DE NOVO CLASSIFICATION REQUEST FOR SPINEOLOGY INTERBODY FUSION SYSTEM

REGULATORY INFORMATION

FDA identifies this generic type of device as:

Intervertebral body graft containment device. An intervertebral body graft containment device is a non-rigid, implanted spinal device that is designed to contain bone graft within its internal cavity. The device is inserted into the intervertebral body space of the spine and is intended as an adjunct to intervertebral body fusion.

NEW REGULATION NUMBER: 21 CFR 888.3085

CLASSIFICATION: Class II

PRODUCT CODE: OQB

BACKGROUND

DEVICE NAME: Spineology Interbody Fusion System

SUBMISSION NUMBER: DEN200010

DATE DE NOVO RECEIVED: February 19, 2020

SPONSOR INFORMATION:

Spineology, Inc.
7800 3rd Street North, Suite 600
Saint Paul, Minnesota 55128

INDICATIONS FOR USE

The Spineology Interbody Fusion System (SIFS) is indicated for use as an adjunct to fusion 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 Grade 1 spondylolisthesis at the involved level. DDD is defined as discogenic back pain with degeneration of the disc confirmed by patient history, physical examination, and radiographic studies. Eligible patients shall have undergone six (6) months of conservative (non-operative) care. SIFS with compatible allograft and autograft is intended for use with supplemental posterior fixation systems intended for use in the lumbar spine.

LIMITATIONS

The sale, distribution, and use of the Spineology Interbody Fusion System are restricted to prescription use in accordance with 21 CFR 801.109.

PLEASE REFER TO THE LABELING FOR A COMPLETE LIST OF WARNINGS, PRECAUTIONS AND CONTRAINDICATIONS.

DEVICE DESCRIPTION

Implant Description:
The Spineology Interbody Fusion System (SIFS) is a lumber intervertebral body fusion device comprised of a PET (polyethylene terephthalate) mesh bag designed to contain compatible allograft and autograft as an adjunct to fusion for the treatment of degenerative disc disease (see Figure 1). The device is placed into the prepared intervertebral disc space and then is packed with bone graft. The resulting SIFS implant is used with posterior supplemental fixation forming the completed SIFS construct (see Figure 2).

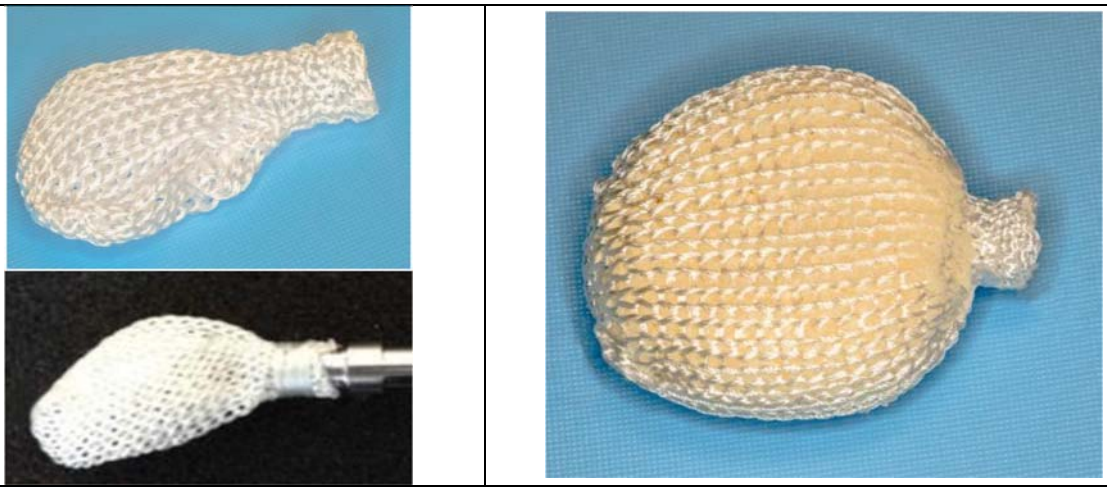

Figure 1: Unfilled SIFS implant (left), SIFS implant filled with bone graft (left)

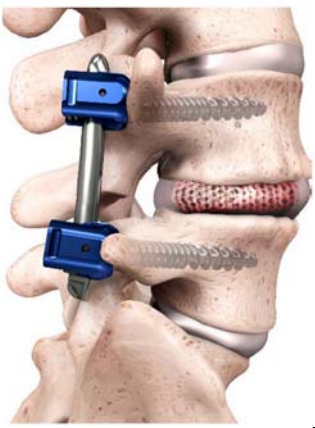

Figure 2: SIFS Construct with pedicle screw fixation

Instrument Description:

The instruments in Table 1, below, and Class I surgical instruments under 21 CFR 888.4540, product code LXH, are provided to implant the SIFS device in the lumbar spine.

