Declaration of Helsinki. This investigation will further be conducted in accordance with applicable federal regulations, specifically, the Title 21 Code of Federal Regulations, Part 812 – IDE Regulations, Part 50 – Informed Consent, Part 54 – Financial Disclosure, Part 56 – IRBs, ISO 14155 (2012), and ICH E6 – Good Clinical Practices (GCPs) Consolidated Guidance.

9.1 INSTITUTIONAL REVIEW BOARD (IRB)

Prior to participating in this investigation, the clinical site will be responsible for obtaining approval from their governing IRB. The Principal Investigator (PI) at the site is responsible for obtaining and maintaining IRB approval to participate in this investigation. A copy of the initial and all periodic review and approvals shall be maintained in the investigative site's administrative binder. A copy of each approval shall be provided to Spineology as the study sponsor and shall be maintained in the respective site administrative files.

9.2 INFORMED CONSENT

Prior to enrolling subjects into this investigation, a site-specific IRB approved Informed Consent Form (ICF) is required. The PI at each site is responsible for obtaining and maintaining the site-specific approved ICF. A copy of the site-specific initial ICF, and any subsequent approved revisions of the ICF, will be provided to Spineology in a timely manner for maintenance in the respective site-specific administrative file.

Subject participation in this investigation is voluntary. In accordance with FDA regulation 21 CFR, Part 50, written informed consent is required of all subjects (or their legal representative) **prior to study participation**. ***Spineology is required to report any failure to obtain subject consent to FDA within 5 working days of learning of such an event (21 CFR, §812.150(b)(8)).***

A sample Informed Consent Form Template for this investigation is provided as **Appendix VI**.

9.3 PATIENT DATA CONFIDENTIALITY

All information and data provided to Spineology concerning subjects and their participation in this clinical investigation will be considered confidential by Spineology. Only authorized sponsor personnel or an appropriately identified FDA representative will have access to these confidential files. All data used in the analysis and reporting of this investigation will be without identifiable reference to specific subject names. Subjects will be identified by a three (3) digit (sequential)

number and a three (3) letter name code. The name code will be determined using the subject's first-middle-last initials. As an example, a subject named John Quincy Smith would have a name code of JQS. In the event a subject does not have a middle name, a dash (-) shall be used in its place. Further, each investigative site is assigned a three (3) digit number as the site identifier code by the sponsor. The site ID together with the subject ID and name code shall constitute the complete subject ID. As an example, if John Quincy Smith was the first subject enrolled at a site assigned a site ID code of 123, he would be identified as subject 123-001 JQS. All subject IDs are unique to the site/subject.

Data collected in this investigation will be obtained in compliance with applicable federal regulations relating to confidentiality and security of protected health information (PHI) including by not limited to the Health Insurance Portability and Accountability Act (HIPAA). HIPAA regulations require a signed subject authorization, which informs the subject of the following:

- What PHI will be collected from trial subjects,
- Who will have access to that information and why, and
- Who will use or disclose that information.

In the event that a subject revokes authorization to collect or use PHI, the Investigator, by regulation, retains the ability to use all information collected prior to the revocation of subject authorization. For subjects who have revoked authorization to collect or use PHI, attempts should be made to obtain permission to collect at least vital status (i.e., that the subject is alive) at the end of their scheduled trial period.

In accordance with HIPAA regulations, subject records leaving the facility for purposes of the investigation should be identified by the Subject ID assigned for the trial and should not include the subject's name, whenever practical. Every effort should be made to "black out" (redact) the subject's name from medical records, including x-rays, prior to sending to Spineology.

This trial is being conducted in compliance with FDA 21 CFR and all personal information pertaining to subjects will be kept confidential. Whenever practical, subjects will be identified only by their subject ID number and initials. Clinical trial documents and hospital and clinic medical records pertaining to trial subjects may be reviewed by Spineology trial personnel or their representatives, FDA, or other health inspectors as needed to assure compliance with trial requirements.

Information obtained in the course of executing this trial, including still and motion photography, may be presented for regulatory, clinical or educational purposes provided no subject is identified. The information collected is the property of Spineology.

9.4 DATA MONITORING COMMITTEE (DMC)

An independent Data Monitoring Committee will be established for this investigation and will function as an advisory group to provide independent oversight of the investigation and to ensure patient safety. The DMC shall be comprised of no less than three (3) physician consultants of appropriate training, expertise and experience in the spinal discipline and a biostatistician. A DMC Chairperson shall be designated to preside over DMC meetings. The DMC may function in the role of a Data Safety Monitoring Board (DSMB) and as a Clinical Events Committee (CEC). The complete DMC Charter is provided as **Appendix V**.

