SUMMARY OF SAFETY & EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Prosthesis, Spinous Process Spacer/Plate
Device Trade Name:	Superion® InterSpinous Spacer (ISS)
Device Product Code:	NQO
Applicant's Name and Address:	VertiFlex®, Incorporated 1351 Calle Avanzado, Suite 100 San Clemente, CA 92673
Date(s) of Panel Recommendation:	February 20, 2015
Premarket Approval Application (PMA) Number:	P140004
Date of FDA Notice of Approval:	May 20, 2015

II. INDICATIONS FOR USE

The Superion® InterSpinous Spacer (ISS) is indicated to treat skeletally mature patients suffering from pain, numbness, and/or cramping in the legs (neurogenic intermittent claudication) secondary to a diagnosis of moderate degenerative lumbar spinal stenosis, with or without Grade 1 spondylolisthesis, confirmed by X-ray, MRI and/or CT evidence of thickened ligamentum flavum, narrowed lateral recess, and/or central canal or foraminal narrowing. The Superion® ISS is indicated for those patients with impaired physical function who experience relief in flexion from symptoms of leg/buttock/groin pain, numbness, and/or cramping, with or without back pain, and who have undergone at least 6 months of non-operative treatment. The Superion® ISS may be implanted at one or two adjacent lumbar levels in patients in whom treatment is indicated at no more than two levels, from L1 to L5.

For this intended use, moderate degenerative lumbar spinal stenosis was defined as follows:

- 25% to 50% reduction in the central canal and/or nerve root canal (subarticular, neuroforaminal) compared to the adjacent levels on radiographic studies, with radiographic confirmation of any one of the following:
  - Evidence of thecal sac and/or cauda equina compression
  - Evidence of nerve root impingement (displacement or compression) by either osseous or non-osseous elements
  - Evidence of hypertrophic facets with canal encroachment
- AND associated with the following clinical signs:
  - Presents with moderately impaired Physical Function (PF) defined as a score of ≥ 2.0 of the Zurich Claudication Questionnaire (ZCQ)
  - Ability to sit for 50 minutes without pain and to walk 50 feet or more.

III. CONTRAINDICATIONS

The Superion® ISS is contraindicated in patients with:

- an allergy to titanium or titanium alloy;
- spinal anatomy or disease that would prevent implantation of the device or cause the device to be unstable *in situ*, such as:
  - instability of the lumbar spine, e.g., isthmic spondylolisthesis or degenerative spondylolisthesis greater than grade 1 (on a scale of 1 to 4);
  - an ankylosed segment at the affected level(s);
  - fracture of the spinous process, pars interarticularis, or laminae (unilateral or bilateral);
  - scoliosis (Cobb angle >10 degrees);
- *Cauda equina* syndrome defined as neural compression causing neurogenic bladder or bowel dysfunction;
- diagnosis of severe osteoporosis, defined as bone mineral density (from DEXA scan or equivalent method) in the spine or hip that is more than 2.5 S.D. below the mean of adult normals;
- active systemic infection, or infection localized to the site of implantation;
- prior fusion or decompression procedure at the index level;
- morbid obesity defined as a body mass index (BMI) greater than 40.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Superion® ISS labeling.

V. DEVICE DESCRIPTION

The Superion® ISS is a one-piece implant that requires no assembly *in situ*. It consists of an implant body, within which resides the actuation mechanism, and two Cam Lobes, or "wings" which – when deployed – rotate away from the axis of the implant body to encompass the lateral aspects of the superior and inferior spinous processes (see Figure 1).

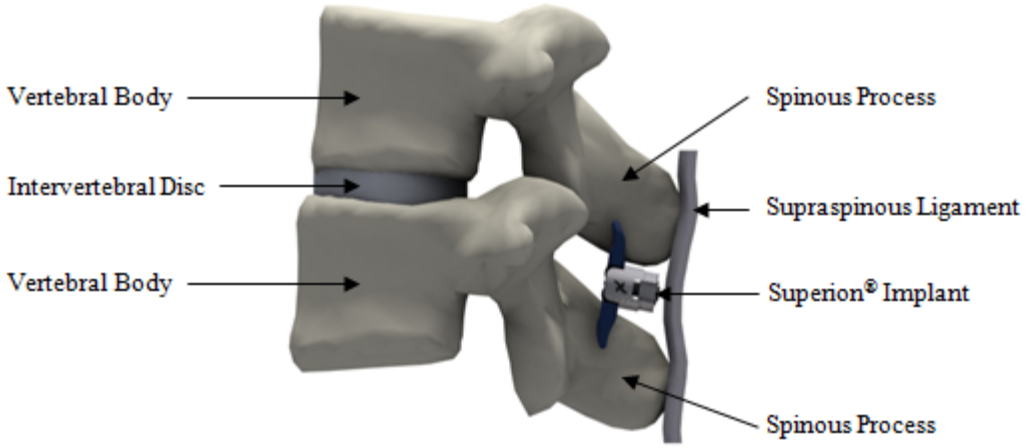


Figure 1: Superion® device in spine model

The Superion® ISS is composed entirely of titanium alloy (Ti6Al-4V ELI conforming to ASTM F136) The Superion® ISS is intended to be implanted via minimally-invasive surgical methods using a set of proprietary accessory instruments provided by VertiFlex® expressly for use with the Superion® ISS device. Together, the implants and manual instruments form a complete system for implantation of the Superion® ISS.

To accommodate variations in patient anatomy, Superion® ISS implants are available in five (5) sizes, ranging from 8mm to 16mm in 2mm increments, each of which is color-coded and laser-etched to indicate implant size. The size selection determines the amount of "spacing" between the two adjacent spinous processes. Implant size is determined by the distance between the bottom of the "saddle" of each of the Cam Lobes, which represents the point at which the adjacent spinous processes would rest within a deployed implant.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Non-surgical alternatives include non-steroidal anti-inflammatory drugs (NSAIDs), analgesics, oral and epidural steroids, rest, exercise, physical therapy, and bracing. Surgical alternatives to the Superion® ISS vary, depending upon the severity of the stenosis, the contribution of back pain, and the presence of instability, among other factors, and can include various direct decompressive procedures (e.g. laminectomy, laminotomy, hemilaminotomy, foraminotomy, etc.), other FDA-approved interspinous distraction devices, direct decompression with non-fusion posterior stabilization devices, and decompression with posterolateral fusion with pedicle screw instrumentation. Each alternative has its own advantages and disadvantages. A patient should discuss these alternatives with his or her physician to select the option that best meets their clinical condition, lifestyle and expectations.

VII. MARKETING HISTORY

The Superion® ISS has been marketed outside of the United States since 2007, and has not been withdrawn from marketing for any reason. The Superion® ISS is marketed in: Germany, Israel, Italy, Mexico, Netherlands, South Africa, Spain and the United Kingdom.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of potential adverse effects (e.g., complications) associated with use of the Superion® ISS. This listing was derived from results of the Superion® ISS clinical trial conducted under Investigational Device Exemption (IDE) #G070118, approved device labeling for other interspinous devices, and published clinical literature. It includes (1) those adverse effects potentially associated with any surgical procedure; (2) those potentially associated with lumbar spine surgery; (3) those potentially associated with lumbar spinal implants, and in particular with interspinous process implants; and (4) those potentially associated with the Superion® ISS in particular. In some instances, additional surgery may be required to correct adverse effects.

1. Risks associated with any surgical procedure include: anesthetic medication reactions; blood loss, blood vessel damage, phlebitis or hematoma; blood transfusion which may cause circulatory collapse, blood incompatibility, kidney damage, hepatitis or infection with HIV; myocardial infarction or circulatory problems; deep vein thrombosis, pulmonary embolism or thrombus formation in other vessels; stroke; fever or infection; pneumonia; injury to muscle, soft tissue or nerves; wound swelling, drainage or delayed healing; discomfort and rehabilitation associated with recovery from surgery; inability to perform certain tasks, such as lifting or exercise; and death.

2. Risks associated with lumbar spine surgery include: damage to nerve roots or the spinal cord causing partial or complete sensory or motor loss (paralysis); loss of bladder and/or bowel functions; dural leaks (tears in the tissue surrounding and protecting the spinal cord); instruments used during surgery may break or malfunction which may cause damage to the operative site or adjacent structures; fracture, damage or remodeling of adjacent anatomy, including bony structures or soft tissues during or after surgery; new or worsened back or leg pain; and surgery at the incorrect location or level.

3. Risks associated with lumbar spine implants and associated instruments include: sensitivity or allergy to the implant material; failure of the device/procedure to improve symptoms and/or function; pain and discomfort associated with the operative site or presence of implants; implant malposition or incorrect orientation; spinous process fracture; production of wear debris which may damage surrounding soft tissues including muscle or nerve; formation of scar tissue at implant site; migration or dislodgement of the implant from the original position so that it becomes ineffective or causes damage to adjacent bone or soft tissues including nerves; loosening, fatigue, deformation, breakage or disassembly of the implant, which may require another operation to remove the implant and may require another method treatment.

4. Risks specifically associated with the Superion® ISS include deformation, breakage or disassembly of the implant, and spinous process fracture.

For the specific adverse events that occurred in the clinical study of the Superion® ISS, please see Section X below.

IX. SUMMARY OF PRECLINICAL STUDIES

A variety of non-clinical tests were conducted to characterize the performance of the Superion® ISS. These tests as are listed below and summarized in Table 1 and Table 2:

A. Laboratory Studies

- Static Axial Compression
- Static Torsion
- Dynamic Axial Compression
- Dynamic Torsion
- Implant Deployment Under Load
- Static Torsion After Repeated Deployment Under Load
- Quantification and Characterization of Wear Debris
- Kinematic and Kinetic Behavior in Human Cadaver Spines
- Role of Supraspinous Ligament in Biomechanical Stability
- Effects of Implant on Canal and Foraminal Dimensions

B. Additional Studies

- Sterilization, Shelf-Life and Packaging
- Biocompatibility
- MRI Compatibility

A. Laboratory Studies

Table 1: Laboratory Studies on Superion® ISS

Test	Purpose	Method	Acceptance Criteria	Results
Static Axial Compression	To evaluate the performance of the Superion® ISS under static axial compressive loading, under worst-case conditions.	Six (6) samples of the largest (16mm) and smallest (8mm) implant were tested in accordance with methods specified by ASTM F1717	Maximum compressive strength must exceed maximum expected *in vivo* spinous process failure load (320N).[1]	Mean yield load was >8,900 N (8mm) and >8,100 N (16mm). These results suggest that the device can resist compressive loads that exceed the anticipated physiologic failure load (320N) in the lumbar spine.

Table 1: Laboratory Studies on Superion® ISS

Test	Purpose	Method	Acceptance Criteria	Results
Static Torsion Testing	To evaluate the performance of the Superion® ISS under static torsional loading, under worst-case conditions.	Six (6) samples of the largest (16mm) and smallest (8mm) implant were tested in accordance with methods specified by ASTM F1717	Maximum torsional strength must exceed maximum expected *in vivo* spinous process failure load (320N).[1]	Mean yield torque was >30.6 N-m (8mm) and >15 N-m (16mm). These results suggest that the device can resist torsional loads that exceed the anticipated physiologic failure load (320N) in the lumbar spine.
Dynamic Axial Compression	To evaluate the performance of the Superion® ISS under dynamic axial compressive loading, under worst-case conditions.	Six (6) samples of the largest (16mm) and smallest (8mm) implant were tested in accordance with methods specified by ASTM F1717	Maximum dynamic runout load to 10 million cycles must exceed maximum expected *in vivo* spinous process failure load (320N).[1]	Dynamic runout load to 10 million cycles for both 8mm and 16mm implant sizes was 1,750 N. These results suggest that the device can resist dynamic compressive loads that exceed the anticipated physiologic failure load (320N) in the lumbar spine.
Dynamic Torsion	To evaluate the performance of the Superion® ISS under dynamic torsional loading, under worst-case conditions.	Six (6) samples of the largest (16mm) and smallest (8mm) implant were tested in accordance with methods specified by ASTM F1717	Maximum dynamic runout torsion to 10 million cycles must exceed maximum expected *in vivo* spinous process failure load (320N).[1]	Dynamic runout load to 10 million cycles was ±2.5 N-m (8mm) and ±3 N-m (16mm). These results suggest that the device can resist dynamic torsional loads that exceed the anticipated physiologic failure load (320N) in the lumbar spine.
Implant Deployment Under Load	To evaluate the ability of the Superion® ISS to be deployed under axial load	Five (5) implants were deployed under constant resisting axial loads of 250, 300, and 350 N.	Implants must deploy without damage or functional failure under axial load exceeding failure strength of the spinous processes (320N).[1]	All implants deployed without failure under axial loads of 250, 300, and 350 N. These results suggest that the device can adequately deploy in the presence of loads that exceed the strength of the spinous processes and anticipated physiologic loads in the lumbar spine.

Table 1: Laboratory Studies on Superion® ISS

Test	Purpose	Method	Acceptance Criteria	Results
Static Torsion Testing After Repeated Deployment Under Load	To evaluate the torsional strength of the Superion® ISS after repeated deployment under resisting axial load.	Five (5) 16mm implants were deployed five (5) times each under constant resisting axial load of 300 N, and tested in accordance with methods specified by ASTM F1717	Maximum torsional strength must not be adversely affected by loaded deployment. Test is for characterization only; no acceptance criteria were identified.	Mean yield torque was 18 N-m. These results suggest that the device is not adversely affected after repeated deployment.
Quantification and Characterization of Wear Debris	To quantify and characterize any wear debris generated from the Superion® ISS during dynamic axial compression testing.	Wear debris generated from 10 million cycle runout samples of size 8mm and size 16mm implants was quantified and characterized in accordance with ASTM F1714.	Types and total volumetric amounts of wear debris must be of a type and amount similar to other legally marketed spinal devices (10 – 12mg).	Total titanium debris amounted to 0.022 mg (8mm) and 0.017 mg (16mm), well below 10-12mg deemed acceptable in scientific literature, and also lower than wear debris volumes seen in previously cleared/approved spinal devices.
Kinematic and Kinetic Behavior in Human Cadaver Spines	Kinematic and kinetic behavior of the Superion® ISS, including range of motion and intradiscal pressures, were characterized in human lumbar spine specimens.	Six (6) lumbar spine specimens (L1 to S1) were tested. The S1 segment was fixed, and a follower load was used to apply compressive preloads up to 400N at the L1 segment. Spine specimens were preconditioned by cycling in each plane (flexion, extension, lateral bending, and rotation) to a maximum bending moment of 7.5N. Implants (undersized, nominal, and oversized) were placed at 1 and 2 levels. Motion of the L1, L2, L3, L4, and L5 vertebrae were then measured, relative to the sacrum, using an optoelectronic motion measurement system, and intradiscal pressures were measured by transducers placed at the implanted and adjacent levels.	Demonstration of normal flexion, rotational, and lateral bending ranges of motion, and restriction of extension. This test was used to generate benchmark physiologic data and there was no acceptance criteria identified.	Angular displacement was reduced in extension in all configurations, with little or no impact upon rotation or lateral bending. These results suggest that the device has no detrimental impact to the kinematics of the functional spinal unit(s).

Table 1: Laboratory Studies on Superion® ISS

Test	Purpose	Method	Acceptance Criteria	Results
Role of Supraspinous Ligament in Biomechanical Stability	To determine if unintended disruption of the supraspinous ligament (SSL) impacts segmental stability after placement of the Superion® ISS.	Three (3) lumbar spine specimens (L1 to S1) were dissected into three (3) L2-L3 motion segments and three (3) L4-L5 segments. The caudal vertebral body of each was fixed in a kinematic profile apparatus, and the cephalad body was left free to move. A 400N preload was applied, and segments were tested intact, with the SSL dilated and a spacer placed, with the SSL 50% transected and a spacer placed, with the SSL 100% transected with a spacer placed, and with the SSL 100% transected but with no spacer placed. Segments were tested to a maximum bending moment of 10N-m in flexion, extension, rotation, and lateral bending. In each test case, motion of the segment was measured, relative to the fixed body, using an optoelectronic motion measurement system.	The Superion® implant must provide segmental stability to a segment having a disrupted SSL equal to or greater than that of an intact segment. This test was used to generate benchmark bending moment data and there was no acceptance criteria identified.	Bending moments of all implanted specimens were 100% to 135% greater in extension than for an intact specimen, and 60% to 75% greater in flexion. There was no difference in bending moments between the 50% or 100% transected SSL segments, and the intact SSL segments.
Effects of Implant on Canal and Foraminal Dimensions	To quantify the effects of spacer implantation upon canal and foraminal dimensions.	Seven (7) human cadaveric lumbar spine segments were dissected into individual motion segments, seven (7) each of L2-L3 and L4-L5 segments. Each was placed in a frame, with the caudal end fixed, and the cephalad end free to move, to a maximum of 10° flexion and 5° extension. Using CT imaging, key dimensions were measured in neutral, flexion and extension, including canal area, subarticular diameter, ligamentum flavum thickness, and foraminal height, width, and area. Measurements were acquired on the intact specimens, on the same specimens after implantation of a spacer, and on the implanted specimens after 60,000 cycles of coupled 15° flexion-extension under 400N axial preload.	To establish that placement of a Superion® spacer increases canal and foraminal dimensions in extension, and reduces ligamentum flavum thickness. This test was used to generate benchmark characterization data and there was no acceptance criteria identified.	These results confirmed that central canal area and foraminal dimensions increased in extension, with little change in neutral or flexion. Ligamentum flavum thickness decreased in extension, neutral and flexion.

[1]White A., Panjabi, M., *Clinical Biomechanics of the Spine*, J.B. Lippincott, Philadelphia. 2nd Edition.

B. Additional Studies

Table 2: Additional Studies on Superion® ISS

Test	Method and Results
Sterilization, Shelf-Life and Packaging	The Superion® ISS is provided in a sterile package ready for use. The Superion® ISS is sterilized using a gamma irradiation dose of 25 kGy to substantiate a sterility assurance level (SAL) of 10^{-6}. Sterilization validation according to ISO 11137, Sterilization of Health Care Products, Parts 1 and 2 was conducted to confirm that the sterility of the implant is achieved, and is maintained by a sterile barrier package. Sterilization validation according to ISO 11137, Sterilization of Health Care Products, Part 1 was conducted to confirm that the recommended sterilization cycle provides sterility of the manual instruments. Shelf life and packaging validation studies, including packaging seal and integrity, accelerated aging, and real-time aging testing, were conducted to demonstrate that the device packaging can maintain a sterile barrier, with a shelf life of 5 years.
Biocompatibility	The Superion® ISS is manufactured from titanium alloy (Ti-6Al-4V ELI) conforming to ASTM F136. This material has a long history of use in medical implants with no significant biocompatibility issues, as shown in the literature.
MRI Compatibility	Non-clinical testing has demonstrated that the Superion® ISS is MR Conditional. The preclinical tests included assessments of magnetic field interaction (translational attraction, migration, and torque), radiofrequency heating, and artifact measurements. All tests conducted were for characterization and labeling purposes and acceptance criteria were not established. The Superion® ISS can be scanned safely at 1.5T or 3.0T under conditions which are identified in the device labeling.