Table 1: Instruments reviewed in DEN200010 as part of this device

Name	Function	Image
Mesh Holder	delivery of the device to prepared space; also holds fill tubes during graft delivery	
Mesh Extender	used for initial device placement into disc space	
Fill Tube	used to hold and deliver graft material	
Cinch String Cutter	used to cut the drawstrings of the device	

SUMMARY OF NONCLINICAL/BENCH STUDIES

BIOCOMPATIBILITY/MATERIALS

The Spineology Interbody Fusion System is manufactured from the following materials:

Description	Material	Direct Patient Contact	Contact Duration
Implant	Polyethylene Terephthalate (PET)	Yes	Permanent (>30 d)
Instruments	Stainless Steel	Yes	Limited (≤24 h)

Biocompatibility evaluation has been completed according to FDA Guidance, *Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process"*

SHELF LIFE/STERILITY

Gamma Sterilization:

The subject implant and certain instruments are provided sterile to the end user. The sterilization method is gamma radiation at a dose of (b) (4). Sterilization was validated

using the VDmax method as per ISO 11137 to ensure that a minimum Sterility Assurance Level (SAL) of 10^{-6} is achieved.

Sterilized samples real-time aged to 5 years were used to determine the shelf life of the device. Distribution testing (ASTM D4169) and package integrity testing (bubble leak test, ASTM F2096), and seal strength testing (ASTM F88/F88M) were used to validate the sterile shelf life of the device. Non-clinical performance testing of the implant was used to assess the performance shelf life of the device. The testing confirmed a 5-year shelf-life.

Ethylene Oxide Sterilization:
Certain subject instruments are provided sterile to the end user via ethylene oxide. This method has been validated in accordance with ISO 11135 to ensure that a minimum a Sterility Assurance Level (SAL) of 10^{-6} is achieved.
.
Sterilized samples real-time aged to 5 years were used to determine the shelf life of the device. Distribution testing (ASTM D4169) and package integrity testing (bubble leak test, ASTM F2096), and seal strength testing (ASTM F88/F88M) were used to validate the sterile shelf life of device. The testing confirmed a 5-year shelf-life.

Reprocessing:
Certain subject instruments are provided non-sterile and are to be cleaned and sterilized by the end-user. Validated reprocessing instructions are included in their own separate labeling document.

Steam sterilization method was validated per ISO 17665 and AAMI ST79 to ensure that a minium Sterility Assurance Level (SAL) of 10^{-6} is achieved. Instruments are to be sterilized using a Pre-vacuum steam autoclave. For the pre-vacuum steam autoclave cycle, the validated parameters call for an exposure time of 4 minutes at 270°F (132°C) and a dry time of 30 minutes at 270°F (132°C). Users are advised to use an FDA- cleared sterilization wrap.

MAGNETIC RESONANCE (MR) COMPATIBILITY

The SIFS implant is a non-ferromagnetic, polymeric device made of PET. The subject device was not evaluated for safety and compatibility in a Magnetic Resonance Environment.

PERFORMANCE TESTING - BENCH

Test	Purpose	Method	Performance Criteria	Results
Burst Test	Evaluate mechanical properties of the bone graft containment device under a compressive load	PET sheets are placed between the top and bottom ring clamp of burst test fixture without tension. A load is applied until failure.	The performance criteria was based on the Sponsor historical batch/lot records	The PET sheets were tested to failure. The report included the bursting strength of each specimen and the average bursting strength for each

Test	Purpose	Method	Performance Criteria	Results
		The test methodology was adapted from ASTM D3787.		specimen along with the standard deviation.
Tensile and Elongation Test	Evaluate mechanical properties of the mesh material under a tensile load	PET tubes are mounted in clamps of the tensile testing machine and a force applied until failure. Elongation is expressed as a ratio of the extension of a material to the length of the material prior to stretching. The test methodology was adapted from ASTM D5034.	The performance criteria was based on the Sponsor historical batch/lot records	The PET tubes were tested to failure. The report included the tensile strength and elongation of each specimen and the average tensile strength and elongation for each specimen along with the standard deviation.
Static Axial Compression	Evaluate mechanical properties of the bone graft containment device when filled with bone graft under Static Axial Compression loading	The SIFS implant filled with representative bone graft were tested under static compression until failure or approximately (b) (4) N was reached. The test methodology is in accordance with ASTM F2077. Additionally, pre- and post-test dimensions (height, width, and length) and mass of the device was taken to characterize the deformation of the device.	There was no pre-determined performance criteria for this test.	The tested device deformed under the applied load and post-test dimensions and mass were provided under the applied load compared to the pre-test dimensions and mass. Representative pre- and post-test images were provided along with the force-displacement graphs. The linear equations used to calculate stiffness was also provided.
Dynamic Axial Compression	Evaluate mechanical properties of the bone graft containment device when filled with bone graft under Dynamic Axial Compression loading	The SIFS implant filled with representative bone graft were tested under dynamic compression to (b) million cycles at (b) Hz. The test methodology is in accordance with ASTM F2077. Additionally, pre- and post-test dimensions (height, width, and length) and mass of the device was taken to characterize the deformation of the device.	There was no pre-determined performance criteria for this test.	The tested device deformed under the applied load and post-test dimensions and mass were provided under the applied load compared to the pre-test dimensions and mass. Representative pre- and post-test images were provided along with the cycle-displacement table.
Static Compression Shear	Evaluate mechanical properties of the bone graft containment device when filled with bone graft under Static Compression-shear loading	The SIFS implant filled with representative bone graft were tested under static compression-shear ((b) (4)°) until failure or approximately (b) (4) N was reached. The test	There was no pre-determined performance criteria for this test.	The tested device deformed under the applied load and post-test dimensions and mass were provided under the applied load compared to the pre-test dimensions and mass. Representative pre- and post-test