DMC DSMB primary responsibility is to ensure subject safety. Additional DMC DSMB responsibilities may include, but are not limited to, review of interim analyses of outcomes, safety data summaries and study performance information. In addition, the DMC DSMB may provide recommendations relative to the study design, stopping rules for trial conduct, and determinations for continuance, modification, or termination of investigation conduct. DMC DSMB meetings will be conducted no less than annually.

DMC CEC responsibilities include review and adjudication of all adverse events reported for this investigation. The DMC CEC shall adjudicate events for seriousness, relatedness and severity. The DMC CEC shall review all events for potential UADE occurrence. DMC CEC meetings shall be conducted on a quarterly basis throughout the duration of this investigation.

9.5 FINANCIAL DISCLOSURE

All clinical investigators shall disclose to the sponsor sufficient and accurate financial information enabling Spineology to submit complete and accurate certification or disclosure statements as appropriate. The investigator shall promptly update this information should any relevant changes occur during the course of the investigation and for one (1) year following completion of this investigation.

9.6 RADIOGRAPHIC CORE LAB

An independent core lab will be established to perform the required qualitative and quantitative x-ray measurements/assessments. In addition, two (2) core lab radiologists will perform fusion assessments at the 12-month and 24-month time points. A third core lab radiologist will function in the role of adjudicator in the event of discrepant readings between Reviewer 1 and Reviewer 2. For greater detail on core lab responsibilities and assessment, refer to the Radiographic and Core Lab Assessment Protocol provided as **Appendix IV**.

9.7 INVESTIGATIONAL DEVICE USE AND DISPOSITION

As previously stated within this investigation protocol, only sites approved by Spineology Clinical Affairs shall receive investigational product.

For this investigation, SIFS product shall be provided to sites on a ship-in/ship-out basis in support of study cases. Accordingly investigational product shall not be stored or maintained at the investigation site. Following case conclusion, the study product shall be returned to sponsor. Inventory accountability will be managed and tracked by sponsor and reported to FDA as a component of the annual reporting requirements. Records pertaining to device shipment shall be maintained by sponsor with copies of device receipt invoices shipped to the site maintained in the respective site's administrative files. Device shipping invoices shall include the name of the consignee, type and quantity of device, date of shipment, and the lot number.

The site primary investigator is responsible for ensuring that investigational devices are made available only to site personnel who are authorized to access them and only to subjects under the Investigator's or sub-Investigator's supervision.

At the completion of the clinical investigation, any investigational product present at the site must be returned to Spineology. Further, a complete, and final, device accountability and reconciliation will be performed by Spineology at investigation conclusion and reported to FDA in accordance with Federal regulation.

10.0 DATA COLLECTION FORMS

The following patient-centric forms shall be used to record data in this investigation. Case report forms (CRFs) shall be completed accurately and in a timely manner. The Principal Investigator at each study site is responsible for oversight of the completion and submission of all clinical data collect at the respective site. For this investigation, data will be collected electronically and in compliance with the Code of Federal Regulations Title 21 Part 11.

The electronic version of the CRF is referred to as the eCRF. The eCRFs displayed in the electronic data capture (EDC) system implemented for this investigation yields additional functionality and form prompting beyond the basic information identified for capture in the paper version of the CRF. The eCRF is completed by the site in the EDC system. The paper version of the forms is provided to investigative sites in the form of worksheets for ease of use. The Inclusion/Exclusion worksheet and the Patient Survey worksheet may function as source documentation and shall be treated accordingly. The site shall provide the sponsor with redacted copies of all supporting source documentation as required to support centralized monitoring capabilities. Sample CRFs are provided as **Appendix VII**.

Screening Log – This log will record each subject enrolled into the investigation. It will additionally include patients screened for potential inclusion that fail to meet study entrance criteria. For screen failures, minimal information is collected to ensure compliance with HIPAA guidelines and to protect patient confidentiality. The eScreening Log should be updated on a regular basis by the site.

Inclusion/Exclusion Entrance Checklist – This form will be used to screen subjects for study entrance criteria to confirm the individual is an appropriate candidate for study participation. The eCRF should be entered in the EDC system as soon as reasonable but no later than 10 working days of subject enrollment.

Baseline/Pre-op History Form – This form captures relevant baseline information such as demographics, diagnosis for procedure, spinal treatment (conservative measures and surgical intervention) history, work status, etc. The eCRF should be entered in the EDC system within 10 working days of subject enrollment.