X. SUMMARY OF CLINICAL STUDY

The applicant performed a clinical study to determine a reasonable assurance of safety and effectiveness of the Superion® ISS for the treatment of moderate degenerative lumbar spinal stenosis in the US under IDE #G070118. Data from this clinical study were the basis of the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

Patients were treated between June 2008 and December 2011. The database for this PMA reflected data collected through July 7, 2014 and included 470 patients. There were 31 investigational sites.

The study was a prospective, multi-center, single-blinded, randomized controlled clinical trial comparing the Superion® ISS to a control group consisting of the X-STOP® IPD®, a legally marketed alternative with similar indications for use. The study evaluated use of the Superion® ISS in the treatment of subjects aged 45 or older suffering from moderate symptoms of neurogenic intermittent claudication, secondary to a confirmed diagnosis of moderate degenerative lumbar spinal stenosis (LSS) at one or two contiguous levels from L1 to L5, i.e., from the L1-L2 level to the L4-L5 level. A maximum of 35 investigative sites in the U.S. and up to 10 sites outside the U.S. were approved to enroll subjects into the trial using a 1:1 randomization assignment and an adaptively selected sample size ranging from 250 to 350 subjects (125-175 enrolled into each group) using a Bayesian adaptive

design. Up to an additional 50 subjects (25 per group) could be enrolled to allow for loss to follow-up. In addition, prior to initiating the randomized trial, clinical sites were permitted to enroll up to 2 non-randomized subjects to receive the Superion® ISS. A maximum of 70 such additional Superion® ISS "training" cases were built into the protocol. Thus, a maximum of 470 subjects were approved to be enrolled into the study. If the study requirements outlined in the Statistical Analysis Plan were met prior to enrolling 470 subjects, the study enrollment could be stopped and the PMA application could subsequently be submitted early. An investigative site was defined as a facility or facilities in the same general geographic location if they are under the control of a local Institutional Review Board (IRB).

All adverse events (device-related or not) were monitored over the course of the study and radiographic assessments were reviewed by an independent core laboratory. Overall success was determined by data collected during the initial 24 months of follow-up. All device-related adverse events, major procedure-related, and adjacent-level-related adverse events and therapeutic failures reported by the clinical investigators were independently adjudicated (for adverse event code, severity and relationship to the device and/or procedure) by a Clinical Events Committee (CEC) composed of three independent spine surgeons. In addition, adverse events reported as having unknown or undetermined relationships to the device by the clinical investigators were to be adjudicated by the CEC.

After implantation of the Superion® ISS or the X-STOP® IPD® device, each investigator provided a postoperative care regimen individualized to the specific needs of each subject. The regimen included but was not limited to: medications, a corset or brace, acupuncture, traction, physical therapy, chiropractic treatment, use of a TENS unit, and massage therapy.

Subjects were required to complete a VAS questionnaire to evaluate pain status at discharge following the index procedure. At each follow-up visit, subjects were interviewed to determine if they had experienced adverse events (AEs) since the previous follow-up visit. A neurological assessment was performed for all subjects at baseline and at all follow-up visits. All subjects were required to complete the Zurich Claudication Questionnaire (ZCQ), Oswestry Disability Index (ODI), Visual Analog Scale (VAS), SF-12 and the VertiFlex Superion® Patient Satisfaction questionnaires to evaluate disability, function, pain, quality of life, and satisfaction at each follow-up visit.

This clinical study was designed as a Bayesian adaptive trial with a minimum of 250 evaluable subjects and a maximum of 350 evaluable subjects, with an additional adjustment for loss-to-follow-up of 15%. The final sample size in the randomized mITT population consisted of 190 Superion® ISS and 201 X-STOP® IPD® control subjects (391 total subjects). The primary hypothesis of this randomized controlled trial was that the clinical performance of the Superion® ISS is non-inferior to the clinical performance achieved with the active control. The study endpoint was the rate of overall subject success at 24 months. A subject was considered a success if they were a success on each of the four individual primary outcome criteria. The hypotheses tested for this primary study endpoint are as follows: H_0: Superion® ISS overall success rate is inferior (Superion® ISS rate – Control rate $< -\Delta$); H_A: Superion® ISS overall success rate is non-inferior (Superion® ISS rate – Control rate $\geq -\Delta$).

A Bayesian approach was used to test for non-inferiority. If the posterior probability of the alternative hypothesis was at least 95.8%, using non-informative uniform (Beta[1,1]) priors for each success rate then the claim of non-inferiority would be made. The choice of non-inferiority margin, Δ (i.e., delta)

was 10% for the overall subject success rate. The value of 0.958 was selected to control the type I error of this design (type 1 error less than 0.05).

An adaptive sample size approach was used to allow for modifications based on interim results, with a maximum of 350 evaluable subjects and a minimum of 250 subjects. The operating characteristics of the adaptive design demonstrate 86.3% power when the Superion® ISS group was superior to the X-STOP® IPD® control group by 5% and 73.6% power when the advantage is 2.5%. In these calculations, the X-STOP® IPD® was assumed to have a 65% success rate.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the Superion® ISS study was limited to subjects who met the following inclusion criteria:

1. Male or female subjects ≥ 45 years of age.
2. Persistent leg/buttock/groin pain, with or without back pain, that is relieved by flexion activities (example: sitting or bending over a shopping cart)
3. Subjects who have been symptomatic and undergoing conservative care treatment for at least 6 months.
4. Diagnosis of degenerative spinal stenosis of the lumbar spine, defined as the narrowing of the midline sagittal spinal canal (central) and/or narrowing between the facet superior articulating process (SAP), the posterior vertebral margin (lateral recess), and the nerve root canal (foraminal).
5. Radiographic confirmation of at least moderate spinal stenosis which narrows the central, lateral, or foraminal spinal canal at one or two contiguous levels from L1-L5. Moderate spinal stenosis is defined as 25% to 50% reduction in lateral/central foramen compared to the adjacent levels, with radiographic confirmation of any one of the following:
    a. Evidence of thecal sac and/or cauda equina compression
    b. Evidence of nerve root impingement (displacement or compression) by either osseous or non-osseous elements
    c. Evidence of hypertrophic facets with canal encroachment

Note: All imaging studies used to confirm LSS were completed within 3 months prior to enrollment. Radiographic (imaging) confirmation of LSS included MRI and/or CT. In the case of a transitional L5/L6 segment with a sufficiently prominent L6 spinous process, these subjects were included by a deviation request from the applicant.

6. Must present with moderately impaired Physical Function (PF) defined as a score of ≥ 2.0 of the Zurich Claudication Questionnaire (ZCQ)
7. Must be able to sit for 50 minutes without pain and to walk 50 feet or more
8. Subjects who are able to give voluntary, written informed consent to participate in this clinical investigation and from whom consent has been obtained
9. Subjects, who, in the opinion of the Clinical Investigator, are able to understand this clinical investigation, cooperate with the investigational procedures and are willing to return for all the required post-treatment follow-ups.

Subjects were not permitted to enroll in the Superion® ISS study if they met any of the following exclusion criteria:

1. Axial back pain only
2. Fixed motor deficit
3. Diagnosis of lumbar spinal stenosis which requires any direct neural decompression or surgical intervention other than those required to implant the control or investigational device
4. Unremitting pain in any spinal position
5. Significant peripheral neuropathy or acute denervation secondary to radiculopathy
6. Lumbar spinal stenosis at more than two levels determined pre-operatively to require surgical intervention
7. Significant instability of the lumbar spine as defined by ≥ 3mm translation or ≥ 5° angulation
8. Sustained pathologic fractures of the vertebrae or multiple fractures of the vertebrae and/or hips
9. Spondylolisthesis or degenerative spondylolisthesis greater than grade 1 (on a scale of 1-4)
10. Spondylolysis (pars fracture)
11. Degenerative lumbar scoliosis with a Cobb angle of > 10° at treatment level
12. Osteopenia or osteoporosis. To confirm eligibility, at the Clinical Investigator's discretion, the following subjects may have a DEXA scan performed:
    - Women 65 or older
    - Postmenopausal women < age 65
    - Subjects with major risk factors for or diagnosed with osteoporosis or osteopenia
        i. If DEXA is required, exclusion is defined as a DEXA bone density measurement T score ≤ -2.5
13. Morbid obesity, defined as Body Mass Index (BMI) greater than 40kg/m^2
14. Insulin-dependent diabetes mellitus
15. Significant peripheral vascular disease (diminished dorsalis pedis or tibial pulses)
16. Prior surgery of the lumbar spine
17. Cauda equina syndrome (defined as neural compression causing neurogenic bowel or bladder dysfunction)
18. Infection in the disc or spine, past or present
19. Evidence of active (systemic or local) infection at time of surgery
20. Active systemic disease such as AIDS, HIV, hepatitis, etc.
21. Paget's disease at involved segment or metastasis to the vertebra, osteomalacia, or other metabolic bone disease
22. Currently undergoing immunosuppressive therapy or long-term steroid use
23. Known allergy to titanium or titanium alloys
24. Tumor in the spine or a malignant tumor except for basal cell carcinoma
25. Known or suspected history of alcohol and/or drug abuse
26. Prisoner or transient
27. Life expectancy less than two years
28. Angina, active rheumatoid arthritis, or any other systemic disease that would affect the subject's welfare or outcome of the clinical investigation
29. Any significant mental illness (e.g., major depression, schizophrenia, bipolar disorder, etc.) that could impair the consent process or ability to complete subject self-report questionnaires
30. Involved in pending litigation of the spine or worker's compensation related to the back

31. Enrolled in the treatment phase of another drug or device clinical investigation (currently or within past 30 days)
32. Congenital defect of the spine
33. Pregnant or lactating

2. Follow-Up Schedule

All subjects were scheduled to return for follow-up examinations at 6 weeks (± 2 weeks), 3 months (± 2 weeks), 6 months (± 1 month), 12 months (± 2 months), 18 months (± 2 months), 24 months (± 2 months) post-treatment and annually thereafter to collect data for the primary evaluation of safety and effectiveness.

The evaluations performed in relation to the index procedure pre-operatively, as well as the assessments performed which were used to assess the endpoints post-operatively, are shown in Table 3. Adverse events were recorded at all visits.

Table 3: Follow-Up Visit Schedule

	Screening-Baseline	Surgical Treatment	Discharge (±0-7 days)	6-week (±2 weeks)	3-month (±2 weeks)	6-month (±1 month)	12-month (±2 months)	18-month (±2 months)	24-month[c] (±2 months)
Study Visit Window		Day 0	0-7 days	4-8 weeks	10-14 weeks	5-7 months	10-14 months	16-20 months	22-26 months
Signed Informed Consent	X								
Demographic Information	X								
Complete History & Physical	X								
Randomization	X								
Standing AP & Lateral Lumbar Spine X-rays	X[a]		X	X	X	X	X	X	X
Flexion / Extension Lateral Lumbar Spine X-rays	X[a]			X	X	X	X	X	X
Lumbar Spine MRI/CT Scan	X[a]								
DEXA Scan[b]	As needed								
SF-12 –Health Survey (v2)	X			X	X	X	X	X	X
Zurich Claudication Questionnaire (ZCQ)	X			X	X	X	X	X	X
Oswestry Disability Index (v2)	X			X	X	X	X	X	X
Neurological Status	X		X	X	X	X	X	X	X
Visual Analogue Scale	X		X	X	X	X	X	X	X
VertiFlex® Patient Satisfaction Questionnaire				X	X	X	X	X	X
Assess Adverse Events		X	X	X	X	X	X	X	X

[a]Lumbar spine x-rays and MRI/CT taken within 3 months of enrollment can be used to confirm eligibility.

[b]In order to confirm eligibility, at the Investigator's discretion, subjects previously diagnosed with osteoporosis, osteopenia, osteomalacia, female subjects over the age of 65, and post-menopausal female subjects under the age of 65 with any of the risk factors for osteoporosis, will have DEXA scans performed prior to study entry.

[c]Subjects may be required to return for additional follow-up visits annually (±2 months) for up to ten (10) years, or until Applicant notifies Investigator of study conclusion at an earlier time.

3. Clinical Endpoints

The effectiveness of the Superion® ISS was assessed using a composite definition of study success as compared to the X-STOP® IPD® control group.

The safety of the Superion® ISS was assessed by comparison to the X-STOP® IPD® control group with respect to the nature and frequency of adverse events (overall and in terms of seriousness and relationship to the implant), secondary surgical procedures as well as maintenance or improvement in neurological status.

The primary endpoint of the investigation was individual patient success, which required the patient to meet all of the following criteria at 24 months:

- Clinically significant improvement in outcomes compared to baseline, as determined by meeting the criterion for at least two of three domains of ZCQ
  - ≥ 0.5 point improvement in physical function
  - ≥ 0.5 point improvement in symptom severity
  - score of ≤ 2.5 points on patient satisfaction domain
- No reoperations, removals, revisions, or supplemental fixation at the index level(s)
- No major implant or procedure-related complications
  - no dislodgement, migration, or deformation
  - no new or persistent worsened neurological deficit at the index level
  - no spinous process fractures
  - no deep infection, death, or other permanent device attributed disability
- No clinically significant confounding treatments:
  - no epidural injections, nerve block procedures at index level, spinal cord stimulators or rhizotomies

B. Accountability of PMA Cohort

At the time of database lock (July 7, 2014), of 391 per protocol patients (190 Superion® ISS and 201 X-STOP® IPD®) enrolled in the PMA study. Overall, 94.6% (183 Superion® ISS and 187 X-STOP® IPD®) of patients enrolled in the study were available for analysis at the study completion (24-month post-operative visit). The Superion® ISS cohort had a follow-up rate of 97.3% and the X-STOP® IPD® cohort had a follow-up rate of 94.9% through 24 months.

The primary analysis cohort for this study was the Modified Intent-to-Treat Cohort, defined as:
Modified Intent-to-treat patient population (mITT): The mITT patient population will include all patients randomized and having an anesthesia start time, where patients will be classified by the group in which they are randomized. Subjects with an anesthesia start time, but that do not receive a device, or receive the wrong device, will be failures.

Confirmatory analysis was performed in the Per Protocol Cohort, defined as:
Per protocol (PP) Population: The PP patient population will include all subjects with 24-month follow-up data and no major protocol deviations and subjects that failed before 24 months.

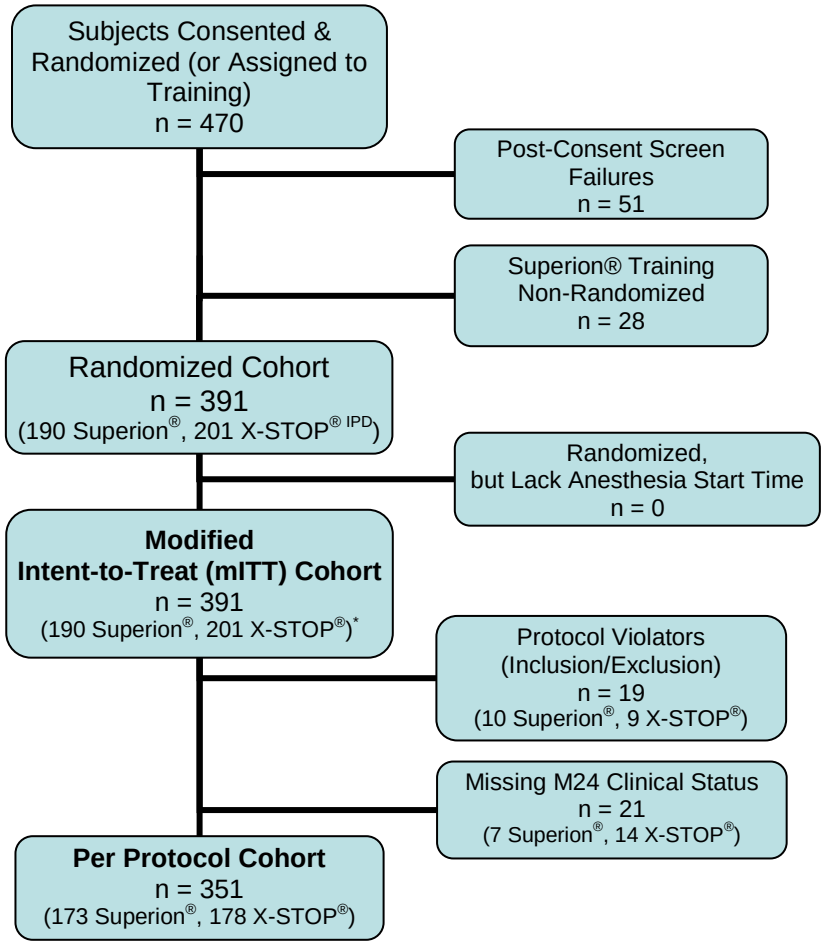
Patient accounting and follow-up (Table 4), a patient accounting tree (Figure 2), and a summary of patient and data accounting at 24 months (Table 5) are provided below.

Table 4: Patient Accounting and Follow-up Compliance Table for Superion® ISS and X-STOP® IPD® mITT Analysis Sets

Date of data transfer 07/07/2014	Pre-op		Week 6		Month 3		Month 6		Month 12		Month 18		Month 24	
	I[1]	C[2]	I	C	I	C	I	C	I	C	I	C	I	C
(1) Theoretical follow-up	190	201	190	201	190	201	190	201	190	201	190	201	190	201
(2) Cumulative deaths	0	0	0	0	1	0	1	0	2	2	2	3	2	5
(3) Cumulative Revisions, Reoperations, and Injections	0	0	3	3	8	11	20	19	40	32	46	48	51	53
(4) Not Yet Overdue	0	0	0	0	0	0	0	0	0	0	0	0	0	0
(5) Deaths + term failures among theoretical due	0	0	3	3	9	11	21	19	42	34	48	51	53	57
(6) Expected due for clinical visit	190	201	187	198	181	190	169	182	148	167	142	150	137	144
(7) Failures among theoretical due	0	0	3	3	8	11	20	19	40	32	46	48	51	53
(8) Expected due + failures among theoretical due	190	201	190	201	189	201	189	201	188	199	188	198	188	197
All Evaluated Accounting (Actual) Among Expected Due Procedures														
(9) # of procedures with any clinical data in interval	190	201	182	193	171	182	164	177	145	162	132	137	131	133
(10) All Evaluated Visit Compliance (%)	100%	100%	97.3%	97.0%	94.5%	95.8%	97.0%	97.3%	98.0%	97.0%	93.0%	91.3%	95.6%	92.4%
(11) XCQ Responder status determined	190	201	181	183	171	182	164	177	145	162	132	137	131	133
(12) Radiographic evaluation	184	194	175	178	165	187	170	182	162	175	147	161	145	150
(13) Composite clinical success	190	201	184	196	179	193	184	197	185	195	179	187	183	187
(14) Actual % Follow-up for CCS	100%	100%	96.8%	97.5%	94.5%	95.8%	97.0%	97.3%	98.0%	97.0%	93.0%	91.3%	97.3%	94.9%
Within Window Accounting (Actual) Among Expected Due														
	I	C	I	C	I	C	I	C	I	C	I	C	I	C
(15) ZCQ Responder status determined	190	201	168	179	169	180	152	167	111	122	129	131	115	113
(16) Radiographic evaluation	184	194	162	162	162	186	154	169	123	131	138	152	127	128
(17) Composite clinical success	190	201	171	182	177	191	172	186	151	154	175	179	166	166
(18) Actual % Follow-up for CCS	100%	100%	89.8%	90.4%	93.4%	94.7%	89.9%	91.8%	75.0%	73.1%	90.8%	87.3%	88.3%	84.3%

I[1] = Superion® ISS, C[2] = X-STOP® IPD®

The patient accounting tree for the Superion® ISS IDE is depicted below in Figure 2.