Test	Purpose	Method	Performance Criteria	Results
		methodology is in accordance with ASTM F2077. Additionally, pre- and post-test dimensions (height, width, and length) and mass of the device was taken to characterize the deformation of the device.		images were provided along with the force-displacement graphs. The linear equations used to calculate stiffness was also provided.
Dynamic Compression Shear	Evaluate mechanical properties of the bone graft containment device when filled with bone graft under Dynamic Compression-shear loading	The SIFS implant filled with representative bone graft were tested under dynamic compression to (b) million cycles at (b) Hz. The test methodology is in accordance with ASTM F2077. Additionally, pre- and post-test dimensions (height, width, and length) and mass of the device was taken to characterize the deformation of the device.	There was no pre-determined performance criteria for this test.	The tested device deformed under the applied load and post-test dimensions and mass were provided under the applied load compared to the pre-test dimensions and mass. Representative pre- and post-test images were provided.
Subsidence	Evaluate mechanical properties of the bone graft containment device when filled with bone graft. Evaluates the implants resistance to subsidence.	The SIFS implant filled with representative bone graft were tested per ASTM F2267. Additionally, pre- and post-test dimensions (height, width, and length) and mass of the device was taken to characterize the deformation of the device.	There was no pre-determined performance criteria for this test.	The tested device deformed under the applied load and post-test dimensions and mass were provided under the applied load compared to the pre-test dimensions and mass. Representative pre- and post-test images were provided. The stiffness and yield were reported.
Expulsion	Evaluate mechanical properties of the bone graft containment device when filled with bone graft. Evaluates the migration potential.	The SIFS implant filled with representative bone graft were placed in polyurethane foam blocks with a compressive pre-load of (b) (4) N. A load was applied until the specimen was displaced.	There was no pre-determined performance criteria for this test.	The report included the force required to displace the device along with the representative pre- and post- test images.
Wear Particulate Analysis	Evaluate the wear debris of the of the bone graft containment device when filled with bone graft.	A wear testing protocol for collection and analyses were conducted based on ISO 17853, ASTM F1877, and ASTM F2025.	There was no pre-determined performance criteria for this test.	The particulates size and morphological characteristics, as well as associated elemental constituents, were reported.

Test	Purpose	Method	Performance Criteria	Results
Simulated Fill Testing	Evaluate the consistency and mechanical features of the bone graft containment device when filled with bone graft by different personnel	Personnel were instructed to fill the SIFS implant with representative bone graft per the protocol. The filled specimens were evaluated under Static Axial compression to evaluate the mechanical properties. Additionally, pre- and post-test dimensions (height, width, and length) and mass of the device was taken to characterize the deformation of the device.	The device is filled consistently and repeatedly across multiple users.	The mechanical properties of this group were compared to the mechanical properties of the experienced group. The specimens deformed under the applied load and post-test dimensions and mass were provided under the applied load compared to the pre-test dimensions and mass. Representative pre- and post-test images were provided along with the force-displacement graphs. The linear equations used to calculate stiffness was also provided.

SUMMARY OF CLINICAL INFORMATION

Study Objective:
The purpose of the clinical trial was to demonstrate the safety and effectiveness of the SIFS implant in instrumented lumbar intervertebral body fusion procedures.

Study Design:
Spineology conducted a 24-month, prospective, single arm, multi-center study (G140140) which was based on their previously conducted prospective, randomized, multi-center study for the same device (G030106). The study enrolled and treated (b) (4) subjects across (b) (4) clinical sites based on inclusion/exclusion criteria. Candidate subjects were skeletally mature adults with low back pain and pain-related disability, who presented with symptomatic single level degenerative disc disease between L2 and S1. The study was designed to meet a pre-determined performance goal at 24 months post-implantation which was based on their previously conducted prospective, randomized, multi-center study.

Inclusion/Exclusion Criteria:

Inclusion Criteria	Exclusion 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	• 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

≥ 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.	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.

Primary Endpoint:
The primary endpoint used to evaluate the subjects implanted with the SIFS filled with compatible allograft and autograft when used with posterior supplementation fixation for lumbar fusion consisted of the following elements (with accompanying success definitions):

- Pain- Improvement in low back pain score as evidenced by a (b) (4) mm reduction on a (b) (4) mm Visual Analog Scale (VAS) when compared to baseline.
- Function- Improvement in low back function as evidenced by a (b) (4)-point decrease of the Oswestry Disability Index (ODI) score compared to baseline.
- 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.