Patient Survey – This survey form collects subjective data consisting of pain rating on a Visual Analog Scale (VAS) for the low back, right leg, left leg and iliac crest as applicable (iliac crest completed at post-op intervals only for subject who underwent iliac crest graft harvest). The survey additionally contains a 10-question Oswestry Disability Index (ODI) to assess low back function and an SF-36 health questionnaire to assess mental and physical components. Lastly, this form allows the subject to rate their level of satisfaction with their surgical outcome and is to be completed only at the post-op follow-up intervals. The eCRF should be entered in the EDC system within 10 working days of the study visit date.

Pain Medication Log – The pain medication log shall be completed at baseline and reviewed at each subsequent study interval follow-up examination. The log shall be updated for changes in pain medication use (start, stop, changes in dosing) as compared to the previous study interval visit. Beyond identifying the prescription information (i.e. medication name, strength and frequency of use), the site shall specify if the pain medication is prescribed for treatment of low back pain or for other reasons. The eLog should be reviewed/updated in the EDC system within 10 working days of the study visit date.

Neurological Evaluation – This form captures relevant neurological testing for the lumbar spine (L2 – S1). Neurological testing includes assessment of bilateral lower extremity deep tendon reflexes (knee and ankle), muscle strength tested against resistance (hips, knees, ankles, and feet), and lumbosacral dermatome sensation (low back, thighs, calves, and feet). The eCRF should be entered in the EDC system within 10 working days of the study visit.

Surgery/Hospitalization – This form records relevant information regarding the study procedure including hospitalization duration, device detail, supplemental fixation detail and operative/intraoperative/postoperative findings. The eCRF should be entered in the EDC system within 10 working days of the subject discharge date.

Follow-Up Evaluation – This form captures relevant information regarding postoperative subject medical care, tobacco use, alcohol consumption, work status and occurrence of adverse events. The eCRF should be entered in the EDC system within 10 working days of the study visit.

Long-Term Follow-Up Questionnaire – This self-administered patient questionnaire captures relevant information regarding postoperative subject tobacco use, alcohol consumption, work status and safety information (occurrence of additional surgical intervention). In the event a subject identifies supplemental surgical intervention has occurred, the study site shall complete a corresponding adverse event form after obtaining the necessary and appropriate information. The questionnaire eCRF should be entered in the EDC system within 10 working days of completed form receipt.

Adverse Event (AE) – This form shall be entered into the EDC system as soon as reasonable for any subject presenting with an adverse event. Beyond eCRF completion, the site shall forward copies of redacted source documentation that support the AE to the sponsor. As noted above, the eCRF shall be entered in the EDC system as soon as reasonable but not greater than 15 working days of discovery of the event. The source documentation copies shall ideally be forwarded to Spineology within 15 working days of the discovery of the event.

Protocol Deviation (PD) – This form documents deviations from the study protocol. Protocol deviations shall be entered into the EDC system within 5 working days of the discovery of the deviation.

Subject Discontinuation (SD) – This form documents a subject's decision to withdraw from the investigation or an investigator's determination to discontinue a subject from study participation. The SD form shall be entered into the EDC system within 15 working days of the discontinuation notification.

Unanticipated Adverse Device Effect (UADE) – The UADE form records any unexpected adverse device effects experienced by a study subject. The investigator is required to notify the sponsor as soon as possible but not later than 10 working days after discovery of the UADE. The UADE form is entered into the EDC system by the site.

11.0 DEFINITIONS

Adverse Event – A secondary disease or condition that develops in addition to, or at an increased rate or severity from, the expected response to treatment, necessitating further evaluation and treatment by a physician. All adverse events, whether related or unrelated to the device or procedure, shall be captured and reported. Further, all adverse events will be adjudicated by the Data Monitoring Committee and reported to FDA per protocol.

Case Report Form (CRF)/Electronic Case Report Form (eCRF)/CRF Worksheet –

- ***CRF*** – A document designated to record protocol required information for each subject participating in an investigation. A CRF may be provided to sites in paper copy or electronic copy. A paper CRF may be used as a worksheet providing the captured information is recorded in the electronic database.
- ***eCRF*** – A database equivalent electronic version of the CRF.
- ***CRF Worksheet*** – A paper version of a CRF used to collect data that will be entered into the eCRF. Worksheets shall be maintained in the relevant study subject's binder at the investigation site.