*There were no subjects with misallocations of randomization, meaning all subjects received the device to which they were randomized. As such, the mITT cohort is identical to the "As-Treated" patient cohort.

Figure 2: Patient Accounting Tree

Of the 51 post-consent screen failures, there were 2 subjects in the training group and 49 that were randomized for the pivotal cohort that did not proceed to treatment. The 49 post-consent screen failures included 28 in the Superion® ISS arm and 21 in the X-STOP® IPD® arm. The subjects that were post-consent screen failures were blinded to treatment group to mitigate bias.

Subjects were expected due at 24 months if they had not terminally failed due to death or clinical failure defined as reoperation, revision or additional treatment. Data were missing for 7 Superion® ISS and 14 X-STOP® IPD® subjects at 24 months.

Table 5: 24 Month Data Accounting for Superion® ISS IDE

Parameter	Superion® ISS	X-STOP® IPD®
Randomized or Assigned to Training	248	222
Withdrawn Prior to Treatment	30	21
Training Patients	28	0
Subjects Treated (mITT)	190	201
Composite Clinical Success Responders	183	187
Deaths + Clinical Failures Among Implanted[1]	53	57
Expected (mITT)	137	144
ZCQ	131	133
VAS Leg and Back Pain	131	133
ODI	131	133
SF-12	128	133
Neurological Evaluation	150	157
Radiographic Evaluation	145	150
Patient Satisfaction Evaluation	152	157

[1]Patients with reoperations, revisions, and epidural steroid injection

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a lumbar interspinous spacer study performed in the US. Baseline demographic information and operative variables are presented in Table 6, Table 7, and Table 8.

Table 2: Summary of Baseline and Demographic Categorical Variables Superion® ISS and X-STOP® IPD® Control mITT Analysis Sets

	Superion® ISS		X-STOP® IPD®	
	N	**%**	**N**	**%**
Number of subjects	190	-	201	-
Males	110	57.9	129	64.2
Females	80	42.1	72	35.8
Race	**N**	**%**	**N**	**%**
White	177	93.2	196	97.5
Asian	0	0.0	1	0.5
African American	8	4.2	1	0.5
American Indian or Alaska Native	0	0.0	0	0.0
Native Hawaiian or Other Pacific Islander	0	0.0	1	0.5
Other	5	2.6	2	1.0
Ethnicity	**N**	**%**	**N**	**%**
Hispanic or Latino	5	2.6	11	5.5
Not Hispanic or Latino	185	97.4	190	94.5
Use of nicotine products	**N**	**%**	**N**	**%**
No	89	46.8	101	50.2
Current Use	24	12.6	24	11.9
Previous Use	77	40.5	76	37.8

Statistical analysis of baseline demographics did not show any significant differences between subjects randomized into the Superion® ISS group compared to those randomized into the X-STOP® IPD® control group.

Table 3: Summary of Baseline and Demographic Continuous Variables Superion® ISS and X-STOP® IPD® mITT Analysis Set

	Superion® ISS			X-STOP® IPD®		
Demographics – All	**N**	**Mean**	**SD**	**N**	**Mean**	**SD**
Age at surgery (yrs)	190	66.9	9.4	201	66.2	10.2
Height (inches)	190	67.2	4.2	201	67.9	3.8
Weight (lbs)	190	189.7	36.5	201	195.8	36.9
BMI (k/m^2)	190	29.5	4.6	201	29.7	4.6
Demographics – Male	**N**	**Mean**	**SD**	**N**	**Mean**	**SD**
Age at surgery (yrs)	110	68.0	9.0	129	66.4	10.2
Height (inches)	110	69.9	2.6	129	70.0	2.8
Weight (lbs)	110	204.9	32.6	129	207.2	32.0
BMI (k/m^2)	110	29.5	4.3	129	29.7	4.0
Demographic – Female	**N**	**Mean**	**SD**	**N**	**Mean**	**SD**
Age at surgery (yrs)	80	65.3	9.7	72	65.8	10.3
Height (inches)	80	63.4	2.8	72	64.2	2.5
Weight (lbs)	80	168.8	31.0	72	175.4	36.3
BMI (k/m^2)	80	29.5	5.0	72	29.8	5.4
Baseline Functional Status	**N**	**Mean**	**SD**	**N**	**Mean**	**SD**
Oswestry (ODI)	190	39.1	13.4	201	39.9	11.6
Zurich Claudication Qx Severity	190	3.33	0.64	201	3.37	0.61
Zurich Claudication Qx Physical	190	2.63	0.43	201	2.72	0.43
SF-12 PCS (Physical)	189	29.4	8.1	201	28.5	6.9
SF-12 MCS (Mental Health)	189	50.0	12.7	201	48.9	12.2
VAS Back pain	190	55.4	27.9	201	55.1	27.4
VAS Leg pain (right leg)	190	55.0	31.3	201	52.9	32.5
VAS Leg pain (left leg)	190	49.6	31.8	201	50.8	31.7

Descriptive comparisons of device group mean differences at baseline, device group differences over time, and change from baseline over time were facilitated using Cohen's standardized effect size. While there were small statistical differences in Race and ZCQ – Physical Function baseline parameters, it was determined that these differences were not clinically important for the investigational and control groups.

Table 4: Operative Variables and Types of Stenosis Superion® ISS and X-STOP® IPD® mITT Analysis Set

	Superion® ISS		X-STOP® IPD®	
	n	**%**	**n**	**%**
Number of Subjects Treated	189	99.5	199	99.0
Subjects Attempted / Not Implanted	1	8.4	2	3.7
Number of Levels Treated	n	%	n	%
1	99	52.4	99	49.7
2	90	47.6	100	50.3
Stenosis Type	n	%	n	%
Central Only	66	34.7	60	29.9
Lateral Only	16	8.4	15	7.5
Central and Lateral Stenosis	100	52.6	118	58.7
Foraminal Stenosis	8	4.2	8	4.0

Baseline differences in operative covariates such as treated levels or stenosis type did not have an overall impact on the clinical success of subjects receiving either Superion® ISS or X-STOP® IPD®.

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the mITT cohort of 391 subjects (190 Superion® ISS subjects and 201 X-STOP® IPD® subjects) available for the 24 month evaluation. When making an assessment of safety, an Adverse Event (AE) was considered as: any undesired clinical response or complication experienced by a subject. All operative and postoperative AEs, whether device-related or not, were recorded on the AE Case Report Forms. Safety outcomes were determined by evaluating the type, frequency, seriousness, and relationship to device of AEs through the 24-month time point for all subjects. AEs were categorized as device-related, procedure-related, adjacent-level-related, or systemic.

AE Device/Procedure-Relatedness

The clinical investigator, on the basis of his or her clinical judgment and the following definitions, determined the severity and relationship of the AE to the device and/or procedure:

- Not related: The AE is clearly not related
- Unknown/Undetermined: The AE is unknown or undetermined to be related
- Related: The AE is clearly related
- Device-related: The AE is related to the Study device or the control device
- Procedure-related: The AE is related to the procedure to implant the investigational or control device.

AE Severity

The severity of an AE was categorized as mild, moderate or severe. Severity was determined by the clinical investigator, using the following definitions:

- Mild: The AE is transient or causes mild discomfort. There usually is no intervention/therapy required and the AE does not interfere with the subject's normal activities.

- Moderate: The AE causes some limitation in activity and some assistance may be needed. There is no or minimal medical intervention/therapy required.
- Severe: The AE causes marked limitation in activity. The subject's usual daily activity is interrupted. The subject may require medical intervention/therapy, hospitalization is possible.

Serious AEs

The AE was regarded as a Serious Adverse Event (SAE) if the injury or illness:

- Results in death
- Is life-threatening,
- Results in or prolongs hospitalization
- Results in permanent impairment of a body function or permanent damage to a body structure, or
- Necessitates medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure.

Serious Adverse Device Effect

A Serious Adverse Device Effect (SADE) is a device-related adverse event that has resulted in any of the consequences characteristic of a serious AE or that might have led to any of these consequences if suitable action had not been taken or intervention had not been made.

Unanticipated Adverse Device Effect

An Unanticipated Adverse Device Effect (UADE) is 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 risks identified for the investigational or control device; or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

Role of the CEC

Adverse events were evaluated by the Medical Monitor. Data were evaluated for safety endpoints by an independent CEC. The CEC had predetermined stopping rules, one of which was greater than 10% postoperative observation of *in situ* study device unlocking with full or partial collapse of the cam lobes at annual review. The first stopping review occurred after a minimum of 30 subjects in the study group had been accrued. This observation was monitored annually throughout the study. Additionally, all device-related events, major procedure-related, and adjacent level-related events and therapeutic failures reported by the clinical investigators were adjudicated by the independent CEC. In addition, events reported as having unknown or undetermined relationships to the device by the clinical investigators were to be adjudicated by the CEC.

The key safety outcomes for this study are presented below in Table 9 through Table 30.

Adverse Effects that Occurred in the PMA Clinical Study

Overall Adverse Events

A summary of the total number of adverse events, adverse events related to the device or procedure, serious adverse events, and serious adverse events that were related to the device or procedure is shown below in Table 9.

The safety profile of the Superion® ISS device is similar to the X-STOP® IPD® device when considering adverse event incidence. The overall incidence of any adverse event (Superion® ISS: 94.7% vs. X-STOP® IPD®: 91.5%), device-related adverse events (Superion® ISS: 11.6% vs. X-STOP® IPD®: 7.5%), procedure-related adverse events (Superion® ISS: 14.2% vs. X-STOP® IPD®: 15.9%), serious adverse events (Superion® ISS: 46.3% vs. X-STOP® IPD®: 45.8%), and device- or procedure-related serious adverse events (Superion® ISS: 21.1% vs. X-STOP® IPD®: 23.4%) were similar between both groups. No device-related or procedure-related deaths were reported during follow-up in either the Superion® ISS or X-STOP® IPD® control groups.

Table 5: Comparisons of Summary Adverse Event Rates between Superion® ISS and X-STOP® IPD® mITT Analysis Sets at 24 Months

	Superion® ISS (N=190)		X-STOP® IPD® (N=201)		I vs. C[1]		
	n	%	n	%	Diff	LB	UB
Any adverse event (per patient)	180	94.7	184	91.5	-3.2	-13.1	6.8
Any device- related AE	22	11.6	15	7.5	-4.1	-14.0	5.8
Any procedure- related AE	27	14.2	32	15.9	1.7	-8.2	11.6
Any serious AE	88	46.3	92	45.8	-0.5	-10.5	9.4
Serious AE that is either device- or procedure-related	16	8.4	19	9.5	1.0	-8.9	10.9
Deaths	6	3.2	5	2.5	-0.7	-10.6	9.3

Notes:
[1] Exact 95% confidence interval for the group difference. Diff signifies difference between percentages of groups. LB signifies lower bound of 95% confidence interval. UB signifies upper bound of 95% confidence interval.

As described above, during the clinical study, adverse events were classified as device-related or procedure-related, not device-related or procedure-related, or as having an "unknown/undetermined" relationship. At FDA's request, an additional analysis was performed that grouped adverse events with an "unknown/undetermined" assessment for device and procedure relation with those events deemed to have a definite device or procedure relation as a "worst case" assessment. These results are presented below in Table 10.

Table 6: Worst Case Comparisons of Summary Adverse Event Rates between Superion® ISS and X-STOP® IPD® mITT Analysis Sets with Unknown/Undetermined Events Grouped with Related Events at 24 Months

	Superion® ISS (N=190)		X-STOP® IPD® (N=201)		I vs. C[1]		
	n	%	n	%	Diff	LB	UB
Any adverse event (per patient)	180	94.7	184	91.5	-3.2	-13.1	6.8
Any device -related AE[2]	73	38.4	79	39.3	0.9	-9.0	10.8
Any procedure-related AE[2]	72	37.9	99	49.3	11.4	1.4	21.1
Any serious AE	88	46.3	92	45.8	-0.5	-10.5	9.4
Serious AE that is either device-or procedure-related	40	21.1	47	23.4	2.3	-7.6	12.2
Deaths	6	3.2	5	2.5	-0.7	-10.6	9.3

Notes:
[1] Exact 95% confidence interval for the group difference.
[2] Includes "Yes" and "Unknown/Undetermined" relationships

Specific adverse events are listed in alphabetical order according to adverse event categories in Table 11. Adverse event rates are based on the number of subjects having at least one occurrence of an adverse event, and divided by the number of subjects in that treatment group. Events per subject are based on the number of adverse events, divided by the total number of subjects in each cohort. Subjects experiencing adverse events in more than one category are represented in each category in which they experienced an adverse event. Regarding specific adverse events, the most common adverse events observed in the Superion® ISS group and X-STOP® IPD® group were Pain - Back, Pain - Leg, Pain - Buttock & Groin, Spinal stenosis symptoms at index level, and Spinous process fracture.

As shown in the detailed overall adverse event table (Table 11), pain-related adverse events were distributed differently between the Superion® ISS and X-STOP® IPD® groups. X-STOP® IPD® patients were more likely to have Pain - Back or Pain - Leg adverse events, while Superion® ISS patients were more likely to have Pain – Buttock & Groin adverse events. Overall, X-STOP® IPD® patients were more likely to have a back, leg, buttock, or groin adverse event compared with Superion® ISS patients. In addition, X-STOP® IPD® patients were more likely to have events related to soft tissue damage or fever. In contrast, Superion® ISS patients were more likely to have an adverse event related to spinous process fracture. In general, there were no clinically important differences in either treatment group, aside from spinous process fracture and device migration/dislodgement, which will be discussed later.

Table 7: Specific Adverse Events in Superion® ISS IDE up to 24 months (mITT cohort)

	Superion® ISS (I) (N=190)			X-STOP® IPD® (C) (N=201)			I vs C[1]		
Adverse Event Type	No. of Events	No. of Pts.	% of Pts.	No. of Events	No. of Pts.	% of Pts.	Diff	LB	UB
Abdominal pain	1	1	0.5	0	0	0	-0.5	-10.4	9.4
Accidental injury	20	15	7.9	22	19	9.5	1.6	-8.4	11.4

Table 7: Specific Adverse Events in Superion® ISS IDE up to 24 months (mITT cohort)

	Superion® ISS (I) (N=190)			X-STOP® IPD® (C) (N=201)			I vs C[1]		
Adverse Event Type	**No. of Events**	**No. of Pts.**	**% of Pts.**	**No. of Events**	**No. of Pts.**	**% of Pts.**	**Diff**	**LB**	**UB**
Adjacent level DDD	1	1	0.5	1	1	0.5	0	-9.9	9.9
Adjacent level stenosis	1	1	0.5	4	2	1	0.5	-9.4	10.4
Allergic reaction	4	4	2.1	6	6	3	0.9	-9	10.8
Anemia	4	3	1.6	1	1	0.5	-1.1	-11	8.8
Angina	3	3	1.6	0	0	0	-1.6	-11.5	8.3
Bronchitis	2	2	1.1	6	5	2.5	1.4	-8.5	11.3
Cancer/Neoplasm	13	11	5.8	14	13	6.5	0.7	-9.3	10.6
Cardiovascular	25	20	10.5	20	16	8	-2.6	-12.5	7.4
Cerebrovascular accident (CVA)	2	2	1.1	1	1	0.5	-0.6	-10.5	9.4
Chronic obstructive pulmonary disease (COPD)	0	0	0	0	0	0	.	.	.
Coronary episode, ischemic	3	2	1.1	5	2	1	-0.1	-10	9.9
Deep infection at the operative site	0	0	0	3	2	1	1	-8.9	10.9
Deep vein thrombosis	2	2	1.1	1	1	0.5	-0.6	-10.5	9.4
Dental	0	0	0	2	2	1	1	-8.9	10.9
Device breakage	0	0	0	1	1	0.5	0.5	-9.4	10.4
Device breakage preventing device placement	0	0	0	0	0	0	.	.	.
Device deformation preventing device placement	1	1	0.5	0	0	0	-0.5	-10.4	9.4
Device dislodgement	1	1	0.5	2	2	1	0.5	-9.4	10.4
Device migration	1	1	0.5	8	7	3.5	3	-7	12.9
Device subsidence	4	4	2.1	0	0	0	-2.1	-12	7.8
Diabetes mellitus	0	0	0	2	2	1	1	-8.9	10.9
Diabetes mellitus inadequate control	0	0	0	1	1	0.5	0.5	-9.4	10.4
Dizziness	5	5	2.6	0	0	0	-2.6	-12.5	7.3
Dural leaks	6	6	3.2	3	3	1.5	-1.7	-11.6	8.3
Dyspnea	0	0	0	1	1	0.5	0.5	-9.4	10.4
Edema	2	2	1.1	4	4	2	0.9	-9	10.8
EENT	2	2	1.1	0	0	0	-1.1	-11	8.9
Endocrine/Metabolic	11	11	5.8	13	11	5.5	-0.3	-10.2	9.6
Facet cyst	4	3	1.6	0	0	0	-1.6	-11.5	8.3
Fever	0	0	0	4	4	2	2	-7.9	11.9
Gallstones	0	0	0	1	1	0.5	0.5	-9.4	10.4
Gastroesophageal reflux disease (GERD)	1	1	0.5	0	0	0	-0.5	-10.4	9.4
Gastrointestinal	9	7	3.7	10	9	4.5	0.8	-9.1	10.7
Gastrointestinal (GI) bleed	2	2	1.1	1	1	0.5	-0.6	-10.5	9.4
Genitourinary	25	22	11.6	17	17	8.5	-3.1	-13	6.8
Headache	1	1	0.5	5	5	2.5	2	-7.9	11.9
Hematologic	0	0	0	2	2	1	1	-8.9	10.9
Hematoma	0	0	0	1	1	0.5	0.5	-9.4	10.4
Immune	0	0	0	1	1	0.5	0.5	-9.4	10.4
Infection*	15	14	7.4	17	16	8	0.6	-9.3	10.5
Instruments breakage or malfunction preventing device placement	0	0	0	0	0	0	.	.	.
Loss of bladder control	0	0	0	2	2	1	1	-8.9	10.9

Table 7: Specific Adverse Events in Superion® ISS IDE up to 24 months (mITT cohort)