Additional Endpoints:
The following additional endpoints that were used to evaluate the safety and effectiveness are:

- 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).

Subject Evaluation:

Subjects were evaluated pre-operatively, intra-operatively, and immediately post-operatively followed by evaluations at 6 weeks, 3 months, 6 months, 12 months, and 24 months. Additionally, longer-term patient questionnaires were completed at the 36- and 48- month interval until the final study subject achieved their 24-month study evaluation. The data collected at each evaluation time point is summarized in Table 1 below:

Table 1: Study Interval Data Collection

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[‡]	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

[‡]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

Subject Accountability and Demographics:

Ten (b) (4) sites participated in the study with a total of (b) (4) subjects enrolled and treated.

Table 2 below provides an account of all subjects enrolled and treated in the study who completed the evaluations at each time point within the windows defined in the investigational protocol.

Table 2: Subject Accountability of the Investigational Cohort Through 48-Months

Exam	Theoretical # Due	Deaths Prior to Visit (Cumulative)	Withdrawals Prior to Visit (including death)	Expected Patients	Missed visit	Pending (Window not yet closed)	# Patients with any follow-up data evaluated	# Patients with complete data in-window	Calculation of follow-up rates (actual # seen/expected x 100)
Baseline	(b) (4)								-
Surgery									100% (102/102)
6-Week									98.0% (99/101)
3-Month									100% (101/101)
6-Month									96.0% (97/101)
12-Month									98.0% (99/101)
24-Month									95.0% (96/101)
36-Month									68.2% (45/66)
48-Month									73.7% (14/19)

*Includes the 3 subjects that had withdrawn early
** Includes the 4 subjects that had withdrawn early.

Table 3 presents the demographic characteristics of the enrolled subjects. The mean age of the enrolled subjects was 57 years old, with 50% of the subjects being male and 50% of the subjects being female. Other demographic data, such as ethnicity, race, BMI and tobacco use, are reported in the table below.

Table 3: Demographic Characteristics of the Investigational Cohort

Parameter	All Subjects Mean ± SD (N) (Median, Min, Max) Or ##/## (%)
Age at Consent (years)	57.0 ± 12.0 (102) 59.0 26.0 - 79.0
Gender	
Male	50.0% (51/102)
Female	50.0% (51/102)
Ethnicity	
Hispanic or Latino	3.9% (4/102)
Not Hispanic or Latino	96.1% (98/102)
Race	
American Indian or Alaskan Native	0.0% (0/100)
Asian	0.0% (0/100)
Black or African American	4.0% (4/100)
Native Hawaiian or Pacific Islander	0.0% (0/100)
White	96.0% (96/100)
BMI	30.6 ± 4.9 (102) 29.9 20.0 - 39.9
Tobacco use	
Current tobacco user (≤30 days)	0.0% (0/102)
Previously but not now (>30 days)	51.0% (52/102)
Never	49.0% (50/102)

Table 4 below shows the baseline assessments for VAS and ODI of the enrolled subjects. The mean VAS scores of all subjects (n=(b) (4) at baseline for Low Back Pain, Right Leg Pain, and Left Leg Pain were (b) (4) and (b) (4) respectively. The mean ODI score of all subjects (n=(b) (4)) at baseline was (b) (4)

Table 4: Baseline Assessments (VAS, ODI) of the Investigational Cohort

Parameter	All Subjects Mean ± SD (N) (Median, Min, Max)
VAS Low Back Pain	(b) (4)
VAS Right Leg Pain	
VAS Left Leg Pain	

ODI	(b) (4)

Table 5 below summarized the intra-operative and hospital data collected on all subjects. A majority of the subjects (66.7% - (b) (4) were treated at L4-L5 followed by the L5-S1 level (b) (4) of (b) (4) subjects). Mean operative time for all subjects (n= (b) (4) was 2.6 hours, and the mean estimated blood loss of all subjects (n= (b) (4) was 137.3 cc. The predominant surgical approach (90.2% - (b) (4) was minimally invasive, and the medium sized device was most commonly used (58.8% - (b) (4)

Table 5: Intra-operative and Hospital Data of the Investigational Cohort

Parameters	All Subjects Mean ± SD (N) Median, Min, Max Or #/# (%)
Surgical Level:	
• L2-L3	(b) (4) (1.0%)
• L3-L4	(b) (4) (3.9%)
• L4-L5	(b) (4) (66.7%)
• L5-S1	(b) (4) (28.4%)
Operative Time (hours)	2.6 ± 0.9 (b) (4) 2.6, 1.0, 5.4 95% CI: 2.5-2.8
Estimated Blood Loss (cc)	137.3 ± 217.4 (b) (4) 75.0, 5.0, 1800.0 95% CI: 94.6-180.0
Length of Hospital Stay (days)	2.3 ± 1.2 ((b) (4) 2.0, 0, 5.0 95% CI: 2.1-2.6
Surgical Approach:	
• Open Procedure	9.8% ((b) (4)
• Minimally Invasive Procedure	90.2% (b) (4)
SIFS Device Used:	
• Small (300-2002)	37.3% (b) (4)
• Medium (300-2302)	58.8% (b) (4)
• Large (300-2702)	3.9% (b) (4)

Clinical Outcomes:

Pain Assessment:

The individual VAS pain scores over time reported for low back, right leg, left leg and iliac crest graft harvest pain are provided in Table 6 below. The average VAS pain scores decreased at 24 months when compared to the baseline (e.g., a mean VAS Low Back Pain score of (b) (4)

was reported for all subjects at the 24-month time point as compared to a mean VAS Low Back Pain score of (b) (4) at baseline).