Centralized Monitoring – A remote evaluation carried out by sponsor personnel or representatives (e.g., clinical monitors, data management personnel, or statistician) at a location other than the site(s) at which the clinical investigation is being conducted.

Device Related – An adverse event that results from the presence, performance or implantation procedure of the investigational device (SIFS mesh).

Enrolled – For this investigation, a subject is considered enrolled after meeting all study entrance criteria, has confirmed agreement to participate in the investigation as documented through completion of the informed consent process, and has been assigned a surgical procedure date. Further, it is expected that prior to enrollment, the investigational site will have successfully negotiated the precertification process as required for pertinent insurance carriers, and obtained documentation of the carrier's precertification approval.

Extended Hospitalization – Increased duration of hospitalization based on determination of the treating investigator.

Functional Disability – In this investigation, functional disability is defined as the subject's self-rated score on the Oswestry Disability Index. The ODI is a commonly used 10 question instrument for assessing patients with back pain. The greater the score achieved, the greater the functional disability. A lower ODI score indicates less back disability (greater back function). A 15 point difference compared to baseline is considered clinically significant.

Hardware Related AE – An adverse event that results from the presence, performance or implantation of the supplemental fixation device hardware or its components.

Informed Consent – A process by which a subject voluntarily confirms his or her willingness to participate in a particular investigation, after having been informed of all aspects of the investigation that are relevant to the subject's decision to participate. Informed consent is

documented by means of a written, signed, and dated informed consent form approved by the site's reviewing IRB.

Institutional Review Board (IRB) – An independent body (a review board or a committee, institutional, regional, or national (centralized) constituted of medical/scientific professionals and non-medical/non-scientific members, whose responsibility it is to ensure the protection of the rights, safety, and well-being of human subjects involved in an investigation and to provide public assurance of that protection, by among other things, reviewing and approving/providing favorable opinion on the investigation protocol, the suitability of the investigator(s), facilities, and the methods and materials s to be used in obtaining and documenting informed consent of the investigation subjects.

Low Back Pain (LBP) – For this investigation, LBP is defined as the self-rated score a subject indicates on a Visual Analog Scale during normal daily activities. When interpreting the VAS, a higher score indicates a greater level of pain severity and a lower score indicates a lesser severity of pain. LBP is captured on a 100mm VAS. A 20mm difference when compared to baseline is considered clinically significant. The same measurement system/guideline is employed for leg pain.

Not Study-Related AE – An event adjudicated by the DMC CEC and determined to not have a causal relationship with either the device or the procedure.

Observation – An observation is an event adjudicated by the DMC CEC and determined to be a non-event and did not require treatment.

On-Site Monitoring – An in-person evaluation of the clinical investigation site that is conducted by sponsor personnel or representatives.

Other Related AE – An adverse event that occurs and is determined to have a relatedness that is not device, hardware general surgery or unknown relatedness.

Procedure Related AE – An adverse event that occurs as a result of the surgical procedure. A procedure related AE may occur as a result of one or more of the following and shall be specified as such for analysis and reporting purposes:

- *Procedure – Device:* Occurs due to the implantation procedure for the investigational device (SIFS mesh)
- *Procedure – Hardware:* Occurs due to the implantation procedure for the supplemental fixation
- *Procedure – General Surgery:* Occurs as a result of the general surgical procedure

Removal – A surgical procedure in which all of the original system (intervertebral device plus supplemental fixation) confirmation is removed, with or without replacement.

Re-Operation – Any surgical procedure at the treated level that does not include removal, modification, or addition of any implanted components.

Revision: Device – A surgical procedure that adjusts or in any way modifies or removes part of the original intervertebral implant configuration, with or without replacement of a component. A revision may also include adjusting the position of the original configuration.

Revision: Hardware – A surgical procedure that adjusts or in any way modifies or removes part of the original supplemental fixation implant configuration, with or without replacement of a component. A revision may also include adjusting the position of the original configuration.

Risk-Based Monitoring – A dynamic assessment procedure that systematically approaches clinical trial monitoring of the individual and global investigation sites, evaluating for data integrity, observable trending and compliance risks that may be associated with the clinical investigation during the trial lifecycle.

Serious Adverse Event (SAE) – An adverse event that requires hospitalization, prolongs or extends the hospitalization, is life-threatening, results in a congenital anomaly/birth defect, or results in death. The device-relatedness or procedure-relatedness of such an event will be adjudicated by the DMC.