	Superion® ISS (I) (N=190)			X-STOP® IPD® (C) (N=201)			I vs C[1]		
Adverse Event Type	**No. of Events**	**No. of Pts.**	**% of Pts.**	**No. of Events**	**No. of Pts.**	**% of Pts.**	**Diff**	**LB**	**UB**
Loss of bowel control	0	0	0	0	0	0	.	.	.
Multi-level DDD	1	1	0.5	0	0	0	-0.5	-10.4	9.4
Muscle damage	1	1	0.5	1	1	0.5	0	-9.9	9.9
Musculoskeletal**	108	78	41.1	100	70	34.8	-6.2	-16.1	3.7
Myocardial infarction	5	5	2.6	3	3	1.5	-1.1	-11	8.8
Nausea	0	0	0	4	4	2	2	-7.9	11.9
Nerve root damage	0	0	0	0	0	0	.	.	.
Neurological disorder	27	22	11.6	13	13	6.5	-5.1	-15	4.8
Ophthalmic	10	8	4.2	6	6	3	-1.2	-11.1	8.7
Osteolysis	0	0	0	1	1	0.5	0.5	-9.4	10.4
Other, specify***	15	14	7.4	10	5	2.5	-4.9	-14.8	5.1
Pain – Back	56	50	26.3	71	66	32.8	6.5	-3.4	16.4
Pain – Back & Buttock	1	1	0.5	0	0	0	-0.5	-10.4	9.4
Pain – Back & Hip	1	1	0.5	0	0	0	-0.5	-10.4	9.4
Pain – Buttock	1	1	0.5	2	2	1	0.5	-9.4	10.4
Pain – Buttock & Groin	23	21	11.1	13	13	6.5	-4.6	-14.5	5.3
Pain – Hip	2	2	1.1	3	3	1.5	0.4	-9.5	10.4
Pain – Leg	41	37	19.5	54	47	23.4	3.9	-6	13.8
Peripheral Vascular Disorder	0	0	0	3	3	1.5	1.5	-8.4	11.4
Pneumonia	5	4	2.1	5	5	2.5	0.4	-9.5	10.3
Presence of osteophyte formation associated with severe disc or facet degeneration	1	1	0.5	1	1	0.5	0	-9.9	9.9
Progression of underlying disease	0	0	0	1	1	0.5	0.5	-9.4	10.4
Psychiatric/Substance abuse	1	1	0.5	4	4	2	1.5	-8.4	11.4
Pulmonary edema	0	0	0	1	1	0.5	0.5	-9.4	10.4
Pulmonary embolism	1	1	0.5	0	0	0	-0.5	-10.4	9.4
Renal failure	3	3	1.6	1	1	0.5	-1.1	-11	8.8
Renal insufficiency	2	2	1.1	2	2	1	-0.1	-10	9.9
Respiratory disorder	4	3	1.6	4	4	2	0.4	-9.5	10.3
Respiratory distress	2	2	1.1	0	0	0	-1.1	-11	8.9
Respiratory infection	0	0	0	2	2	1	1	-8.9	10.9
Rheumatoid arthritis	1	1	0.5	0	0	0	-0.5	-10.4	9.4
Sensory loss	3	2	1.1	4	4	2	0.9	-9	10.8
Shortness of breath	0	0	0	1	1	0.5	0.5	-9.4	10.4
Skin and subcutaneous tissue	2	2	1.1	10	8	4	2.9	-7	12.8
Soft tissue damage	1	1	0.5	7	7	3.5	3	-7	12.9
Spinal stenosis symptoms at index level	37	35	18.4	38	34	16.9	-1.5	-11.4	8.4
Spinous process fracture	24	22	11.6	14	13	6.5	-5.1	-15	4.8
Stroke	1	1	0.5	1	1	0.5	0	-9.9	9.9
Syncope	0	0	0	2	2	1	1	-8.9	10.9
Transient ischemic attack (TIA)	0	0	0	1	1	0.5	0.5	-9.4	10.4
Urinary tract infection	8	7	3.7	6	6	3	-0.7	-10.6	9.2
Vertebral compression fractures	1	1	0.5	3	3	1.5	1	-8.9	10.9
Wound dehiscence or delayed healing	0	0	0	1	1	0.5	0.5	-9.4	10.4
Wound drainage	1	1	0.5	4	4	2	1.5	-8.4	11.4

[1] Exact 95% confidence interval for the group difference.

*Infection AEs are defined as: including superficial infections and seroma at the surgical site, as well as infections at remote sites (e.g., sinus or throat infection)
**Musculoskeletal AEs are defined as: including weakness, cramping, joint pain, joint surgery or replacement, and other disorders in non-lumbar spinal tissues
***Other adverse events includes events not fitting a specific existing adverse event category, including insomnia, psychological disorder, weight loss, general weakness, ganglion cyst, and drug withdrawal.

Table 12 provides the actual counts of specific events by time of onset. Most adverse events were evenly distributed throughout the course of the study up to 24 months. The exception is the occurrence of spinous process fracture. The majority of these fractures occurred within the first 6 months post-operatively in both cohorts. No other clinically important trends in adverse event occurrence were demonstrated by the data.

Table 12: Counts of Specific Adverse Events by Time of Occurrence up to 24 Months (mITT cohort)

	Day of Surgery		**Immed. Post-Op to Month 3 (Day 1-90)**		**>Mo. 3 to Mo. 6 (Day 91-180)**		**>Mo. 6 to Mo. 12 (Day 181-365)**		**>Mo. 12 to Mo. 24 (Day 365-730)**		**Post Month 24 (Day >730)**		**Totals**	
	I[1]	**C[2]**	**I**	**C**	**I**	**C**	**I**	**C**	**I**	**C**	**I**	**C**	**I**	**C**
Abdominal pain	**0**	0	**0**	0	**0**	0	**0**	0	**1**	0	**0**	0	**1**	**0**
Accidental Injury	**1**	0	**2**	5	**1**	2	**7**	5	**6**	8	**2**	2	**19**	**22**
Adjacent Level DDD	**0**	0	**0**	0	**1**	0	**0**	1	**0**	0	**0**	0	**1**	1
Adjacent Level Stenosis	**0**	0	**0**	3	**0**	0	**0**	1	**0**	0	**1**	0	**1**	4
Allergic reaction	**0**	1	**1**	1	**0**	1	**1**	2	**2**	1	**0**	0	**4**	**6**
Anemia	**0**	0	**3**	0	**0**	0	**1**	0	**0**	1	**0**	0	**4**	**1**
Angina	**0**	0	**1**	0	**1**	0	**1**	0	**0**	0	**0**	0	**3**	**0**
Bronchitis	**0**	0	**0**	2	**0**	1	**0**	2	**2**	1	**0**	0	**2**	**6**
Cancer/Neoplasm	**0**	0	**2**	2	**2**	2	**3**	5	**4**	4	**2**	1	**13**	14
Cardiovascular	**1**	0	**2**	2	**5**	3	**3**	0	**12**	10	**2**	5	**25**	20
Cerebrovascular accident (CVA)	**0**	0	**0**	0	**0**	1	**0**	0	**1**	0	**1**	0	**2**	**1**
Chronic obstructive pulmonary disease (COPD)	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0	**0**	**0**
Coronary episode, ischemic	**0**	0	**1**	4	**1**	0	**0**	0	**1**	1	**0**	0	**3**	**5**
Deep infection at the operative site	**0**	0	**0**	2	**0**	1	**0**	0	**0**	0	**0**	0	**0**	**3**
Deep vein thrombosis	**0**	0	**0**	0	**0**	0	**0**	1	**0**	0	**2**	0	**2**	**1**
Dental	**0**	0	**0**	2	**0**	0	**0**	0	**0**	0	**0**	0	**0**	2
Device breakage	**0**	1	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0	**0**	1
Device breakage preventing device placement	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0	**0**	**0**
Device deformation preventing device placement	**1**	0	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0	**1**	**0**
Device dislodgement	**0**	0	**1**	1	**0**	1	**0**	0	**0**	0	**0**	0	**1**	2
Device erosion	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0
Device migration	**0**	0	**1**	4	**0**	2	**0**	0	**0**	2	**0**	0	**1**	8
Device subsidence	**0**	0	**0**	0	**3**	0	**1**	0	**0**	0	**0**	0	**4**	0
Dextroscoliosis	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0
Diabetes mellitus	**0**	0	**0**	0	**0**	0	**0**	1	**0**	1	**0**	0	**0**	**2**
Diabetes mellitus inadequate	**0**	0	**0**	0	**0**	0	**0**	0	**0**	1	**0**	0	**0**	**1**

Table 12: Counts of Specific Adverse Events by Time of Occurrence up to 24 Months (mITT cohort)

	Day of Surgery		Immed. Post-Op to Month 3 (Day 1-90)		>Mo. 3 to Mo. 6 (Day 91-180)		>Mo. 6 to Mo. 12 (Day 181-365)		>Mo. 12 to Mo. 24 (Day 365-730)		Post Month 24 (Day >730)		Totals	
	I[1]	C[2]	I	C	I	C	I	C	I	C	I	C	I	C
control														
Disc bulge	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0
Dizziness	**0**	0	**3**	0	**0**	0	**1**	0	**0**	0	**1**	0	**5**	**0**
Dural leaks	**2**	0	**0**	0	**0**	1	**2**	0	**2**	1	**0**	1	**6**	**3**
Dyspnea	**0**	0	**0**	0	**0**	0	**0**	0	**0**	1	**0**	0	**0**	**1**
Edema	**0**	0	**2**	0	**0**	0	**0**	2	**0**	2	**0**	0	**2**	**4**
EENT	**0**	0	**0**	0	**1**	0	**0**	0	**1**	0	**0**	0	**2**	0
Endocrine/Metabolic	**0**	3	**2**	2	**1**	2	**3**	1	**2**	4	**3**	1	**11**	13
Facet cyst	**0**	0	**1**	0	**0**	0	**1**	0	**2**	0	**0**	0	**4**	0
Fever	**0**	0	**0**	2	**0**	0	**0**	0	**0**	0	**0**	2	**0**	**4**
Gallstones	**0**	0	**0**	0	**0**	0	**0**	0	**0**	1	**0**	0	**0**	**1**
Gastroesophageal reflux disease (GERD)	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0	**1**	0	**1**	**0**
Gastrointestinal	**0**	0	**1**	2	**1**	2	**2**	2	**1**	2	**4**	2	**9**	10
Gastrointestinal (GI) bleed	**0**	0	**0**	0	**1**	0	**0**	0	**1**	1	**0**	0	**2**	**1**
Genitourinary	**6**	1	**9**	7	**2**	2	**4**	2	**3**	3	**1**	2	**25**	17
Headache	**0**	0	**1**	3	**0**	0	**0**	0	**0**	2	**0**	0	**1**	**5**
Hematologic	**0**	0	**0**	0	**0**	0	**0**	0	**0**	2	**0**	0	**0**	2
Hematoma	**0**	0	**0**	1	**0**	0	**0**	0	**0**	0	**0**	0	**0**	**1**
Immune	**0**	0	**0**	0	**0**	1	**0**	0	**0**	0	**0**	0	**0**	1
Infection*	**0**	0	**4**	4	**3**	2	**5**	3	**3**	6	**0**	2	**15**	**17**
Instruments breakage or malfunction preventing device placement	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0	**0**	**0**
Loss of bladder control	**0**	0	**0**	0	**0**	0	**0**	0	**0**	2	**0**	0	**0**	**2**
Loss of bowel control	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0	**0**	**0**
Multi-level DDD	**0**	0	**0**	0	**0**	0	**0**	0	**1**	0	**0**	0	**1**	0
Muscle damage	**0**	0	**1**	0	**0**	0	**0**	1	**0**	0	**0**	0	**1**	**1**
Musculoskeletal**	**1**	0	**29**	24	**12**	13	**20**	12	**32**	38	**14**	13	**108**	100
Myocardial Infarction	**0**	0	**1**	0	**0**	0	**2**	2	**1**	1	**1**	0	**5**	**3**
Nausea	**0**	3	**0**	0	**0**	0	**0**	0	**0**	1	**0**	0	**0**	**4**
Nerve root damage	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0	**0**	**0**
Neurological disorder	**0**	2	**6**	3	**2**	1	**6**	2	**10**	4	**3**	1	**27**	**13**
Ophthalmic	**2**	0	**3**	0	**0**	0	**3**	2	**1**	4	**1**	0	**10**	6
Osteolysis	**0**	0	**0**	0	**0**	0	**0**	1	**0**	0	**0**	0	**0**	1
Other***	**0**	2	**4**	3	**1**	0	**3**	3	**6**	2	**1**	0	**15**	**10**
Pain – Back	**0**	1	**14**	23	**12**	7	**8**	19	**14**	15	**8**	6	**56**	**71**
Pain - Back & Buttock	**0**	0	**0**	0	**0**	0	**0**	0	**1**	0	**0**	0	**1**	0
Pain – Back & Hip	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0	**1**	0	**1**	0
Pain - Back & Leg	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0
Pain - Buttock	**0**	0	**0**	1	**0**	0	**1**	1	**0**	0	**0**	0	**1**	2
Pain - Buttock & Groin	**0**	0	**7**	5	**2**	2	**4**	3	**8**	2	**2**	0	**23**	**12**
Pain - Buttocks and Hip	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0

Table 12: Counts of Specific Adverse Events by Time of Occurrence up to 24 Months (mITT cohort)

	Day of Surgery		Immed. Post-Op to Month 3 (Day 1-90)		>Mo. 3 to Mo. 6 (Day 91-180)		>Mo. 6 to Mo. 12 (Day 181-365)		>Mo. 12 to Mo. 24 (Day 365-730)		Post Month 24 (Day >730)		Totals	
	I[1]	C[2]	I	C	I	C	I	C	I	C	I	C	I	C
Pain - Hip	**0**	0	**1**	2	**0**	0	**0**	0	**0**	1	**1**	0	**2**	3
Pain – Leg	**1**	0	**12**	17	**6**	10	**7**	13	**12**	10	**2**	4	**40**	**54**
Peripheral Vascular Disorder	**0**	0	**0**	0	**0**	1	**0**	1	**0**	1	**0**	0	**0**	3
Pneumonia	**0**	0	**0**	0	**1**	1	**1**	1	**2**	2	**1**	1	**5**	**5**
Presence of osteophyte formation associated with severe disc or facet degeneration	**0**	0	**0**	0	**0**	0	**0**	0	**1**	0	**0**	1	**1**	**1**
Progression of underlying disease	**0**	0	**0**	0	**0**	0	**0**	0	**0**	1	**0**	0	**0**	1
Psychiatric/Substance abuse	**0**	0	**0**	1	**0**	1	**1**	0	**0**	1	**0**	1	**1**	4
Pulmonary edema	**0**	1	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0	**0**	**1**
Pulmonary embolism	**0**	0	**1**	0	**0**	0	**0**	0	**0**	0	**0**	0	**1**	**0**
Renal failure	**0**	0	**0**	0	**1**	0	**0**	0	**2**	1	**0**	0	**3**	**1**
Renal insufficiency	**0**	0	**0**	1	**0**	0	**1**	0	**0**	1	**1**	0	**2**	**2**
Respiratory disorder	**0**	3	**0**	0	**0**	1	**0**	0	**2**	0	**2**	0	**4**	**4**
Respiratory distress	**0**	0	**0**	0	**0**	0	**1**	0	**1**	0	**0**	0	**2**	**0**
Respiratory infection	**0**	0	**0**	0	**0**	0	**0**	0	**0**	1	**0**	1	**0**	**2**
Rheumatoid arthritis	**0**	0	**0**	0	**1**	0	**0**	0	**0**	0	**0**	0	**1**	**0**
Sensory loss	**0**	0	**1**	2	**1**	0	**1**	1	**0**	1	**0**	0	**3**	**4**
Shortness of breath	**0**	0	**0**	0	**0**	0	**0**	0	**0**	1	**0**	0	**0**	**1**
Skin and subcutaneous tissue	**0**	0	**1**	4	**0**	2	**0**	0	**0**	4	**1**	0	**2**	10
Soft tissue damage	**0**	0	**0**	0	**0**	2	**0**	1	**1**	2	**0**	2	**1**	**7**
Spinal stenosis symptoms associated with non-index condition	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0
Spinal stenosis symptoms at index level	**0**	0	**10**	10	**8**	5	**12**	7	**4**	12	**3**	4	**37**	**38**
Spinous process fracture	**4**	2	**13**	9	**3**	1	**2**	1	**1**	1	**1**	0	**24**	**14**
Stroke	**0**	0	**0**	0	**0**	1	**0**	0	**1**	0	**0**	0	**1**	**1**
Syncope	**0**	0	**0**	2	**0**	0	**0**	0	**0**	0	**0**	0	**0**	**2**
Synovial cyst	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0
Transient ischemic attack (TIA)	**0**	0	**0**	1	**0**	0	**0**	0	**0**	0	**0**	0	**0**	**1**
Urinary tract infection	**1**	1	**3**	1	**3**	0	**1**	1	**0**	3	**0**	0	**8**	**6**
Vertebral compression fractures	**0**	0	**0**	1	**0**	0	**1**	0	**0**	1	**0**	1	**1**	**3**
Wound dehiscence or delayed healing	**0**	0	**0**	1	**0**	0	**0**	0	**0**	0	**0**	0	**0**	**1**
Wound drainage	**0**	0	**0**	3	**0**	1	**0**	0	**1**	0	**0**	0	**1**	**4**

I[1] = Superion® ISS, C[2] = X-STOP® IPD®

*Infection AEs are defined as: including superficial infections and seroma at the surgical site, as well as infections at remote sites (e.g., sinus or throat infection)

**Musculoskeletal AEs are defined as: including weakness, cramping, joint pain, joint surgery or replacement, and other disorders in non-lumbar spinal tissues

***Other adverse events includes events not fitting a specific existing adverse event category, including insomnia, psychological disorder, weight loss, general weakness, ganglion cyst, and drug withdrawal.

Device-Related Adverse Events

The most frequent device-related adverse events were spinous process fractures, as noted in Table 13 below, which occurred in 7.9% of Superion® ISS patients and 2.5% of X-STOP® IPD® patients. There were no large numerical differences in the number of device-related adverse events, with the exception of Deep infection at the operative site, Device dislodgement, Device migration, Device subsidence, Spinal stenosis symptoms at index level, and Spinous process fractures. However, given the low incidences of the aforementioned device-related adverse events, it is difficult to draw conclusions regarding the clinical importance of these differences.

Table 13: Specific Device-Related Adverse Events in Superion® ISS IDE up to 24 months (mITT cohort)

	Superion® ISS (N=190)			X-STOP® IPD® (N=201)		
Adverse Event Type	**No. of Events**	**No. of Pts.**	**% of Pts.**	**No. of Events**	**No. of Pts.**	**% of Pts.**
Deep infection at the operative site	0	0	0.0	2	1	0.5
Device breakage	0	0	0.0	1	1	0.5
Device deformation preventing device placement	1	1	0.5	0	0	0.0
Device dislodgement	1	1	0.5	2	2	1.0
Device migration	1	1	0.5	5	5	2.5
Device subsidence	4	4	2.1	0	0	0.0
Dural leaks	1	1	0.5	0	0	0.0
Loss of bowel control	0	0	0.0	1	1	0.5
Pain - Back	1	1	0.5	0	0	0.0
Pain - Leg	1	1	0.5	0	0	0.0
Spinal stenosis symptoms at index level	0	0	0.0	3	3	1.5
Spinous process fracture	16	15	7.9	5	5	2.5

Procedure-Related Adverse Events

The most frequent procedure-related adverse events, as noted in Table 14 below, were spinous process fractures, which occurred in 7.9% of Superion® ISS patients and 2.5% of X-STOP® IPD® patients. There were no large numerical differences in the number of procedure-related adverse events, with the exception of Deep infection at the operative site, Device migration, Device subsidence, Dural leaks, Spinal stenosis symptoms at index level, Spinous process fracture and Wound drainage. However, given the low incidences of the aforementioned procedure-related adverse events, it is difficult to draw conclusions regarding the clinical importance of these differences.