Table 6: Mean VAS Pain Scores of the Investigational Cohort Through 24 Months

	Mean ± SD (N) (Min, Median, Max)					
	Baseline	6-Week	3-Month	6-Month	12-Month	24-Month
Low Back Pain						
At Follow-Up Exam	(b) (4)					
95% Confidence Interval						
Change from Baseline						
95% Confidence Interval						
Right Leg Pain						
At Follow-Up Exam	(b) (4)					
Confidence Interval						
Change from Baseline						
Confidence Interval						
Left Leg Pain						
At Follow-Up Exam	(b) (4)					
95% Confidence Interval						
Change from Baseline						
95% Confidence Interval						
Iliac Crest Graft Site Pain						
At Follow-Up Exam	(b) (4)					
95% Confidence Interval						

Function Assessment

The ODI scores over time are provided in Table 7 below. The average ODI score decreased at each successive time point, with the mean ODI score at 24 months reported as (b) (4) as compared to the mean ODI score at baseline reported as (b) (4)

Table 7: Mean ODI Scores of the Investigational Cohort Through 24 Months

ODI Score	Mean ± SD (N) (Min, Median, Max)					
	Baseline	6-Week	3-Month	6-Month	12-Month	24-Month
At Follow-Up Exam	(b) (4)					
95% Confidence Interval						
Change from Baseline						
95% Confidence Interval						

Radiographic Assessment:

Fusion was assessed by independent radiologists at the 12-month time point, and again at 24 months for those subjects who had not fused. At 12 months, (b) (4) subjects were evaluated for fusion. (b) (4) subjects were determined to be fused. (b) (4) subjects did not have a designation of "fused" at 12 months, and one of those (b) (4) subjects was not imaged due to pregnancy. At the 24-month time point, (b) (4) of those (b) (4) subjects were determined to be fused. The (b) (4) patient that was determined not fused was the subject who was pregnant at the 12-month time point. Overall, at 24 months, the fusion rate for all evaluated subjects is 99.0% (b) (4) when considering the 12- and 24-month fusion assessments, and similarly, 99.0% (b) (4) when considering subjects who were evaluated at 24 months. The fusion status is summarized in Table 8 below.

Table 8: Fusion Status of the Investigational Cohort as Assessed by Evidence of Bridging Bone Through 24-Months

Bridging Bone (Fusion) Status Determination	12-Month Visit	24-Month Visit	Combined 12/24-Month Status (n=(b) (4)
All Subjects 12 & 24 Combined (n=(b) (4)			
Bridged	97.9% (b) (4)	75.0% (b) (4)	99.0% (b) (4)
95% Confidence Interval	92.7%, 99.7%	19.4%, 99.4%	94.5%, 100.0%
Only Subjects Achieving a 24-Month Evaluation (n=(b) (4)			
Bridged	97.9% (b) (4)	75.0% (b) (4)	99.0% (b) (4)

Radiographic imaging also assessed for device expulsion, subsidence, radiolucency and adjacent segment degeneration and summarized in Table 9 below. (b) (4) subjects were determined to have subsidence at the 12-month time point. All (b) (4) subjects who had subsidence also had bone bridging at 12 months per the imaging. (b) (4) subjects had radiolucency at the 12-month time point. Of those (b) (4) subjects, (b) (4) subject had bone bridging at the 12-month time point and the other subject had bone bridging at the 24-month timepoint.

Table 9: Device Expulsion, Subsidence, Radiolucency and Adjacent Segment Degeneration of the Investigational Cohort Through 24-Months

Parameter	% (#/#)		
	12-Month	24-Month	Combined 12-/24-Month
Expulsion (device moved outside the disc space)			
At Follow-Up Exam	0.0% (b) (4)	0.0% (b) (4)	0.0% (b) (4)
95% Confidence Interval	0.0%, 3.7%	0.0%, 60.2%	0.0%, 3.7%
Subsidence (>5 mm migration of implant from original position)			
At Follow-Up Exam	3.1% (b) (4)	0.0% (b) (4)	3.0% (b) (4)
95% Confidence Interval	0.6%, 8.8%	0.0%, 60.2%	0.6%, 8.6%
Radiolucency (> 50% of implant/endplate interface shows true lucency (true lucency is black not gray)			
At Follow-Up Exam	2.1% (b) (4)	0.0% (b) (4)	1.0% (b) (4)
95% Confidence Interval	0.3%, 7.3%	0.0%, 60.2%	0.0%, 5.5%
Adjacent Level Degeneration (>5 mm loss of disc height; >3 mm translation on flexion/extension			
At Follow-Up Exam	0.0% (b) (4)	0.0% (b) (4)	0.0% (b) (4)
95% Confidence Interval	0.0%, 3.7%	0.0%, 60.2%	0.0%, 3.7%