Study-Related Event – An event that meets the definition of an Adverse Event and in addition is determined to have a causal relationship to the study and/or attributable to study participation. The application of a Study-Related Adverse Event status is determined by the Data Monitoring Committee (DMC) as a component of the adjudication process. While all events regardless of status, categorization or relatedness are adjudication by the DMC and reported to FDA, only those events determined to be Study-Related Adverse Events will be included in the final statistical analysis for this trial.

Unknown Related AE – An adverse event that cannot be determined to have a causal relationship with either the investigational device, supplemental fixation hardware or its components, general surgery, or other relatedness.

Unanticipated Adverse Device Effect (UADE) – Any serious adverse effect on health or safety, 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 application; or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

12.0 PROTOCOL DEVIATION

Deviations from protocol shall be document on a Protocol Deviation (PD) Form. PDs are reportable to the investigator's reviewing IRB and to FDA as a component of the periodic (annual) reporting requirements, unless otherwise directed by the reviewing IRB requirements or as the specific circumstance dictates.

Every attempt shall be made to adhere to the investigation protocol. Should an investigator deviate from the protocol to protect the life or physical wellbeing of a study subject in an emergent circumstance, such notice shall be given to the sponsor as soon as possible, but not more than five (5) working days from the date the emergency occurred. With the exception of the emergent circumstance, prior approval from the study sponsor is required for any change in, or deviation from, the investigation protocol considered to be major as such changes may affect the scientific soundness of the clinical investigation or the rights, safety, and welfare of study subjects.

For reporting purposes, deviations from protocol shall be grouped into the below categories. Examples are provided to ensure consistent reporting.

- *Major Protocol Deviation* – a deviation from the study protocol that ***impacts*** the risks and benefits of the study; impacts participant safety, affects the integrity of study data, or affects a participants willingness to participate in the study. For example:
    - Failure to obtain informed consent
    - Informed consent obtained after the study procedure is performed
    - Use of an invalid Informed Consent Form, i.e., consent form without IRB approval stamp, or outdated/expired consent form
    - Enrolling subjects outside the study entrance criteria
    - Failure to perform the final (24-month) study examination/required testing as this impacts the study integrity

- *Minor Protocol Deviation* – a deviation from the study protocol that ***does not impact*** participant's safety, compromise the integrity of the study data, or affect participants' willingness to participate in the study. For example:
    - Study visit conducted outside the required timeframe
    - Failure to perform a required interval evaluation – excluding the final (24-month) exam
    - Failure to perform a required research activity

13.0 COMPLIANCE

It is expected that investigational sites (investigators, study coordinators, ancillary site personnel, and subjects) will be compliant with the investigation protocol. Should it be determined that the site is noncompliant, reasonable efforts will be made to secure compliance. These efforts/actions will be documented in writing and maintained within the sponsor study administration file. Should it be determined significant site compliance or site management issues present, these will be documented in a clinical corrective and preventative action (cCAPA) plan. The cCAPA shall define the infraction, outline an action plan to achieve resolution, and be signed by the sponsor representative and the principal investigator at the site. A copy of the signed cCAPA shall be maintained at the investigational site with the original being maintained by the sponsor in the site-specific administrative files.

14.0 INVESTIGATOR RESPONSIBILITY

Investigators are responsible for ensuring the investigation is conducted in accordance with the study protocol and applicable federal regulations (21 CFR, Subpart E). Investigators are additionally responsible for:

- Obtaining IRB approval for study conduct and re-approval as applicable. If more than one (1) investigator at a site is participating in the investigation, the Principal Investigator (PI) shall be responsible for obtaining initial IRB approval and subsequent IRB approvals for the duration of time the site is participating in the trial.
- Obtaining informed consent of study subjects prior to enrollment into the investigation
- Protecting the subject's rights, safety and welfare
- Maintenance of subject records and confidentiality
- Record retention as defined per federal regulations 21 CFR, §812.140 (a), (d), and (e)
- Management of investigation and study related activities in accordance with the Clinical Trial Agreement (CTA)
- Submission of site-specific study closure report to the reviewing IRB within three (3) months of notification from the sponsor. If more than one (1) investigator is participating in the trial at a given site, the PI is responsible for submission of the closure report to the reviewing IRB.
- Return of any unused investigational product to the study sponsor upon request by Spineology or at the conclusion of the investigation.

Note: In the event that an Investigator withdraws from the responsibility to maintain records for the required period of retention required for this investigation, a transfer of custody of records shall be permitted. The transfer of custody must be to an individual willing to accept responsibility for the records in accordance with Federal regulation. Further, a notice of transfer of records shall be provided to FDA no later than 10 working days after the transfer occurs.