Table 14: Specific Procedure- Related Adverse Events in Superion® ISS IDE up to 24 months (mITT cohort)

	Superion® ISS (N=190)			X-STOP® IPD® (N=201)		
Adverse Event Type	**No. of Events**	**No. of Pts.**	**% of Pts.**	**No. of Events**	**No. of Pts.**	**% of Pts.**
Coronary episode, ischemic	0	0	0.0	4	1	0.5
Deep infection at the operative site	0	0	0.0	3	2	1.0
Device deformation preventing device placement	1	1	0.5	0	0	0.0
Device dislodgement	1	1	0.5	1	1	0.5
Device migration	1	1	0.5	4	4	2.0
Device subsidence	2	2	1.1	0	0	0.0
Dural leaks	3	3	1.6	0	0	0.0
Fever	0	0	0.0	1	1	0.5
Genitourinary	1	1	0.5	2	2	1.0
Hematoma	0	0	0.0	1	1	0.5
Infection*	2	2	1.1	2	1	0.5
Nausea	0	0	0.0	1	1	0.5
Neurological disorder	0	0	0.0	1	1	0.5
Pain – Back	1	1	0.5	1	1	0.5
Pain – Leg	1	1	0.5	0	0	0.0
Skin and subcutaneous tissue	0	0	0.0	2	2	1.0
Spinal stenosis symptoms at index level	0	0	0.0	3	3	1.5
Spinous process fracture	18	17	8.9	7	7	3.5
Wound drainage	0	0	0.0	4	4	2.0

*Infection AEs are defined as: including superficial infections and seroma at the surgical site, as well as infections at remote sites (e.g., sinus or throat infection).

As noted in Tables 13 and 14 above, the adverse events as determined by the CEC demonstrated that the Superion® ISS patients experienced more device-related adverse events (Superion® ISS, 11.6%; X-STOP® IPD®, 7.5%), while X-STOP® IPD® patients experienced more procedure-related adverse events (Superion® ISS, 14.2%; X-STOP® IPD®, 15.9%).

Specific Adverse Events with More than a 2% Difference Between Treatment Groups

For additional clarity, specific adverse events where the difference between Superion® ISS and X-STOP® IPD® were more than 2% are shown in Table 15.

Table 15: Specific Adverse Events in Superion® IDE with > 2% Difference

	Superion® ISS (N=190)			X-STOP® IPD® (N=201)		
Adverse Event Type	**No. of Events**	**No. of Pts.**	**% of Pts.**	**No. of Events**	**No. of Pts.**	**% of Pts.**
Cardiovascular	25	20	10.5	20	16	8.0
Device migration	1	1	0.5	8	7	3.5
Device subsidence	4	4	2.1	0	0	0.0
Dizziness	5	5	2.6	0	0	0.0
Genitourinary	25	22	11.6	17	17	8.5
Musculoskeletal*	108	78	41.1	100	70	34.8
Neurological disorder	27	22	11.6	13	13	6.5
Other**	15	14	7.4	10	5	2.5
Pain – Back	56	50	26.3	71	66	32.8
Pain – Buttock & Groin	23	21	11.1	12	12	6.5
Pain – Leg	40	37	19.5	54	47	23.4
Skin and subcutaneous tissue	2	2	1.1	10	8	4.0
Soft tissue damage	1	1	0.5	7	7	3.5
Spinous process fracture	24	22	11.6	14	13	6.5

*Musculoskeletal AEs are defined as: including weakness, cramping, joint pain, joint surgery or replacement, and other disorders in non-lumbar spinal tissues

**Other adverse events includes events not fitting a specific existing adverse event category, including insomnia, psychological disorder, weight loss, general weakness, ganglion cyst, and drug withdrawal.

Serious Adverse Events

Serious adverse events occurred in 46.3% (88/190) of Superion® ISS patients compared with 45.8% (92/201) of X-STOP® IPD patients. A listing of the specific serious adverse events which occurred during this study is shown in Table 16 below.

Table 16: Specific Serious Adverse Events in Superion® ISS IDE up to 24 months (mITT cohort)

	Superion® (I) (N=190)			X-STOP® IPD® (C) (N=201)			I vs C[1]		
Adverse Event Type	**No. of Events**	**No. of Pts.**	**% of Pts.**	**No. of Events**	**No. of Pts.**	**% of Pts.**	**Diff**	**LB**	**UB**
Abdominal pain	1	1	0.5	0	0	0	-0.5	-10.4	9.4
Accidental injury	4	3	1.6	4	4	2	0.4	-9.5	10.3
Adjacent level DDD	1	1	0.5	1	1	0.5	0	-9.9	9.9
Adjacent level stenosis	0	0	0	3	2	1	1	-8.9	10.9
Allergic reaction	1	1	0.5	1	1	0.5	0	-9.9	9.9
Anemia	3	2	1.1	0	0	0	-1.1	-11	8.9
Angina	1	1	0.5	0	0	0	-0.5	-10.4	9.4
Cancer/Neoplasm	8	7	3.7	6	6	3	-0.7	-10.6	9.2
Cardiovascular	11	8	4.2	9	7	3.5	-0.7	-10.6	9.2
Cerebrovascular accident (CVA)	2	2	1.1	1	1	0.5	-0.6	-10.5	9.4
Coronary episode, ischemic	0	0	0	5	2	1	1	-8.9	10.9
Deep infection at the operative site	0	0	0	3	2	1	1	-8.9	10.9

Table 16: Specific Serious Adverse Events in Superion® ISS IDE up to 24 months (mITT cohort)

	Superion® (I) (N=190)			X-STOP® IPD® (C) (N=201)			I vs C[1]		
Adverse Event Type	**No. of Events**	**No. of Pts.**	**% of Pts.**	**No. of Events**	**No. of Pts.**	**% of Pts.**	**Diff**	**LB**	**UB**
Deep vein thrombosis	1	1	0.5	1	1	0.5	0	-9.9	9.9
Device Dislodgement	0	0	0	2	2	1	1	-8.9	10.9
Device Migration	1	1	0.5	4	3	1.5	1	-8.9	10.9
Device Subsidence	1	1	0.5	0	0	0	-0.5	-10.4	9.4
Dizziness	2	2	1.1	0	0	0	-1.1	-11	8.9
Dural leaks	6	6	3.2	2	2	1	-2.2	-12	7.8
Dyspnea	0	0	0	1	1	0.5	0.5	-9.4	10.4
Edema	0	0	0	1	1	0.5	0.5	-9.4	10.4
Fever	0	0	0	2	2	1	1	-8.9	10.9
Gastrointestinal	4	4	2.1	3	3	1.5	-0.6	-10.5	9.3
Gastrointestinal (GI) bleed	1	1	0.5	1	1	0.5	0	-9.9	9.9
Genitourinary	8	8	4.2	4	4	2	-2.2	-12.1	7.7
Hematoma	0	0	0	1	1	0.5	0.5	-9.4	10.4
Infection*	2	2	1.1	1	1	0.5	-0.6	-10.5	9.4
Musculoskeletal**	13	12	6.3	24	21	10.4	4.1	-5.8	14
Myocardial infarction	5	5	2.6	3	3	1.5	-1.1	-11	8.8
Nausea	0	0	0	2	2	1	1	-8.9	10.9
Neurological disorder	3	3	1.6	3	3	1.5	-0.1	-10	9.8
Other***	5	5	2.6	3	2	1	-1.6	-11.5	8.3
Pain - Back	8	8	4.2	13	13	6.5	2.3	-7.7	12.1
Pain - Buttock	1	1	0.5	0	0	0	-0.5	-10.4	9.4
Pain - Buttock & Groin	3	3	1.6	2	2	1	-0.6	-10.5	9.3
Pain - Hip	1	1	0.5	0	0	0	-0.5	-10.4	9.4
Pain - Leg	13	12	6.3	11	10	5	-1.3	-11.3	8.6
Peripheral Vascular Disorder	0	0	0	1	1	0.5	0.5	-9.4	10.4
Pneumonia	4	3	1.6	2	2	1	-0.6	-10.5	9.3
Presence of osteophyte formation associated with severe disc or facet degeneration	0	0	0	1	1	0.5	0.5	-9.4	10.4
Pulmonary edema	0	0	0	1	1	0.5	0.5	-9.4	10.4
Pulmonary embolism	1	1	0.5	0	0	0	-0.5	-10.4	9.4
Renal failure	3	3	1.6	1	1	0.5	-1.1	-11	8.8
Respiratory disorder	2	2	1.1	1	1	0.5	-0.6	-10.5	9.4
Respiratory distress	2	2	1.1	0	0	0	-1.1	-11	8.9
Respiratory infection	0	0	0	1	1	0.5	0.5	-9.4	10.4
Sensory loss	0	0	0	1	1	0.5	0.5	-9.4	10.4
Soft tissue damage	0	0	0	1	1	0.5	0.5	-9.4	10.4
Spinal stenosis symptoms at index level	21	20	10.5	16	15	7.5	-3.1	-13	6.9
spinous process fracture	11	10	5.3	5	5	2.5	-2.8	-12.7	7.2
stroke	1	1	0.5	0	0	0	-0.5	-10.4	9.4
Transient ischemic attack (TIA)	0	0	0	1	1	0.5	0.5	-9.4	10.4
Urinary tract infection	0	0	0	2	2	1	1	-8.9	10.9
Vertebral compression fracture	0	0	0	1	1	0.5	0.5	-9.4	10.4
Wound dehiscence or delayed healing	0	0	0	1	1	0.5	0.5	-9.4	10.4
Wound drainage	1	1	0.5	0	0	0	-0.5	-10.4	9.4

[1] Exact 95% confidence interval for the group difference.
*Infection AEs are defined as: including superficial infections and seroma at the surgical site, as well as infections at remote sites (e.g., sinus or throat infection)
**Musculoskeletal AEs are defined as: including weakness, cramping, joint pain, joint surgery or replacement, and other disorders in non-lumbar spinal tissues
***Other adverse events includes events not fitting a specific existing adverse event category, including insomnia, psychological disorder, weight loss, general weakness, ganglion cyst, and drug withdrawal.

Device- or Procedure-Related Serious Adverse Events

In regards to serious adverse events which were device- or procedure-related, X-STOP® IPD® patients exhibited a slightly higher rate of serious adverse events that were device- or procedure-related (X-STOP® IPD®: 9.5% (19/201), Superion® ISS: 8.4% (16/190)). These device- or procedure-related serious adverse events primarily occur the day of surgery through Month 3 postoperatively.

Table 17: Counts and Percentages of Serious Device or Procedure Related Adverse Events in Superion® ISS IDE up to 24 months (mITT cohort)

	Superion® (I) (N=190)			X-STOP® (C) (N=201)		
Adverse Event Type	**No. of Events**	**No. of Pts.**	**% of Pts.**	**No. of Events**	**No. of Pts.**	**% of Pts.**
Coronary episode, ischemic	0	0	0.0	4	1	0.5
Deep infection at the operative site	0	0	0.0	3	2	1.0
Device dislodgement	0	0	0.0	2	2	1.0
Device migration	1	1	0.5	2	2	1.0
Device subsidence	1	1	0.5	0	0	0.0
Dural leaks	3	3	1.6	0	0	0.0
Genitourinary	1	1	0.5	2	2	1.0
Hematoma	0	0	0.0	1	1	0.5
Infection*	1	1	0.5	0	0	0.0
Nausea	0	0	0.0	1	1	0.5
Pain – Back	1	1	0.5	0	0	0.0
Pain – Leg	1	1	0.5	0	0	0.0
Respiratory disorder	0	0	0.0	1	1	0.5
Spinal stenosis symptoms at index level	0	0	0.0	4	4	2.0
Spinous process fracture	11	10	5.3	5	5	2.5

*Infection AEs are defined as: including superficial infections and seroma at the surgical site, as well as infections at remote sites (e.g., sinus or throat infection)

Overall Conclusions from Review of Adverse Events

The overall adverse event rates of the Superion® ISS and X-STOP® IPD® cohorts subjects were similar, but there were differences in the types of adverse events. While the devices each had different associated adverse event rates associated with individual types of events (e.g., spinous process fracture or migration/dislodgement), the balance of these events, either severe or non-severe, and overall adverse event rate, were not preferential to one device or another. More specifically, Superion® ISS subjects experienced more device-related adverse events; as

compared with X-STOP® IPD® subjects who numerically experienced more procedure-related adverse events, although the differences were similar between the two groups. The data presented demonstrates a reasonable assurance of the safety of the Superion® ISS device compared to an approved device (X-STOP® IPD®) for the same intended patient population of moderate degenerative lumbar spinal stenosis.

Subsequent Surgical Interventions

A time course listing of subsequent surgical interventions is provided in Table 18 (Superion® ISS) and Table 19 (X-STOP® IPD®). In the modified intent-to-treat patient population (mITT) through 24 months (as part of the primary endpoint), there were a total of 38 reoperations or revisions in the Superion® ISS group (38/190, 20.0%) compared with 29 reoperations or revisions in the X-STOP® IPD® group (29/201, 14.4%). Reoperations and revisions in subjects prior to 24 months of treatment were considered to be failures in the primary endpoint.

In the modified intent-to-treat patient population (mITT) through the last available follow-up (included time points past 24 months) there were a total of 49 reoperations or revisions in the Superion® ISS group (49/190, 25.8%) compared with 44 reoperations or revisions in the X-STOP® IPD® group (44/201, 21.9%). The majority of reoperations and revisions were performed for pain adverse events (either back pain or leg pain, or combined back and leg pain). Similar numbers of subjects had decompression and device removal (Superion® ISS [13.7% (26/190)]; X-STOP® IPD® [11.4% (23/201)]), device removal and fusion (Superion® ISS [6.8% (13/190)]; X-STOP® IPD®[6.5% (13/201)]) and device removal (Superion® ISS [0.5% (1/190)]; X-STOP® IPD® [1.0% (2/201)]) between the 2 groups.

A higher percentage of Superion® ISS subjects had supplemental decompression (Superion® ISS [2.1% (4/190)]; X-STOP® IPD® [0.0% (0/201)]). Two (2) X-STOP® IPD® subjects had an intraoperative complication preventing implantation (1.0% - 2/201), compared with one (1) Superion® ISS patient (0.5% - 1/190). The primary reason for reoperation or revision in both Superion® ISS and X-STOP® IPD® subjects was related to continued pain.

Table 18: Reoperation and Revision Events in the Superion® ISS Arm – (mITT) Population

Superion® ISS, n=190										
Reoperation or Revision Type*	**Event Time Course (months)**								**Total (events)**	**Reasons**
	<1.5	**1.5-3**	**3-6**	**6-12**	**12-24**	**24-36**	**36-48**	**48-60**		
Decompression and Device Removal	-	3 (1.6%)	4 (2.1%)	8 (4.2%)	4 (2.1%)	7 (3.7%)	-	-	26 (13.7%)	20 leg and/or low back pain, 2 bone-related fracture, 2 neurological decline, 1 device deployment issue, 1 facet cyst
Device Removal and Fusion	1 (0.5%)	-	-	4 (2.1%)	5 (2.6%)	2 (1.1%)	1 (0.5%)	-	13 (6.8%)	9 leg and/or low back pain, 2 bone-related fracture, 1 neurological decline, 1 unknown
Device Removal	-	-	-	1 (0.5%)	-	-	-	-	1 (0.5%)	1 leg and/or low back pain
Fusion (no device removal)	-	-	-	1 (0.5%)	1 (0.5%)	1 (0.5%)	-	-	3 (1.6%)	2 leg and/or low back pain, 1 synovial cyst
Supplemental Decompression	-	-	2 (1.1%)	1 (0.5%)	1 (0.5%)	-	-	-	4 (2.1%)	3 leg and/or low back pain, 1 synovial cyst
I&D and Device Removal	1 (0.5%)	-	-	-	-	-	-	-	1 (0.5%)	1 dural tear
Intraoperative Failure	1 (0.5%)	-	-	-	-	-	-	-	1 (0.5%)	1 dural tear
Subtotal Events	3 (1.6%)	3 (1.6%)	6 (3.2%)	15 (7.9%)	11 (5.8%)	10 (5.3%)	1 (0.5%)	-	49 (25.8%)	

*Single patients may be listed in more than one category

Table 19: Reoperation and Revision Events in the X-STOP® IPD® Arm - (mITT) Population

X-STOP® IPD®, n=201										
Reoperation or Revision Type*	**Event Time Course (months)**								**Total (events)**	**Reasons**
	<1.5	**1.5-3**	**3-6**	**6-12**	**12-24**	**24-36**	**36-48**	**48-60**		
Decompression and Device Removal	1 (0.5%)	1 (0.5%)	3 (1.5%)	3 (1.5%)	8 (4.0%)	4 (2.0%)	2 (1.0%)	1 (0.5%)	23 (11.5%)	18 leg and/or low back pain, 3 device dislodgement, 1 neurological decline, 1 herniated disc
Device Removal and Fusion	-	-	-	1 (0.5%)	5 (2.5%)	5 (2.5%)	2 (1.0%)	-	13 (6.5%)	12 leg and/or low back pain, 1 bone-related fracture
Device Removal	-	-	-	1 (0.5%)	-	1 (0.5%)	-	-	2 (1.0%)	1 leg and/or low back pain, 1 bone-related fracture
Device Replacement	-	1 (0.5%)	-	1 (0.5%)	-	-	-	-	2 (1.0%)	2 leg and/or low back pain
Intraoperative Failure	2 (1.0%)	-	-	-	-	-	-	-	2 (1.0%)	2 bone-related fracture
Irrigation and Debridement	2 (1.0%)	-	-	-	-	-	-	-	2 (1.0%)	2 deep infection
Subtotal Events	5 (2.5%)	2 (1.0%)	3 (1.5%)	6 (4.0%)	13 (6.5%)	10 (5.0%)	4 (2.0%)	1 (0.5%)	44 (21.9%)	

*Single patients may be listed in more than one category

Additional Treatments (Epidurals, Rhizotomies and Spinal Cord Stimulators)

Following index surgery, 25 of the 190 (13.2%) Superion® ISS mITT subjects received an epidural steroid injection or nerve block at the level(s) of surgery prior to Month 24. In contrast, 33 of the 201 (16.4%) X-STOP® IPD® mITT subjects received an epidural steroid injection or nerve block at the level(s) of surgery prior to Month 24. All subjects who received an epidural steroid injection or nerve block at the level(s) of surgery prior to Month 24 were considered study failures.

Following index surgery, 0 of the 190 (0.0%) Superion® ISS mITT subjects received a rhizotomy at the level(s) of surgery prior to Month 24. One (1) of the 201 (0.5%) X-STOP® IPD® mITT subjects received a rhizotomy and was therefore considered a study failure. No subject in either group received a spinal cord stimulator at the level(s) of surgery through 24 months.

As shown in Table 20, in the immediate post-operative period (up to Week 6), 142 of the 190 (74.7%) Superion® ISS mITT subjects were treated with narcotics. 155 of the 201 (77.1%) X-STOP® IPD® mITT subjects were treated with narcotics during the immediate post-operative period. Narcotic use declined following the immediate post-operative period with 64 of the 190 (33.6%) Superion® ISS mITT subjects using narcotics during the Week 6 through Month 24 time period. Similarly, 61 of the 201 (30.3%) X-STOP® IPD® mITT subjects were treated with narcotics during the Week 6 through Month 24 period. At all time-points, narcotic use was increased in subjects with pre-existing orthopedic or musculoskeletal comorbidities. Narcotic use was not a study failure criterion.