Additionally, radiographic assessments at the index level for angulation and translation, disc height, and sagittal alignment is summarized in Table 10 below. The mean angulation at 12 months is 1.6 degrees (n=(b) (4) of motion and 1.4 degrees at 24 months (n=(b) (4) The mean translation at 12 months is 0.7 millimeters (n=(b) (4) and 0.9 millimeters at 24 months (n=(b) (4)

Table 10: Mean Quantitative Assessment (angulation, translation) for Motion at Index level of the Investigational Cohort Through 24 Months

Parameter	6-Month	12-Month	24-Month
(b) (4)			

The change of the mean disc height over time is summarized in Table 11 below. The baseline measurement post-op was used to compare the disc height to each time point. Immediately post-operatively, the mean disc height increased from 6.5 mm (n=(b) (4) at baseline to 9.6 mm (n=(b) (4) However, this gain in disc height gradually decreased over time, with a mean disc height of 7.0 mm (n=(b) (4) at 24 months.

Table 11: Mean Disc Height at Index Level of the Investigational Cohort Through 24 Months

Parameter	Pre-op	Baseline Post-op	6-Month	12-Month	24-Month
(b) (4)					

The change of the mean sagittal alignment at the index segment over time is summarized in Table 12 below. Immediately post-operatively, the mean sagittal alignment (lordosis) increased from 14.9 degrees at baseline (n=(b) (4) to 15.8 degrees (n=(b) (4) However, this gain in sagittal alignment gradually decreased over time, with a mean sagittal alignment of 12.7 degrees (n=(b) (4) at 24 months.

Table 12: Mean Sagittal Alignment-Index Segment of the Investigational Cohort Through 24 Months

Parameter	Pre-op	Baseline Post-op	6-Month	12-Month	24-Month
(b) (4)					

Safety Assessment

A Clinical Events Committee (CEC) was utilized for the study to mitigate reporting bias of safety-related events. Each event was evaluated for applicability (event versus observation), relatedness to the study (study-related event versus non study-related event), and additional classifications of seriousness (serious adverse events, unanticipated adverse device effects, neither) and severity (mild, moderate, severe).

One hundred and twenty-five (125) events were reported in this study of which 6 were non-events. The events are classified in Table 13 below:

Table 13: Adverse Event Classification of the Investigational Cohort (All Reported During Study)

Characteristic	# of events	# of subjects	Rate
Includes all adverse events (excludes the 6 non-events/observations)			
All Adverse Events	119	69	67.6%
Not Study-Related Adverse Events	48	32	31.4%
All Study-Related Adverse Events	71	54	52.9%
Severe Study-Related Adverse Events (SAE)	15	13	12.7%
All procedure related adverse events	41	35	34.3%
Procedure – General Surgery	40	34	33.3%
Procedure – Hardware-Related	1	1	1.0%
Procedure – Investigation Device-Related	0	0	0.0%
Hardware-Related Adverse Events	15	13	12.7%
Investigation Device-Related Adverse Events	2	2	2.0%
Serious Procedure-Related Adverse Events	10	8	7.8%
General Surgery	10	8	7.8%
Hardware	0	0	0.0%
Device	0	0	0.0%
Serious Procedure-Related Adverse Events	10	8	7.8
Serious Hardware-Related Adverse Events	0	0	0.0%
Serious Investigation Device-Related Adverse Events	0	0	0.0%

Some adverse events resulted in subsequent surgical interventions. Subsequent surgical interventions (SSIs) were prospectively classified as revisions, removals, reoperations, supplemental fixations, or other qualified events per FDA's Guidance, *Clinical Data Presentations for Orthopedic Device Applications (2004)*. Overall, there were 8 SSIs in 7 subjects, with 2 device removals, 4 reoperations, 2 surgeries which added supplemental fixation, 3 events categorized as other spinal surgeries, and no device revisions.

Table 14: SSI Summary Table for the Investigational Cohort (All Reported During Study)

Additional Surgeries	# of Surgeries	# of Subjects	Percent of Subjects (%)
Index Site Surgery	8	7	6.9%
Device Revision	0	0	0.0%
Device Removal	2	2	2.0%
Reoperation	4	4	3.9%
Supplemental Fixation	2	2	2.0%
Other Spinal Surgeries	3	3	2.9%
Other Non-spinal Surgeries	10	10	9.8%