15.0 SPONSOR RESPONSIBILITY

The study sponsor, Spineology, is responsible for ensuring the investigation is conducted in accordance with the study protocol and applicable federal regulations, specifically, Title 21 Code of Federal Regulations, Part 812, Part 50, Part 54, Part 56 and Good Clinical Practices (GCPs).

Although included in the above citation, Spineology is additionally responsible for the following:

- Selecting qualified investigators and providing study investigators with appropriate information for study conduct (21 CFR 812.40)
- Ensuing review and approval process for reviewing IRB(s) is obtained (21 CFR 812.40)
- Appropriate monitoring of the clinical investigation (21 CFR 812.46)
- Appropriating reporting in accordance with federal regulation (21 CFR, 812.150(b)(1-10)
- Record maintenance and retention per federal regulation (21 CFR, 812.140 (b)(d) and (e))
- Prompt notification of FDA, IRBs, and al investigators of unanticipated adverse device effects (21 CFR 812.150(b)(1))
- Submission of progress reports in accordance with federal regulation (21 CFR 812.150(b)(5)
- Submission of final study closure report that details the cumulative study experience to FDA, governing IRBs, and Investigators within six (6) months of completing the clinical investigation, in addition to fulfilling semi-annual and annual reporting requirements (21 CFR 812.150(b)(7))

16.0 MONITORING PLAN

This clinical investigation will be monitored by Spineology personnel, or a designated Spineology representative, for appropriate study conduct, compliance and date integrity. In accordance with the Food and Drug Administration's Guidance for Industry, Oversight of Clinical Investigations – A Risk-Based Approach to Monitoring (August 2013) publication, risk-based monitoring practices shall be implemented for the present investigation. Monitoring efforts shall employ periodic on-site monitoring visits and centralized (remote) monitoring that align with Spineology Standard Operating Procedures for clinical site and investigation monitoring.

On-site monitoring shall be conducted to identify data entry errors and discrepancies, missing data, missing data in source records/documents, provide assurance of appropriate source documentation existence, educate sponsor personnel on site-specific procedures, assess site compliance with protocol, and evaluate sites for maintenance or changes in staff, facility, and resources.

Centralized monitoring shall be conducted for remote source data verification, site characteristics and performance metrics to assess for trends, detect high risk type errors and evaluate for other potential risk factors. High risk indicators include, but are not limited to, elements of:

- *Protocol Integrity* – randomization/blinding, study entrance criteria, protocol procedure deviation, and lost-to-follow-up.
- *Patient Safety* – adverse events, serious adverse events, unanticipated adverse device effects, inclusion deviations, and informed consent deviation.
- *Regulatory Compliance* – Institutional Review Board approval and investigational device handling/management.
- *Data Quality* – Query resolution, missing data, and missed visit deviations.

For data evaluation, should discrepancies be identified between the comparison of source data and submitted data, data queries will be assigned by the monitor and resolved by the investigational site. Following conclusion of the investigation, Spineology monitors will conduct a site specific study closure visit. The study closure visit will consist of reconciliation of data inconsistencies, outstanding data queries, review of previously unresolved adverse event to either obtain resolution or a current status determination if unable to resolve, and review of administrative materials. In addition, Spineology will perform a device reconciliation of all investigational product ensuring that any and all investigational product that may be at an investigational site is returned to the sponsor. Study closure visits will occur within three (3) months following study conclusion.

Monitoring of this clinical investigation will be accomplished by Spineology, Inc., and performed under the supervision of:

[redacted]
Spineology, Inc.
7800 3rd Street North, Suite 600
Saint Paul, MN 55128-5455

[redacted]

Record retention for this investigation shall be in accordance with Federal regulation (21 CFR §812.140 (a) (b). Accordingly, Investigator and sponsor investigation records shall be maintained for a period of two (2) years or after the latter of the following two (2) dates:

- The date on which the investigation is terminated or completed, or
- The date that the records are no longer required for purposes of supporting the sponsor's premarket approval application or a notice of completion of a product development protocol.

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18.0 STUDY SPONSOR

Comments or correspondence pertinent to this study should be directed to:

[redacted]
Spineology, Inc.
7800 3rd Street North
Suite 600
Saint Paul, MN 55128-5455
[redacted]

Or

[redacted]

19.0 REVISION HISTORY

Revision	Effective Date	DCO Ref. #	Reason/Description of Change
A	03Sep2014	4618	Origination