Table 20: Narcotic Use

	Superion® ISS	**X-STOP® IPD®**
Immediate Post-Operative Period (up to Week 6)	74.7% (142/190)	77.1% (155/201)
Week 6 to Month 24	33.6% (64/190)	30.3% (61/201)

Surgery and Hospitalization Data

The operative details from the IDE subjects are shown in Table 21 and Table 22. The Superion ISS was implanted via a minimally-invasive or “mini-open” approach, compared to X-STOP® IPD® which was implanted via an open approach. As expected, Table 21 shows that mean blood loss was numerically greater with the X-STOP® IPD® device, likely due to the surgical approach. Operative time, however, was numerically greater in the Superion® ISS group.

Table 21: Perioperative Results from Superion® ISS IDE (mean ± SD)

Operative Detail	Superion® ISS (n=190)	X-STOP® IPD® (n=200)
Blood Loss (cc)	13.5 ± 15.9	38.7 ± 43.8
Hospital Length of Stay (days)	1.80 ± 1.5	1.90 ± 1.5
Operative Time (min)	56.3 ± 26.8	47.2 ± 18.8

Repair of the supraspinous ligament was performed in approximately half of the Superion® ISS group. This procedure was not performed in any of the X-STOP® IPD® group. As shown in Table 22, additional procedures which could be interpreted as decompression procedures (e.g., facet debulking, osteophyte removal, soft tissue removal), were performed in 11 levels in 9 Superion® ISS subjects and 16 levels in 12 X-STOP® IPD® subjects.

Table 22: Operative Variables from the Superion® ISS Clinical Trial (mITT cohort)

	Superion® ISS		X-STOP® IPD®	
	n	**%**	**n**	**%**
Number of Subjects Treated	189		199	
Subjects Attempted / Not Implanted	1	8.4	2	3.7
Number of Levels Treated	n	%	n	%
1	99	52.4	99	49.7
2	90	47.6	100	50.3
One Level Treated	**n**	**%**	**n**	**%**
L1-L2	1	1.0	0	0.0
L2-L3	0	0.0	5	5.1
L3-L4	7	7.1	9	9.1
L4-L5	91	91.9	85	85.9
Two Levels Treated	**n**	**%**	**n**	**%**
L1-L2/L2-L3	2	2.2	1	1.0
L2-L3/L3-L4	8	8.9	7	7.0
L2-L3/L4-L5	0	0.0	1	1.0
L3-L4/L4-L5	80	88.9	91	91.0
L4-L5/L5-S1	0	0.0	0	0.0
Anesthesia Type (all patients)	**n**	**%**	**n**	**%**
General	156	82.1	179	89.1
Conscious IV Sedation	25	13.2	18	9.0
Local	14	7.4	11	5.5
Surgical Approach (as treated patients by level)	**n**	**%**	**n**	**%**
Percutaneous	131	46.8	0	0.0
Mini-Open	149	53.2	0	0.0
Open	0	0.0	299	100.00
Device Size (as treated patients by level)	**n**	**%**	**n**	**%**
6 mm (X-STOP® IPD® only)	N/A	N/A	2	0.7
8 mm	2	0.7	9	3.0
10 mm	36	12.9	71	23.8
12 mm	95	33.9	131	43.8
14 mm	117	41.8	79	26.4
16 mm (Superion®)	30	10.7	7	2.3
Supraspinous Ligament sutured? (AT by level)	**n**	**%**	**n**	**%**
Yes	130	46.4	N/A	N/A
No	150	53.6	N/A	N/A

Table 22: Operative Variables from the Superion® ISS Clinical Trial (mITT cohort)

	Superion® ISS		X-STOP® IPD®	
	n	%	n	%
Additional Procedure (as treated patients by level)	**n**	**%**	**n**	**%**
Any additional procedures	11	3.9	16	5.4
Facet(s) debulking	0	0.0	2	0.7
Osteophyte removal	3	1.1	3	1.0
Soft tissue removal	6	2.1	13	4.4
Laminectomy / wide decompression	0	0.0	1	0.3
Other	2	0.7	1	0.3

Radiographic Data Potentially Related to Safety

Radiographic observations were reported in the Superion® ISS IDE based on independent radiographic review of all radiographs. The overall incidence of radiographic observations is presented in Table 23.

Following index surgery through 24 months, 31 of the 190 (16.3%) Superion® ISS mITT subjects had a spinous process fracture identified by the radiographic core lab. In contrast, 17 of the 201 (8.5%) X-STOP® IPD® mITT subjects had a spinous process fracture through 24 months. By 24 months, healed fractures were noted (as determined by independent radiographic review) in 10 of the 31 Superion® ISS subjects (32.3%) and 7 of the X-STOP® IPD® subjects (41.2%). In addition, 24 of the 201 (11.9%) X-STOP® IPD® subjects had a device dislodgement or migration, as reported by independent radiographic assessment. These results are outlined in Table 23. In contrast, none of the Superion® ISS subjects exhibited device dislodgement or migration, using the same assessment standards. In contrast to the X-STOP® IPD®, once placed, the Superion® ISS appeared to retain its postoperative position between the spinous processes.

Table 23: Subjects with Radiographic Observations in the Superion® IDE

Radiographic Observation	Superion® ISS (n=190)		X-STOP® IPD® (n=201)	
	N	%	n	%
Spinous Process Fracture (any time)	31	16.3%	17	8.5%
Spinous Process Fracture (non-healed at 24 months)	21	11.1%	10	5.0%
Device Migration (>5mm)	0	0.0%	13	8.0%
Device Dislodgement	0	0.0%	20	10.0%
Any Radiographic Observation (any time)	31	16.3%	34*	16.9%
Any Radiographic Observation (24 months)	21	11.1%	28	13.9%

*Significant overlap was present in X-STOP® IPD® subjects having spinous process fractures, device migration, and device dislodgement.

It should be noted that the study demonstrated a discrepancy between spinous process fractures as determined by the investigators (investigational group - 13; control group - 10), by the radiographic core lab (investigational group - 31; control group - 17), and by the CEC (investigational group - 24; control group - 14) as shown below in Table 24. The results from independent radiographic review were used in the final Clinical Composite Success (CCS)

analysis and are also shown in Table 24 below. The applicant has explained the discrepancy between site reported observations, observations by the CEC, and observations by the radiographic core lab by stating that the radiographic core lab was equipped with more sensitive imaging equipment and some of the fractures were asymptomatic. The applicant has provided an analysis of ZCQ, ODI, and VAS (Leg and Back) scores at 24 months in support of this statement (see Table 28 below). The core laboratory determined that 21 investigational and 10 control fractures remained unhealed at 24 months.

Table 24: Fracture Identification and Reporting in the Superion® IDE

Number of Spinous Process Fractures According to Reporting Method	Training Cohort		Superion® ISS mITT Cohort		X-STOP® IPD® mITT Cohort	
	Events	Subjects	Events	Subjects	Events	Subjects
Adverse Events						
Site Reported*	0	0	13	11	10	9
CEC Adjudicated**	3	3	24	22	14	13
Independent Radiographic Review	6	6	31	31	17	17
Non-Healed Fractures (M24)***	2	2	21	21	10	10

*Site reported fractures are those adverse events originally placed in the "spinous process fracture" category by the investigators.
**Note that the CEC had access to the results of the independent radiographic review as reported by the Radiology Core Laboratory and re-categorized several adverse events as spinous process fractures.
***Incidences of non-healed fractures at 24 months post index procedure as determined by the Radiology Core Laboratory.

Spinous process fractures observed via independent radiographic review were further characterized by the timing of fracture diagnosis on imaging studies. The time course of spinous process fractures in both treatment groups is shown in Table 25. As demonstrated in Table 25 below, the majority of spinous process fractures in both treatment groups were observed within 6 weeks of device implantation. In addition, 4/31 (12.9%) of Superion® ISS subjects and 1/17 (5.9%) X-STOP® IPD® subjects with fractures had an observation of fracture in the immediate post-operative x-ray.

Table 25: Time Course of Spinous Process Fractures in Superion® ISS & X-STOP® IPD® Patients

	Post-op	Week 6	Month 3	Month 6	Month 12	Month 18	Month 24	Total
Superion® ISS	4	23	3	-	1	-	-	31
X-STOP® IPD®	1	13	2	1	-	-	-	17
Superion® ISS	30/31 (96.7%) btw 0-3 months			1/31 (3.2%) btw 6-24 months				
X-STOP® IPD®	16/17 (94.1%) btw 0-3 months			1/17 (5.8%) btw 6-24 months				

Table 26 and Table 27 provide additional details regarding the characteristics of the spinous process fractures. The majority of fractures in the Superion® ISS group were located in continuity with the device, while those in the X-STOP® IPD® group were located anterior to the device. Specifically, in the Superion® ISS group, a majority of the fractures (80.6%) present were coincident or in contact with the device, while in the X-STOP® IPD® group, a majority of the fractures (70.6%) were present anterior to the location of the device. Healing (Table 26) was observed at 24 months at a higher rate in fractures that were anterior to the device (Superion® ISS [50.0% (2/4)]; X-STOP® IPD® [50.0% (6/12)]) compared with those fractures coincident with the device (Superion® ISS [28.0% (7/25)]; X-STOP® IPD® [20.0% (1/5)]).

Table 26: Fracture Healing by Location

Device	Coincident with Device			Anterior to Device		
	n	% of Fractures	% Healed by 24M	n	% of Fractures	% Healed by 24M
Superion® ISS[1]	25	80.6%	28.0% (7/25)	4	12.9%	50.0% (2/4)
X-STOP® IPD®	5	29.4%	20.0% (1/5)	12	70.6%	50.0% (6/12)

[1] Location of spinous process fracture information was not available for 2 Superion® ISS subjects with fractures

The majority of fractures in both Superion® ISS [83.9% (26/31)] and X-STOP® IPD® [88.2% (15/17)] groups were displaced fractures (Table 27). A displaced fracture was defined by the applicant as no contact between the fragment and the remaining vertebra with at least a 2mm wide gap at some point along the fracture gap. However, the applicant notes that healing of the displaced fractures was observed in a subset of patients. Healing of displaced spinous process fractures was noted in 23.1% (6/26) of Superion® ISS subjects and 40.0% (6/15) of X-STOP® IPD® subjects.

Table 27: Fracture Healing in Subjects with Displaced and Non-displaced Fractures

Device	Displaced Fractures			Non-Displaced Fractures		
	n	% of Fractures	% Healed by 24M	n	% of Fractures	% Healed by 24M
Superion® ISS[1]	26	83.9%	23.1% (6/26)	3	9.6%	100.0% (3/3)
X-STOP® IPD®	15	88.2%	40.0% (6/15)	2	11.8%	50.0% (1/2)

[1] Displacement of spinous process fracture information was not available for 2 Superion® ISS subjects with fractures

Clinical outcomes were also correlated with the presence of spinous process fractures identified by the independent radiographic core lab, as reported in Table 28 below. When reviewing the possible clinical sequelae of spinous process fractures, there were no notable differences demonstrated in ZCQ, ODI, VAS Back pain, VAS Leg pain, and SF-12 in either the Superion® ISS or X-STOP® IPD® groups, as compared to patients in each group that were not diagnosed with a spinous process fracture. These results are shown in Table 28 below.

Table 28: Clinical Outcome Measurements Stratified by Presence or Absence of Spinous Process Fracture at Any Time Point, 24 Months (mITT cohort)

24 Month Clinical Outcomes	Superion® ISS		X-STOP® IPD®	
	Fracture	No Fracture	Fracture[1]	No Fracture
Pain				
VAS Back: ≥20mm decrease	78.3% (18/23)	64.8% (70/108)	46.2% (6/13)	70.8% (85/120)
VAS Leg (Worse): ≥20mm decrease	73.9% (17/23)	75.9% (82/108)	69.2% (9/13)	78.3% (94/120)

24 Month Clinical Outcomes	Superion® ISS		X-STOP® IPD®	
	Fracture	No Fracture	Fracture[1]	No Fracture
Back & Stenosis-Related Outcomes				
ZCQ Physical Function: ≥0.5 point decrease	73.9% (17/23)	72.2% (78/108)	76.9% (10/13)	80.8% (97/120)
ZCQ Symptom Severity: ≥0.5 point decrease	78.3% (18/23)	76.9% (83/108)	69.2% (9/13)	81.7% (98/120)
ZCQ Patient Satisfaction ≤2.5 points	73.9% (17/23)	86.1% (93/108)	84.6% (11/13)	92.5% (111/120)
ODI: ≥15 point decrease	65.2% (15/23)	63.0% (68/108)	61.5% (8/13)	67.5% (81/120)

[1]Subjects in the fracture group for X-STOP® include those subjects who had an incidence of both spinous process fracture and migration and/or dislodgement.

Additional treatments were also assessed for subjects with and without spinous process fractures (Table 29). Superion® ISS subjects and X-STOP® IPD® subjects presenting with spinous process fractures had lower re-operation and epidural injection rates compared to subjects without fractures. These data demonstrate that subjects observed to have a spinous process fracture by the independent radiographic lab required an additional treatment at a lower rate than study subjects without spinous fractures. These results, coupled with the clinical outcomes presented in Table 28, suggest that some of these spinous process fractures may have been asymptomatic.

Table 29: Additional Treatments Stratified by Presence or Absence of Spinous Process Fracture at Any Time Point, 24 Months

Treatment Type	Superion® ISS		X-STOP® IPD®	
	Fracture	No Fracture	Fracture	No Fracture
Reoperation or Revision	12.9% (4/31)	21.4% (34/159)	11.8% (2/17)	14.7% (27/184)
Epidural Steroid Injection or Nerve Root Block	12.9% (4/31)	13.2% (21/159)	17.6% (3/17)	16.3% (30/184)
Overall Additional Treatment*	**19.4% (6/31)**	**27.7% (44/159)**	**23.5% (4/17)**	**27.7% (51/184)**

*Subjects could have both a reoperation and injection during follow-up.

Neurologic Status Outcomes

Neurologic success was defined as maintenance or improvement in neurological status as assessed by motor, sensory and deep tendon reflex examination. The rate of neurologic failures was similar for both Superion® ISS and X-STOP® IPD® groups. The Superion® ISS patient population had seven (7) patients (3.7%) that developed new or worsening persistent motor or sensory neurologic assessments at 24 months, while the X-STOP® IPD® population had five (5) failures (2.5%) as shown in Table 30 below. The applicant also provided an analysis of ZCQ scores at 24 months for these patients. Only one Superion® ISS patient that was a neurologic failure was also a ZCQ failure.

Table 30: Neurological Outcome Failures in the Superion® IDE Trial (mITT Patient Population)

Type of Neurological Failure	Superion® ISS		X-STOP® IPD®	
	n	%	n	%
Motor Failure	3	1.6	3	1.5
Sensory Failure	3	1.6	1	0.5
Motor & Sensory Failure	1	0.5	1	0.5

2. Effectiveness Results

The analysis of effectiveness was based on the 391 evaluable subjects at the 24-month time point. Key effectiveness outcomes are presented in Tables 31 to 37.

Primary Effectiveness Analysis

The primary composite endpoint, termed Composite Clinical Success (CCS), was developed to measure the safety and effectiveness of the Superion® ISS when compared to X-STOP® IPD® for the treatment of moderate degenerative lumbar spinal stenosis. This primary composite success measurement at 24 months included measurements of clinical efficacy (ZCQ Success), absence of subsequent treatments (e.g., epidurals, rhizotomy, and spinal cord stimulators), neurological success, safety (absence of device revision or removal), and absence of implant or procedure-related complications (absence of dislodgement, migration, spinous process fracture, or serious device-related adverse events).

As demonstrated in Table 31, non-inferiority of Superion® ISS was established in the primary effectiveness cohort with a Bayesian Posterior Probability > 0.958 (as described in the Statistical Analysis Plan), in the mITT cohort that included all subjects with an anesthesia start time in the Superion® ISS IDE. Further, the demonstration of non-inferiority in the Per Protocol cohort provides confirmation of the non-inferiority result of the Superion® ISS IDE and demonstrates the robustness of the overall statistical determination.

Table 31: Composite Clinical Success in Superion® ISS IDE at 24 months

	Number and Percentage Achieving Month 24 Overall Success						Posterior Probability of Non-Inferiority
	Superion® ISS			X-STOP® IPD®			
Analysis Cohort	N	n	%	N	n	%	
mITT[1]	183	95	52.7%	187	93	50.2%	0.9927
Per Protocol	173	92	53.1%	178	88	49.4%	0.9944

[1]As described in the statistical analysis plan, missing data for the posterior probability were handled using Bayesian multiple imputation methodologies. The %'s, as well as the posterior probability reported for the Bayesian multiple imputation (MI) are based on the mean over 5000 multiple imputations. The (SD's) over multiple imputations for these estimates were 52.7% (0.6%), 50.2% (0.9%), and 0.9927 (0.4%), respectively. The reported N and n values for this row reflect only the numbers of patients with complete Month 24 CCS. All

190 Superion® ISS and 201 X-STOP® IPD® patients were included in the primary analysis using Bayesian multiple imputation.

Table 32 shows the success rates for each of the individual components of the CCS for the mITT patient population at 24 months. As seen in Table 32, the Superion® ISS demonstrates greater than 80% success in each individual sub-component of the CCS.

Table 32: Primary Endpoint Component Success (mITT Patient Population)

	Component Success	
	Superion® ISS	**X-STOP® IPD®**
Clinical Success (2/3 ZCQ Domains)	81.7% (107/131)	87.2% (116/133)
No Re-operations & Revisions	80.0% (152/190)	86.6% (174/201)
No Major Related Complications	86.3% (164/190)	82.6% (166/201)
No Confounding Additional Treatments	86.8% (165/190)	83.1% (167/201)

Table 33 lists the specific elements of the individual component results of the CCS at 24 months, resulting in an overall success rate of 51.9% for Superion® ISS and 49.7% for X-STOP® IPD® in the "completers" population.