Neurological assessment was performed at baseline, prior-to-discharge from the hospital, and at each study evaluation thereafter through 24 months. At each timepoint, subjects were evaluated to ascertain if their neurological status (reflexes, sensory, and strength) was improved, maintained, or worsened when compared to pre-op. Most subjects were reported to have improved or maintained their neurological status, with 5.3% (5/95), 2.1% (2/96) and 1.0% (1/96) of subjects reported to have worsened in their reflex, sensory and strength neurological

assessments, respectively. A summary for each neurological status (reflexes, sensory, and strength) is provided in Table 15 below:

Table 15: Neurological (reflexes, sensory, strength) Status of the Investigational Cohort Through 24 Months

	Pre-surgery	Surgery	6 Weeks	3 Months	6 Months	12 Months	24 Months
Neurological deficiency - Reflexes	**44.6%** (b) (4)	**31.4%** (b) (4)	**28.3%** (b) (4)	**31.0%** (b) (4)	**27.1%** (b) (4)	**28.3%** (b) (4)	**24.0%** (b) (4)
Changes in REFLEXES compared to pre-surgery							
Improved		16.8% (b) (4)	21.4% (b) (4)	17.2% (b) (4)	24.2% (b) (4)	22.4% (b) (4)	25.3% (b) (4)
No Change		79.2% (b) (4)	73.5% (b) (4)	78.8% (b) (4)	70.5% (b) (4)	70.4% (b) (4)	69.5% (b) (4)
Worsened		4.0% (b) (4)	5.1% (b) (4)	4.0% (b) (4)	5.3% (b) (4)	7.1% (b) (4)	5.3% (b) (4)

	Pre-surgery	Surgery	6 Weeks	3 Months	6 Months	12 Months	24 Months
Neurological deficiency - Sensory	**37.3%** (b) (4)	**17.6%** (b) (4)	**23.2%** (b) (4)	**19.0%** (b) (4)	**24.0%** (b) (4)	**18.2%** (b) (4)	**13.5%** (b) (4)
Changes in SENSORY compared to pre-surgery							
Improved		22.5% (b) (4)	22.2% (b) (4)	22.0% (b) (4)	18.8% (b) (4)	23.2% (b) (4)	25.0% (b) (4)
No Change		74.5% (b) (4)	69.7% (b) (4)	74.0% (b) (4)	77.1% (b) (4)	72.7% (b) (4)	72.9% (b) (4)
Worsened		2.9% (b) (4)	8.1% (b) (4)	4.0% (b) (4)	4.2% (b) (4)	4.0% (b) (4)	2.1% (b) (4)

	Pre-surgery	Surgery	6 Weeks	3 Months	6 Months	12 Months	24 Months
Neurological deficiency - Strength	**5.9%** (b) (4)	**3.9%** (b) (4)	**3.0%** (b) (4)	**3.0%** (b) (4)	**3.1%** (b) (4)	**2.0%** (b) (4)	**1.0%** (b) (4)
Changes in STRENGTH compared to pre-surgery							
Improved		2.9% (b) (4)	4.0% (b) (4)	4.0% (b) (4)	4.2% (b) (4)	5.1% (b) (4)	6.3% (b) (4)
No Change		96.1% (b) (4)	93.9% (b) (4)	95.0% (b) (4)	94.8% (b) (4)	93.9% (b) (4)	92.7% (b) (4)
Worsened		1.0% (b) (4)	2.0% (b) (4)	1.0% (b) (4)	1.0% (b) (4)	1.0% (b) (4)	1.0% (b) (4)

Overall Conclusion:

As stated earlier, this prospective, single arm, multi-center study was designed to meet a pre-determined performance goal at 24 months which was based on a previously conducted prospective, randomized, multi-center study on the same device. The performance goal was based on four (4) parameters: pain (evaluated by VAS), function (evaluated by ODI, fusion

(evaluated by imaging), and safety (evaluated by adverse events). These identified parameters are also in-line with the FDA Guidance Document, *Preparation and Review of Investigational Device Exemption Applications (IDEs) for Total Artificial Discs*. (b) (4) of the (b) (4) subjects (85.4%) had at least a 20 mm improvement in VAS pain score. (b) (4) of the (b) (4) subjects (81.3%) had at least a 15-point improvement in ODI score. (b) (4) of the (b) (4) subjects (99.0%) achieved a fusion. (b) (4) of the (b) (4) subjects (92.9%) for freedom from device-related Serious Adverse Events and secondary surgical interventions at the index level. The results are summarized in the table below:

Table 16: Overall

Parameter	Results- % (#/#)
At least 20 mm improvement in VAS	85.4% (82/96)
At least 15-point improvement in ODI	81.3% (78/96)
Fusion	99.0% (96/97)
Freedom from investigational device-related serious adverse events at the index level and free of surgical intervention at index level	92.9% (91/98)

The results provided from the study have comparable clinical outcomes as compared to previously published literature related to lumbar fusion (Brantigan,J[1]; Fritzell P[2], Ghogawala[3]) for lumbar interverbal body fusion devices. The valid scientific evidence presented in the preceding sections demonstrates that the subject device is demonstrated to have a reasonable assurance of safety and effectiveness, and the benefits of using the subject device for its intended use/indications for use outweigh the risks to health.

References:
1. Brantigan JW, Steffee AD, Lewis ML, Quinn LM, Persenaire JM. Lumbar interbody fusion using the Brantigan I/F cage for posterior lumbar interbody fusion and the variable pedicle screw placement system: two-year results from a Food and Drug Administration investigational device exemption clinical trial. Spine, 2000, 25(11):1437-1446.
2. Fritzell P, Hägg O, Wessberg P, Nordwall A; Swedish Lumbar Spine Study Group. 2001 Volvo Award Winner in Clinical Studies: Lumbar fusion versus nonsurgical treatment for chronic low back pain: a multicenter randomized controlled trial from the Swedish Lumbar Spine Study Group. Spine, 2001, 26(23):2521-2534.
3. Ghogawala Z, Dziura J, Butler WE, et al. Laminectomy plus Fusion versus Laminectomy Alone for Lumbar Spondylolisthesis. N Engl J Med, 2016, 374(15):1424-1434.

Pediatric Extrapolation:

In this De Novo request, existing clinical data were not leveraged to support the use of the device in a pediatric patient population.

LABELING

The labeling consists of the following: device description, indications for use, instructions for use including surgical steps and device removal, principles of device operation, identification of device materials, contraindications, warnings, precautions, MR compatibility, and a list of potential adverse effects. Furthermore, the sterile packaging includes a shelf life for the device, and the labeling includes reprocessing instructions for the reusable instruments. The labeling meets the requirements of 21 CFR 801.109 for prescription devices.

RISKS TO HEALTH

The table below identifies the risks to health that may be associated with use of and the measures necessary to mitigate these risks.

Identified Risks to Health	Mitigation Measures
Adverse tissue reaction	Design characteristics Biocompatibility evaluation Sterilization/reprocessing validation Labeling
Infection	Sterilization/reprocessing validation Labeling
Loosening/migration due to device failure or failure at the bone/implant interface	Design characteristics Clinical performance testing Non-clinical performance testing Biocompatibility evaluation Labeling
Tissue injury	Labeling
Pseudarthrosis due to device failure or failure at the bone-implant interface	Clinical performance testing Non-clinical performance testing Biocompatibility evaluation Labeling
Adverse clinical sequelae	Clinical performance testing Labeling
Use error/Improper device use	Labeling

SPECIAL CONTROLS

In combination with the general controls of the FD&C Act, the intervertebral body graft containment device is subject to the following special controls:

(1) Clinical performance testing must include an assessment of any adverse events observed during clinical use, as well as intervertebral body fusion, and compare this to a clinically acceptable fusion rate.
(2) Non-clinical performance testing must demonstrate the mechanical function and durability of the implant, as well as the ability of the device to be inserted, deployed, and filled with bone graft consistently.
(3) Device must be demonstrated to be biocompatible.
(4) Validation testing must demonstrate the cleanliness and sterility of, or the ability to clean and sterilize, the device components, and device-specific instruments.
(5) Design characteristics of the device, including engineering schematics, must ensure that the geometry and material composition are consistent with the intended use.
(6) Labeling must bear all information required for the safe and effective use of the device, specifically including the following:
    (i) A clear description of the technological features of the device including identification of device materials, compatible components in the fusion construct, and the principles of device operation;

(ii) Intended use and indications for use, including levels of fixation;
(iii) Identification of magnetic resonance (MR) compatibility status;
(iv) Cleaning and sterilization instructions for devices and instruments that are provided non-sterile to the end user; and
(v) Detailed instructions of each surgical step, including device removal.

BENEFIT-RISK DETERMINATION

The sponsor has collected adequate data to assess the safety profile of the subject device and has identified that there are benefits. The study has demonstrated reduction of pain and functional improvement as discussed in the clinical section. The most common study-related adverse events were pain (15.7%- 16/102), symptomatic adjacent level DDD (5.9% -6/102), and lumbar muscle spasm/strain (4.9%- 5/102). The list of potential adverse effects is provided in the labeling. In conclusion, the benefits of using the subject device for its intended use/indications for use outweigh the risks to health.

Patient Perspectives

This submission did not include specific information on patient perspectives for this device.

Benefit/Risk Conclusion

In conclusion, given the available information above, for the following indication statement:

> The Spineology Interbody Fusion System (SIFS) is indicated for use as an adjunct to fusion 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 Grade 1 spondylolisthesis at the involved level. DDD is defined as discogenic back pain with degeneration of the disc confirmed by patient history, physical examination, and radiographic studies. Eligible patients shall have undergone six (6) months of conservative (non-operative) care. SIFS compatible allograft and autograft is intended for use with supplemental posterior fixation systems intended for use in the lumbar spine.

The probable benefits outweigh the probable risks for the Spineology Interbody Fusion System. The device provides benefits and the risks can be mitigated by the use of general controls and the identified special controls.

CONCLUSION

The De Novo for the Spineology Interbody Fusion System is granted and the device is classified as follows:

Product Code: OQB
Device Type: Intervertebral Body Graft Containment Device
Regulation Number: 21 CFR 888.3085
Class: II