Table 33: Superion® ISS and X-STOP® IPD® mITT Analysis Set - Descriptive Comparisons of the Percentages of Subjects Achieving CCS Component Success

	Number and Percentage Meeting Criteria					
	Superion® ISS			X-STOP® IPD®		
	N	n	%	N	n	%
(1) ZCQ Responder (at least two of three ZCQ domains)	**131**	**107**	**81.7**	**133**	**116**	**87.2**
Improvement in physical function by ≥ 0.5 points	131	95	72.5	133	107	80.5
Improvement in symptom severity by ≥ 0.5 points	131	101	77.1	133	107	80.5
Mean satisfaction ≤ 2.5 points (1=very sat., 2=somewhat sat., 3=somewhat dis, 4=very dis.)	131	110	84.0	133	122	91.7
(2) No re-operations, revisions, removals or supplemental fixation at the index level(s) (Up to Day 730)	**190**	**152**	**80.0**	**201**	**174**	**86.6**
(3) No major device- or procedure-related complications defined as:	**190**	**164**	**86.3**	**201**	**166**	**82.6**
Failure from dislodgement or migration at any time	190	190	100.0	201	177	88.1
New or persistent worsened neurological deficit at the index level	150	143	95.3	157	152	96.8
Spinous process fractures at the index level(s)	190	169	88.9	201	191	95.0
Deep infection at the operative site requiring hospitalization, surgical draining, or IV antibiotics	190	190	100.0	201	199	99.0
Death or other permanent disability attributed to the device	190	190	100.0	201	201	100.0
(4) No clinically significant confounding treatments:	**190**	**165**	**86.8**	**201**	**167**	**83.1**
No epidural injections or nerve block procedures to treat spinal stenosis symptoms at the index level(s) at any time	190	165	86.8	201	168	83.6
No spinal cord stimulators or rhizotomies	190	190	100.0	201	200	99.5
Composite Clinical Success	**183**	**95**	**51.9**	**187**	**93**	**49.7**

Zurich Claudication Questionnaire

For the components of ZCQ, both treatments improved symptoms; however, the Superion® ISS device demonstrated slightly less improvement compared to the X-STOP® IPD®. Immediate relief of clinical symptoms was seen in the three ZCQ domains with improvement maintained through 24 months. These findings were not nominally significant.

Reoperations, Removals, Revisions, or Supplemental Fixation

For the component of "no re-operations, removals, revisions, or supplemental fixation at the index level(s)," in the modified intent-to-treat patient population, through 24 months (as part of the primary endpoint), there were a total of 38 reoperations or revisions in the Superion® ISS group (38/190, 20.0%) compared with 29 reoperations or revisions in the X-STOP® IPD® group (29/201, 14.4%).

Beyond 24 months, there were a total of 49 reoperations or revisions in the Superion® ISS group (49/190, 25.8%) compared with 44 reoperations or revisions in the X-STOP® IPD® group (44/201, 21.9%) through the last available follow-up, which included time points past 24 months for many patients. Reoperations and revisions in patients prior to day 730 of treatment were considered to be failures in the primary endpoint although there was an increased number of reoperations and revisions in the X-STOP® IPD® arm, vs. the Superion® ISS arm, at time points after 2 years.

Implant-and Procedure-Related Complications

For the component of dislodgement, migration or deformation, 24 of the 201 (11.9%) X-STOP® IPD® mITT subjects had a device dislodgement or migration, and none of the Superion® ISS subjects experienced this type of event. In terms of spinous process fractures that were considered CCS failures, 21 of the 190 (11.1%) Superion® ISS mITT subjects had a spinous process fracture that did not heal by Month 24. In contrast, 10 of the 201 (5.0%) X-STOP® IPD® mITT subjects had a spinous process fracture that did not heal by the 24-month time point.

The rate of neurologic failures was similar for both Superion® ISS and X-STOP® IPD® groups. The Superion® ISS patient population had seven (7) failures (3.7%) that had new or worsening persistent motor or sensory neurologic assessments, while the X-STOP® IPD® population had five (5) failures (2.5%) of these criteria.

Clinically Significant Confounding Treatments

Following index surgery, 0 of the 190 (0.0%) Superion® ISS mITT subjects received a rhizotomy at the level(s) of surgery prior to Month 24. In contrast, 1 of the 201 (0.5%) X-STOP® IPD® mITT subjects received a rhizotomy and was therefore considered a study failure. No subject in either group received a spinal cord stimulator at the level(s) of surgery prior to Month 24. Following index surgery, 25 of the 190 (13.2%) Superion® ISS mITT subjects received an epidural steroid injection or nerve block at the level(s) of surgery prior to month 24 and were considered study failures as a result. In contrast, 33 of the 201 (16.4%) X-STOP® IPD® mITT subjects received an epidural steroid injection or nerve block at the level(s) of surgery prior to Month 24.

Additional Stratified Outcomes

As the device was indicated for one- or two-level treatments, additional analyses were performed stratifying CCS results by level implanted and number of levels. Non-inferiority of the Superion® ISS device was also demonstrated comparing the results of one- and two-level procedures.

Secondary Effectiveness Analysis

The secondary endpoints included ODI, VAS (Back and Leg), SF-12 Short Form Survey (Physical Function and Mental Health), and an applicant-derived patient satisfaction survey (VertiFlex® Patient Satisfaction Survey).

Analysis of secondary clinical endpoints demonstrated similar trends in both the Superion® ISS and X-STOP® IPD® cohorts (Table 34). In general, the Superion® ISS demonstrated improvement in pain and function as measured with ODI, and less pain as measured through

VAS. The similarities in clinical endpoint outcomes between groups further demonstrate the similar effectiveness of the Superion® ISS device to the control X-STOP® IPD® device. Even when investigating each demographic population, no substantial trends could be found that would demonstrate greater effectiveness of one device over the other.

Table 34: Superion® ISS and X-STOP® IPD® Control mITT Analysis Set- Secondary Endpoint Successes at 24 Months

	Number and Percentage Meeting Criteria					
	Superion® ISS			X-STOP® IPD®		
	N	n	%	N	n	%
Improvement of at least 15 pts in ODI	131	83	63.4	133	89	66.9
Improvement of at least 20mm on leg pain (worst) VAS	131	99	75.6	133	103	77.4
Improvement of at least 20mm on back pain VAS	131	88	67.2	133	91	68.4
Maintenance or improvement of SF-12 PCS	128	103	80.5	133	119	89.5
Maintenance or improvement of SF-12 MCS	128	77	60.2	133	89	66.9

ODI mean scores demonstrated an improvement in ODI of at least 15 points in both the Superion® ISS and X-STOP® IPD® by 3 months. This improvement was maintained through 24 months. Improvement in mean VAS Back pain score was demonstrated at 6 weeks. Similarly mean VAS leg (worse) scores also improved by 3 months and maintenance of this improvement was maintained through 24 months. These improvements in pain and function are considered clinically meaningful. In particular, the improvement in leg pain may be significant to patients and their treating physicians as this symptom is a component of intermittent neurogenic claudication. The data does not, however, demonstrate that this improvement in pain and function is maintained with motion and walking.

As shown in Table 35 and Table 36 below, both the SF-12 Physical Component Summary scores and Mental Health Component Summary scores increased by 3 months and improvement was maintained through 24 months.

Table 35: Time Course of Percentage of Subjects Maintaining or Improving SF-12 Physical Function Component (mITT Patient Population)

	Number and Percentage Meeting Criteria					
	Superion®			X-STOP®		
	N	n	%	N	N	%
Week 6	180	143	79.4%	193	163	84.5%
Month 3	169	140	82.8%	180	155	86.1%
Month 6	164	131	79.9%	177	153	86.4%
Month 12	143	121	84.6%	161	141	87.6%
Month 18	130	110	84.6%	137	124	90.5%
Month 24	128	103	80.5%	133	119	89.5%

Table 36: Time Course of Percentage of Subjects Maintaining or Improving SF-12 Mental Health Component (mITT Patient Population)

	Number and Percentage Meeting Criteria					
	Superion			X-STOP		
	N	n	%	N	N	%
Week 6	180	102	56.7%	193	134	69.4%
Month 3	169	101	59.8%	180	120	66.7%
Month 6	164	89	54.3%	177	116	65.5%
Month 12	143	86	60.1%	161	108	67.1%
Month 18	130	68	52.3%	137	96	70.1%
Month 24	128	77	60.2%	133	89	66.9%

Patient satisfaction was measured using a questionnaire (Table 37). At 24 months, 86.2% of subjects in the Superion® ISS group and 88.5% of subjects in the X-STOP® IPD® group were "Satisfied" or "Somewhat Satisfied." Also, 82.9% of Superion® ISS patients vs. 84.1% of X-STOP® IPD® patients answered "Definitely Yes" or "Probably Yes" to whether they would have the same treatment again.

Table 37: Patient Satisfaction at Month 24 by Treatment Group - mITT Analysis Set

	Superion® ISS		X-STOP® IPD®	
How satisfied were you with your treatment?	**n**	**%**	**n**	**%**
Satisfied	114	75.0	123	78.3
Somewhat Satisfied	17	11.2	16	10.2
Somewhat Dissatisfied	0	0.0	0	0.0
Dissatisfied	21	13.8	18	11.5
Would you have the same treatment again?	**n**	**%**	**n**	**%**
Definitely yes	96	63.2	108	68.8
Probably yes	30	19.7	24	15.3
Probably no	14	9.2	16	10.2
Definitely no	12	7.9	9	5.7

Overall, there was a trend toward slightly better effectiveness outcomes for the X-STOP® IPD® in the secondary endpoints at 24 months; but the results remained comparable between the two groups.

Radiographic Analysis

Additional Radiographic Assessments

The additional radiographic effectiveness assessments measured by the radiographic core lab were:

- Range of Motion
- Translation
- Disc Angle
- Anterior Disc Height
- Posterior Disc Height
- Spinous Process Distance
- Foraminal Height
- Spondylolisthesis Progression

Range of Motion

The applicant presented data regarding the range of motion (ROM) arc over time. The quantitative ROM data is presented below in Table 38. The ranges of motion between the 2 study arms are comparable. There is minimal change in ROM over time in either treatment group, and the applicant characterizes the data as maintenance of motion. The applicant states that the investigational device functions by extension blockage; however, data separating flexion from extension was not captured in the study, thus the data is not clear in determining if this was achieved.

Table 38: Flexion Extension - Rotation (F to E) (deg), Superion® and X-STOP® mITT Analysis Sets

	Superion® ISS			X-STOP® IPD®		
	At level(s) of Implant (per level)					
	N	Mean	SD	N	Mean	SD
Pre-Op	274	4.41	3.47	288	4.60	3.39
Month 24	216	3.37	3.08	222	3.78	3.11

Translation

The applicant presented data regarding the translational motion (flexion to extension) over time. The quantitative translational motion data is presented below in Table 39. The ranges of motion between the 2 study arms are comparable. There is minimal change in translational motion over time in either treatment group, and the applicant characterizes the data as maintenance of motion. Data separating flexion from extension was not captured in the study.

Table 39: Translation (F to E) (mm), Superion® and X-STOP® mITT Analysis Sets

	Superion® ISS			X-STOP® IPD®		
	At level(s) of Implant (per level)					
	N	Mean	SD	N	Mean	SD
Pre-Op	270	1.00	0.87	288	1.05	0.90
Month 24	215	0.98	0.90	220	1.02	0.97

Disc Angle

In terms of disc angle, the changes from the pre-operative disc angle measurements are nominally significant at every time point from post-operative through 24 months, as shown in Table 40. At every time point, the changes were smaller in the Superion® ISS group. This is consistent with other radiographic data that suggest the X-STOP® IPD® devices are designed with an oval shape; thereby affecting distraction. The applicant states that the radiographic data suggests the larger distraction caused by the X-STOP® IPD® devices reduces the disc angle. In other words, the natural lordosis present at the pre-operative evaluation decreases when the spinous process distance increases.

Table 40: Static Alignment Disc Angle (deg) - Superion® ISS and X-STOP® IPD mITT Analysis Sets

	Superion® ISS						X-STOP® IPD®					
	At level(s) of Implant (per level)											
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max
Pre-Op	279	9.23	4.59	9.3	-4.7	21.8	296	9.5	4.32	9.3	-2.9	21.4
Post-Op	270	5.09	4.25	5.1	-5.5	19.1	289	4.41	3.92	4.1	-5.9	14.3
Week 6	269	8.1	4.44	8.3	-3.8	19.6	293	6.96	4.52	6.7	-6.2	20.7
Month 3	251	8.18	4.46	8.3	-4.4	19	287	7.45	4.48	7.3	-5.3	21.2
Month 6	257	8.57	4.47	8.9	-6.4	19.7	279	7.67	4.42	7.3	-4.8	20.9
Month 12	242	8.68	4.46	8.9	-8.4	20.7	266	7.75	4.58	7.8	-4.2	21.4
Month 18	221	8.6	4.57	8.8	-5.4	20.2	243	7.89	4.6	7.9	-4.8	21.3
Month 24	218	8.39	4.54	8.4	-4.9	19.6	222	7.8	4.68	7.6	-5.1	20.7

Anterior Disc Height

The applicant presented data regarding the anterior disc height over time. The quantitative anterior disc height data is presented below in Table 41. Anterior disc height changes from the pre-operative measurements at the index level are nominally different at 6 weeks through 18 months in both treatment groups. At each time point, the X-STOP® IPD® group had a larger decrease in anterior disc height.

Table 41: Anterior Disc Height (mm) - Superion® ISS and X-STOP® IPD mITT Analysis Sets

	Superion® ISS						X-STOP® IPD®					
	At level(s) of Implant (per level)											
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max
Pre-Op	275	10.6	3.23	10.9	1.1	19.8	296	10.6	3.04	11	2.7	18.1
Post-Op	266	9.7	3.09	9.9	1.8	19.4	287	9.5	2.9	9.8	1.4	16
Week 6	267	10.2	3.17	10.3	1.6	18.5	293	9.8	3.1	10	0.8	17.2
Month 3	249	10.1	3.15	10.2	1.6	18.4	285	9.9	3.13	10.3	0.4	17.3
Month 6	256	10.1	3.12	10.4	0.7	18	277	9.9	3.14	10.1	0.6	17.5
Month 12	241	9.9	3.15	10.2	0.1	16.4	264	9.8	3.19	10.2	0.1	16.4
Month 18	220	9.8	3.21	10	0.7	16.9	241	9.7	3.3	10	0	16
Month 24	217	9.5	3.26	9.7	0.5	16.6	220	9.6	3.28	10	0	16.2

Posterior Disc Height

The applicant presented data regarding the posterior disc height over time. The quantitative posterior disc height data is presented below in Table 42 Posterior disc height increases following surgery in both treatment groups. However, there is a decrease in posterior disc height over time compared to the post-operative measurements, with the decrease more pronounced in the Superion® ISS group. At 24 months, the mean posterior disc height is lower than the pre-operative measurements.

Table 42: Posterior Disc Height (mm) - Superion® ISS and X-STOP® IPD mITT Analysis Sets

	Superion® ISS						X-STOP® IPD					
	At level(s) of Implant (per level)											
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max
Pre-Op	275	5	1.68	4.9	1.1	9.5	296	4.9	1.74	4.9	0.5	10.2
Post-Op	266	6.6	2.06	6.5	1.6	12.7	287	6.8	2	6.9	1.4	12.3
Week 6	267	5.3	1.84	5.2	1	11	293	5.5	1.8	5.6	1.2	10.2
Month 3	249	5.1	1.78	5	1.1	10.7	285	5.3	1.76	5.4	1.2	10.2
Month 6	256	4.9	1.75	4.9	1.1	9.9	277	5.2	1.75	5.3	0.8	10.4
Month 12	241	4.7	1.77	4.6	0.7	9.4	264	5	1.78	5.2	0.7	10
Month 18	220	4.6	1.78	4.5	0.4	9.1	241	4.9	1.73	5.1	0.7	9.3
Month 24	217	4.5	1.78	4.5	0.4	9.1	220	4.8	1.79	4.8	0.6	10.4

Spinous Process Distance

In regards to spinous process distance, there are no statistically significant differences between the Superion® ISS and X-STOP® IPD® groups as shown below in Table 43. In both groups, there is an immediate increase in the post-op measurements, followed by a slight decrease that can be attributed to patient mobility and device settling. At 24 months, the spinous process distance is greater than the pre-operative condition for both groups.

Table 43: Spinous Process Distance (mm) - Superion® ISS and X-STOP® IPD mITT Analysis Sets

	Superion® ISS						X-STOP® IPD					
	At level(s) of Implant (per level)											
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max
Pre-Op	176	45.3	7.5	44.7	29.9	67.8	190	45.1	7.1	45	30.7	66.6
Post-Op	146	51.1	7	50.9	35.8	67.6	149	51.9	7	51.9	34.3	70.6
Week 6	116	48.7	6.9	49.2	31.9	64.3	154	48.7	6.7	48.1	34	67
Month 3	104	48.5	6.7	48.7	33.8	62.8	145	47.8	6.7	47.4	33.7	67.4
Month 6	111	47.9	6.8	48.1	34.1	63	137	47.8	6.7	47.1	34.4	67.5
Month 12	100	47.2	6.9	46.4	33.7	62.8	128	48	7	47.2	34.4	68
Month 18	89	47.6	7.2	47.7	33.9	62.8	118	47.5	7	47	33.9	68.1
Month 24	82	47.2	6.9	46.1	33.8	62.2	104	48	6.5	47.2	35.6	64.4

Foraminal Height

The applicant presented data regarding the foraminal height over time. The quantitative foraminal height data is presented below in Table 44. Foraminal height increases following surgery in both treatment groups. However, there is a decrease in foraminal height over time compared to the post-operative measurements, with the decrease more pronounced in the Superion® ISS group. At 24 months, the mean foraminal height is nominally lower than the pre-operative measurements in the Superion® ISS group.

Table 44: Foraminal Height (mm) - Superion® ISS and X-STOP® IPD mITT Analysis Sets

	Superion® ISS						X-STOP® IPD®					
	At level(s) of Implant (per level)											
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max
Pre-Op	275	16.6	2.8	16.7	9.8	24.9	294	16.6	2.7	16.6	9.3	27.8
Post-Op	266	18.5	3.2	18.8	9.2	27.6	287	18.9	2.9	18.8	10.7	29.5
Week 6	267	17	2.9	17.1	9.4	25.9	293	17.5	2.8	17.4	9.5	27.6
Month 3	249	16.8	2.8	16.9	9.6	25.9	285	17.2	2.8	17.2	9.4	27.5
Month 6	256	16.7	2.8	16.9	9.2	25.5	277	17.1	2.7	17.1	11	27.5
Month 12	241	16.4	2.8	16.8	8.9	25.2	264	16.9	2.7	16.9	10.8	27.3
Month 18	220	16.4	2.9	16.4	9	25.2	241	16.8	2.8	16.7	8.9	26.9
Month 24	217	16.3	2.9	16.5	7.9	25.4	220	16.6	2.9	16.6	8.9	27

Spondylolisthesis Progression

For spondylolisthesis progression, there were no notable differences between Superion® ISS and X-STOP® IPD® at the index levels as shown in Table 45. In all cases, spondylolisthesis was slightly decreased. The values suggest spondylolisthesis measurements were maintained from pre-op to month 24. These results are expected since the devices are not intended to reduce the presence of spondylolisthesis. The data also demonstrate the investigational and control devices do not encourage greater spondylolisthesis.

Table 45: Spondylolisthesis (mm) - Superion® ISS and X-STOP® IPD mITT Analysis Sets

	Superion® ISS						X-STOP® IPD ®					
	At level(s) of Implant (per level)											
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max
Pre-Op	275	-0.4	3.14	0.4	-10.2	5.7	296	-0.2	3	0.5	-9.1	5.7
Post-Op	266	-0.45	2.77	0.2	-9.4	4.7	287	-0.24	2.8	0.3	-8.6	5.5
Week 6	267	-0.58	3.16	0.2	-9.7	5.5	293	-0.46	3.08	0.3	-9.4	5.7
Month 3	249	-0.58	3.2	0.2	-9.8	5.5	285	-0.39	3.08	0.4	-9.5	5.8
Month 6	256	-0.58	3.2	0.1	-9.8	4.8	277	-0.45	3.08	0.3	-11	5.9
Month 12	241	-0.58	3.22	0	-10.2	5.2	264	-0.4	3.11	0.4	-11.7	6.2
Month 18	220	-0.58	3.21	0.2	-10.4	6.8	241	-0.51	3.05	0.3	-12.3	5.4
Month 24	217	-0.66	3.22	0.1	-10.3	4.6	220	-0.51	3.05	0.2	-9.5	6.1

Longer Term Clinical Results (36 Months)

The applicant provided an analysis of their 36-month data using the same parameters as the primary composite endpoint (CCS). For subjects theoretically due for 36 month follow-up, the Superion® ISS cohort had a follow-up rate of 90.2% and the X-STOP® IPD® cohort had a follow-up rate of 91.4%. Table 46 shows the CCS results at 36 months, as well as the success rates of the individual sub-components of the CCS. At 36 months, the Superion® ISS success rate (52.5%) remains comparable to the X-STOP® IPD® (38.0%). Table 47 presents VAS, ZCQ and ODI secondary endpoint outcomes at 36 months for both treatment cohorts. While these analyses were not pre-specified, the results suggest that the Superion® ISS remains comparable to the X-STOP® IPD® for these clinical outcomes at 36 months as well.

Table 46: Superion® ISS and X-STOP® IPD® mITT Analysis Set - Descriptive Comparisons of the Percentages of Subjects Achieving CCS Component Success at 36 Months*

	Number and Percentage Meeting Criteria					
	Superion® ISS			X-STOP® IPD®		
	N	n	%	N	n	%
(1) ZCQ Responder (at least two of three ZCQ domains)	81	71	87.7	75	63	84.0
(2) No re-operations, revisions, removals or supplemental fixation at the index level(s)	138	112	81.2	148	118	79.7
(3) No major device- or procedure-related complications	138	125	90.6	148	126	85.1
(4) No clinically significant confounding treatments	138	120	87.0	148	118	79.7
Composite Clinical Success	**120**	**63**	**52.5**	**129**	**49**	**38.0**

*Outcomes based on all data available 7/7/14

Table 47: Clinical Primary and Secondary Outcomes at 36 Months

36 Month Clinical Outcomes*	Superion® ISS	X-STOP® IPD®
Pain		
VAS Back: ≥20mm decrease	76.8% (63/82)	69.7% (53/76)
VAS Leg (Worse): ≥20mm decrease	84.1% (69/82)	69.7% (53/76)
Back & Stenosis-Related Outcomes		
ZCQ Physical Function: ≥0.5 point decrease	80.5% (66/82)	77.9% (60/77)
ZCQ Symptom Severity: ≥0.5 point decrease	82.9% (68/82)	75.3% (58/77)
ZCQ Patient Satisfaction: ≤2.5 points	91.5% (75/82)	88.3% (68/77)
ODI: ≥15 point decrease	69.5% (57/82)	71.4% (55/77)

*Outcomes based on all data available 7/7/14

3. Subgroup Analyses

A number of other exploratory analyses were performed to determine if various baseline pre-existing spinal conditions or surgical effects had an effect on poolability, treatment success, and Superion® ISS safety and effectiveness. In addition, several exploratory analyses were performed

on subjects who were observed to have spinous process fractures at any time point based upon independent radiographic review.

These exploratory analyses included migrations/dislodgements, level poolability, stenosis locations, smoking status, presence or absence of spondylolisthesis, supraspinous ligament repair, spinous process fractures, instrumentation sets, anesthesia types, learning curves, device sizes, comorbidity analyses, and presence or absence of bone-implant interface changes.

The exploratory analyses suggest that subjects treated with the Superion® ISS exhibit comparable clinical outcomes regardless of pre-existing conditions, such as 1- or 2-level disease, various types of stenosis, up to Grade I spondylolisthesis, and smoking status. In addition, intra-operative details, such as supraspinous ligament repair and instrumentation set versions, do not appear to have an effect on the clinical outcomes produced following implantation with the Superion® ISS. Furthermore, the presence of radiographic findings, such as spinous process fractures and bone-implant interface changes, did not affect the clinical outcomes observed with the Superion® ISS.

There were no pre-specified analyses related to weight, age, or gender. Post-hoc analyses were performed for weight, age, and gender, and there were no notable differences between groups.

A. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 33 Investigators of which none were full-time or part-time employees of the applicant and 1 had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: none
- Significant payment of other sorts: 1
- Proprietary interest in the product tested held by the investigator: none
- Significant equity interest held by investigator in applicant of covered study: 1

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Statistical analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. The information provided does not raise any questions about the reliability of the data.

XI. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

A. Panel Meeting Recommendation

At an advisory meeting held on February 20, 2015, the Orthopaedic and Rehabilitation Devices Panel voted 5-1 (2 abstentions) that there is reasonable assurance the device is safe, 5-1 (2 abstentions) that there is reasonable assurance that the device is effective, and 4-2 (2 abstentions) that the benefits of the device do outweigh the risks in subjects who meet the criteria specified in the proposed indication. The 24-hour Panel Summary is located at the following link: *http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/OrthopaedicandRehabilitationDevicesPanel/UCM435258.pdf*

B. FDA's Post-Panel Action

Following the Panel meeting, the applicant worked with FDA to develop post-approval studies to address the outstanding issues highlighted by the Panel, namely, the need for longer-term follow-up and comparison of the Superion® ISS to decompression. The Panel also identified the potential risk of radiation posed by the use of CT scans.

The applicant has adequately addressed the outstanding issues raised by the Panel relating to comparison of the Superion® ISS to decompression at 60 months through the design of their new enrollment post-approval study. FDA agrees with the applicant's submitted five-point summary protocol plan, and has determined that the information the applicant has submitted to address the Panel's concern is acceptable.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

Effectiveness Conclusions

In this study, subjects were enrolled, treated, and followed up through the 24 month post-operative visit. Follow-up was satisfactory and 97.3% of the Superion® cohort and 94.9% of the control cohort had data available for analysis at the completion of the study. Assessment of effectiveness was performed using the mITT and the per protocol populations. All 190 Superion® ISS and 201 X-STOP® IPD® subjects were included in the primary analysis of the mITT cohort. Statistical analysis demonstrated that the results from all sites were poolable to determine safety and effectiveness. Analysis of patient demographic and baseline data showed the Superion® ISS and X-STOP® IPD® groups to be comparable.

To meet the primary effectiveness endpoint, individual subjects were considered a success if they 1) demonstrated improvement in two of the three domains of the ZCQ (physical function, symptom severity, and patient satisfaction); 2) experienced no re-operations or revisions; 3) experienced no device- or procedure-related complications; and 4) required no spinal cord stimulators, rhizotomies, or epidural injections.

The applicant has met the protocol specified primary composite endpoint with a posterior probability for non-inferiority of 0.9927 for the mITT and 0.9944 for the Per Protocol analysis cohorts. Note that 0.958 is the pre-specified threshold to declare statistical success. This was calculated through a Bayesian model using Bayesian imputation for the missing data, assuming

they were missing at random. The estimated overall success rates were 52.7% in the Superion® ISS group and 50.2% in the X-STOP® IPD® group.

Overall success as defined in the study protocol was comparable in both Superion® ISS and X-STOP® IPD® for both populations analyzed (mITT and Per Protocol). The results of overall success indicate that the Superion® ISS group is statistically non-inferior to the X-STOP® IPD® control group at 24 months. Although non-inferiority was demonstrated, both Superion® ISS and X-STOP® IPD® success rates were below the 65% rate used to calculate the trial sample size. To assess the impact of subjects with unknown outcomes at 24 months or other potential biases, various sensitivity analyses were conducted. Non-inferiority was demonstrated with these analyses. At every assessment time period, the percentage of Superion® ISS subjects achieving composite success was comparable to control. When considering the individual components of composite success, the ZCQ and re-operations components numerically favored the control, while complications and confounding treatments favored the Superion® device. Analysis shows that the demonstration of non-inferiority between the Superion® ISS and X-STOP® IPD® is robust to missing data.

It should be noted that 24 of the 201 (11.9%) X-STOP® IPD® mITT subjects had a device dislodgement or migration, and none of the Superion® ISS subjects experienced this type of event. In terms of spinous process fractures that were considered CCS failures, 21 of the 190 (11.1%) Superion® ISS mITT subjects had a spinous process fracture that did not heal by Month 24. In contrast, 10 of the 201 (5.0%) X-STOP® IPD® mITT subjects had a spinous process fracture that did not heal by the 24-month time point.

A worst-case analysis of all unresolved spinous process fractures being analyzed as study failures was conducted, and under these conditions, non-inferiority was still demonstrated when comparing the Superion® ISS to the X-STOP® IPD®.

In conclusion, the clinical study data indicate that, at 24 months post-operatively, the Superion® ISS has a reasonable assurance of effectiveness for the treatment of moderate degenerative lumbar spinal stenosis.

Safety Conclusions

The risks of the device are based on non-clinical laboratory as well as data collected in a clinical study conducted to support PMA approval as described above. The clinical data from the mITT population were used in the safety analysis. Data considered were adverse events, re-operations, and neurological status at 24 months. The rate of Superion® ISS subjects having at least one adverse event, or an events classified as severe, device-related or procedure-related as adjudicated by the CEC was comparable to the observed adverse event rates in the X-STOP® IPD® control group. The rate of secondary surgery for the Superion® ISS group was also similar to the X-STOP® IPD® control group at 24 months. Neurological success, defined as maintenance of improvement in neurological status at 24 months was comparable between Superion® ISS and X-STOP® IPD® groups.

The clinical study noted the presence of additional spinous process fractures in a number of subjects identified by the independent radiographic lab, and not by the investigators, in both Superion® ISS and the X-STOP® IPD® groups. There were more fractures noted in the Superion® ISS subjects than in the X-STOP® IPD® group, and two-thirds of these fractures had not healed by the evaluation at 24 months. However, based on an analysis of the primary composite endpoint, including the ZCQ, VAS, and ODI assessments, the presence of the fractures did not demonstrate clinical significance at 24 months. The long term significance of these fractures, however, is unknown.

In conclusion, the clinical study data indicate that, at 24 months post-operatively, the Superion® ISS has a reasonable assurance of safety, and is at least as safe as the X-STOP® IPD®, in regards to adverse events, re-operations and neurological status. It also demonstrates a numerically greater incidence of spinous process fractures when compared to the X-STOP® IPD® which had no clinical significance at 24 months, but the long term effects of which are unknown.

Benefit-Risk Conclusions

The probable benefits of the device are also based on data collected in a clinical study conducted to support PMA approval as described above.

Over the 24-month time period studied, the following benefits were observed with use of the Superion® ISS when compared to the X STOP® IPD® (control):

1) Improvement in neurogenic intermittent claudication symptoms as measured by the Zurich Claudication Questionnaire (ZCQ) Score at 24 months post-operatively compared to baseline (proportion of subjects achieving protocol defined ZCQ success: Superion® ISS, 81.7%; X-STOP® IPD®, 87.2%).
2) Functional improvement measured by the improvement in Oswestry Disability Index (ODI) scores at 24 months post-operatively compared to baseline (proportion of subjects achieving protocol defined ODI success: Superion® ISS, 64.3%; X-STOP® IPD®, 66.9%).
3) Maintenance or improvement in neurological status at 24 months post-operatively (proportion of subjects achieving protocol defined neurologic success: Superion® ISS, 95.3%; X-STOP® IPD®, 96.8%).
4) Despite longer operative times, less blood loss (numerically different, not statistically significant) was reported during the surgical implantation of the Superion® ISS device as compared to the control device (mean operative time: Superion® ISS, 56.2 minutes; X-STOP® IPD®, 47.2 minutes; estimated blood loss: Superion® ISS, 13.5cc; X-STOP® IPD®, 38.7cc).

Additional factors that were considered in determining probable risks and benefits for the Superion® ISS included:

1) The overall rate of adverse events with the Superion® ISS device was comparable to the control device (Superion® ISS, 94.7%; X-STOP® IPD®, 91.5%).
2) The rate of serious adverse events with the Superion® ISS device was comparable to the control device (Superion® ISS, 46.3%; X-STOP® IPD®, 45.8%).

3) The rate of serious adverse events that were either device- or procedure-related with the Superion® ISS device was comparable to the control device (Superion® ISS, 8.4%; X-STOP® IPD®, 9.5%).
4) The incidence of spinous process fractures observed with the Superion® ISS device was higher than those observed with the control device (Superion® ISS, 16.3%; X-STOP® IPD®, 8.5%; as reported by the independent radiographic reviewers), and the long-term effect of these fractures on safety and effectiveness is unclear.
5) Through 24 months, there were a total of 38 reoperations or revisions in the Superion® ISS group (38/190, 20.0%) compared with 29 reoperations or revisions in the X-STOP® IPD® group (29/201, 14.4%).

In conclusion, given the available information above, the data supports that for moderate degenerative lumbar spinal stenosis, the probable benefits of using the Superion® ISS outweigh the probable risks.

Overall Conclusions

The data in this PMA application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. Based on the clinical study results, it is reasonable to conclude that a portion of the indicated patient population will achieve clinically significant results. The clinical benefits of the use of the Superion® ISS in terms of functional improvement, reduction in pain and maintenance or improvement in neurological status outweigh the risks associated with the device and surgical procedure through 24 months follow-up when used in the indicated population and in accordance with the directions for use. In conclusion, the Superion® ISS represents a reasonable alternative to other treatment options for subjects suffering from moderate degenerative lumbar spinal stenosis.

XIII. CDRH DECISION

CDRH issued an approval order on May 20, 2015. The final conditions of approval cited in the approval order are described below.

In addition to the Annual Report requirements, the applicant must conduct two Post-Approval Studies to provide long-term device performance and to evaluate device performance under actual conditions of use.

1. ***Extended Follow-up of Premarket Cohort.*** The "Superion® Post-Approval Clinical Evaluation and Review (SPACER)" study is described as follows:

   Based on the study plan received on May 1, 2015, the applicant must perform a 60-month post-approval study (PAS) to evaluate the longer term safety and effectiveness of the Superion® ISS as compared to the X-STOP® Interspinous Process Decompression (IPD®) System ("X-STOP® IPD®") by following all patients from the pivotal investigational device exemption (IDE) study G070118 with device survival to 24 months (137 Superion® and 144 X-STOP® randomized patients had not died or

terminally failed as of the 24 month visit) annually through 60 months at 25 study sites. Thus, the post-approval study duration is approximately 36 months as all patients have reached 24 months prior to the start of this study.

At each annual (±3 month) visit, the applicant will collect the following data: Zurich Claudication Questionnaire (ZCQ); neurological status as determined by physical exam; radiographic information; maintenance of distraction; all adverse events regardless of cause; incidence of epidural injections regardless of the cause and spinal level injected; incidence of analgesic narcotics usage; reoperations, revisions, removals or supplemental fixation at the index levels; SF-12 Short Form Health Survey, Version 2; VertiFlex® Patient Satisfaction Survey; Visual Analog Scale (VAS); Oswestry Disability Index (ODI), return to work and to activities of daily living, and rehabilitation utilization. In addition, the applicant will report information on the length of hospital stay, operative time, estimated blood loss, and type of anesthesia.

Radiographic information collected will include: standing anteroposterior and lateral lumbar radiographs, range of motion on lateral standing flexion/extension films (at implanted and adjacent level(s)), radiolucency, device displacement or migration, and radiographic observations such as incidence of total and per patient spinous process fractures or heterotopic ossification. Adverse events will be evaluated by the Medical Monitor. Data will be evaluated for safety endpoints by an independent Clinical Events Committee (CEC).

The primary hypothesis of this extended follow-up post approval study is that performance of the Superion® ISS remains clinically non-inferior to X-STOP® IPD® at 60 months post-surgery using the same non-inferiority margin (δ=-0.10) as was used at 24 Months. An individual subject will be considered a success if they meet all of the following conditions at the 60-month follow-up:

Clinically significant improvement in outcomes compared to baseline, as determined by meeting the following:

- At least two of three domains of the Zurich Claudication Questionnaire (ZCQ)
    - Improvement in physical function by $\geq$ 0.5 points
    - Improvement in symptom severity by $\geq$ 0.5 points
    - "Satisfied" or "somewhat satisfied" as defined by a score of $\leq$ 2.5 points on the patient satisfaction domain
- No re-operations, revisions, removals, or supplemental fixation at the index level(s)
- No major implant-or procedure-related complications:
    - No dislodgement, migration, or deformation
    - No new or persistent worsened neurological deficit at the index level
    - No spinous process fractures
    - No deep infection, death, or other permanent device attributed disability
- No clinically significant confounding treatments:
    - No epidural injections or nerve block procedures at index level, spinal cord stimulators or rhizotomies

The secondary study objective is to demonstrate the superiority of Superion® ISS to X-STOP® IPD® in effectively treating moderately impaired LSS patients as measured by 60 months postoperative overall success rates.

FDA will expect at least 85% follow-up at the 60-month time point to provide sufficient data to evaluate safety and effectiveness as well as sensitivity analyses to address missing data.

2. ***New Enrollment Study.*** The "Superion® New Enrollment Study" is described as follows:

The applicant will recruit 358 subjects to ensure that at minimum 304 (152 per treatment group) patients will be followed through 60-months. Nine clinical visits will occur at the following intervals: screening (< 4 weeks before surgery), surgery, 6 weeks (±2 weeks), 6 months (±2 months), 12 months (±2 months), 24 months (±2 months), and annually (±4 months) thereafter through 60 months of follow-up. At each post-operative visit, the applicant will collect the following data: ZCQ; neurological status as determined by physical exam; radiographic information; all adverse events regardless of cause; incidence of epidural injections regardless of the cause and spinal level injected; incidence of analgesic narcotics usage; reoperations, revisions , removals or supplemental fixation at the index levels; Patient satisfaction Survey; VAS; ODI, return to work and to activities of daily living and rehabilitation utilization. In addition, the applicant will collect information on the length of hospital stay, operative time, estimated blood loss, and type of anesthesia.

The imaging data will be collected during screening (< 4 weeks before surgery) and during all post-operative visits via x-rays in the following positions: anteroposterior, lateral, flexion and extension. In addition, standing anteroposterior and lateral lumbar radiographs will be taken at time of discharge of index surgery. Computed tomography (CT) imaging will be captured in lieu of x-rays at 24 months for all patients, pending individual IRB approval, in the Superion® cohort. CT imaging may be performed in lieu of x-rays for Superion® patients at 60 months per surgeon discretion. CT imaging will be utilized to observe spinous process fractures.

- The primary objective of this study is to demonstrate that the composite clinical success (CCS) of Superion® device performance will be non-inferior (δ=-0.125) to decompression at 60-months. The CCS is defined as following:
    - A clinically significant improvement in at least two of the three domains of the ZCQ
    - No re-operations, revisions, removals, or supplemental fixation at the index level(s)
    - No ≥2 injections or series of injections for the treated level, or nerve block procedures performed to treat spinal stenosis for the index level(s), or a single injection within 12 months of the 60-month endpoint.

A secondary endpoint with alternative CSS for the primary objective will also be evaluated at 60 months where CSS is defined as above with the exception of point number three where success will be defined as:

- No injections or series of injections at any level at any time.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

Directions for Use: See device labeling
Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.
Post-approval Requirements and Restrictions: See Approval Order.