Instructions for Use

SUPERION® INTERSPINOUS SPACER

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CAUTION: Federal (United States) law restricts this device to sale by or on the order of a Physician.

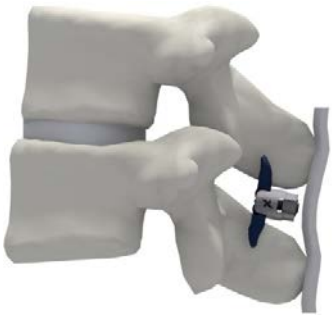
Rx only

HOW SUPPLIED
Implant Components – Sterile
Surgical Instruments – Non-sterile (unless otherwise noted on the package label)

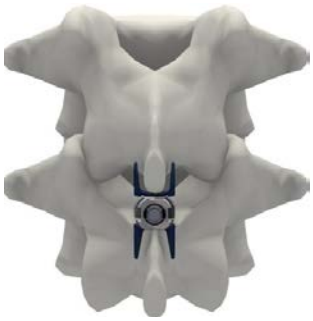
DEVICE DESCRIPTION

The Superion® Interspinous Spacer is a titanium implant that is designed to fit between the spinous processes of the lumbar spine. It is composed of titanium 6Al-4V ELI alloy, and consists of a single component with deployable superior and inferior projections that engage the spinous processes to secure it in place. The Superion® Interspinous Spacer is provided sterile in sizes of 8mm, 10mm, 12mm, 14mm, and 16mm.

The Superion® Interspinous Spacer is implanted by percutaneous means through a cannula inserted between adjacent spinous processes. Once inserted into the interspinous process space the Superion® Interspinous Spacer is deployed, or opened, to provide distraction at the affected spinal segment.



Superion® Spacer in situ – Lateral View



Superion® Spacer in situ – A/P View

The Superion® ISS System includes a set of proprietary instruments necessary to deliver the Superion® Implant percutaneously. Instruments specifically designed for implanting the Superion® implant consist of a cannula, dilators, an interspinous reamer, an interspinous gauge, and an inserter with driver utilized to deploy the device once in position. Additional general purpose instruments included in the instrument set consist of a mallet, retractor, a handle for the cannula, and forceps. Refer to the Superion® Surgical Technique Manual for comprehensive instructions on instrument use.

CAUTION: The Superion® Interspinous Spacer is manufactured from titanium alloy, which is known to produce MRI artifacts. Patients should be warned to disclose the presence of the Superion® Interspinous Spacer prior to an MRI exam. Failure to do so may affect the quality of diagnostic information obtained from the scans.

INDICATIONS FOR USE

The Superion® Interspinous Spacer 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 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 narrowing. The Superion® Interspinous Spacer is indicated for those patients with impaired physical function who experience relief in flexion from symptoms of leg/buttock/groin pain, with or without back pain, who have undergone at least 6 months of non-operative treatment. The Superion® Interspinous Spacer may be implanted at one or two adjacent lumbar levels in patients in whom operative 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:
  - o Evidence of thecal sac and/or *cauda equina* compression
  - o Evidence of nerve root impingement (displacement or compression) by either osseous or non-osseous elements
  - o Evidence of hypertrophic facets with canal encroachment

- AND Associated with the following clinical signs:
  - o Presents with moderately impaired Physical Function (PF) defined as a score of ≥ 2.0 of the Zurich Claudication Questionnaire (ZCQ)
  - o Ability to sit for 50 minutes without pain and to walk 50 feet or more.

CONTRAINDICATIONS

The Superion® Interspinous Spacer 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:
  - o instability of the lumbar spine, e.g., isthmic spondylolisthesis or degenerative spondylolisthesis greater than grade 1.0 (on a scale of 1 to 4);
  - o an ankylosed segment at the affected level(s);
  - o fracture of the spinous process, pars interarticularis, or laminae (unilateral or bilateral);
  - o 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.

WARNINGS

The Superion® Interspinous Spacer must be placed in the concavity between the spinous processes. If correct placement of the implant cannot be achieved due to variant anatomy, the physician should consider aborting the procedure because incorrect placement may result in device dislodgement, particularly if the patient experiences a traumatic event postoperatively.

The Superion® ISS should only be used by surgeons who are experienced and have undergone training in the use of the device. Only surgeons who are familiar with the implant components, instruments, procedure, clinical applications, biomechanics, adverse events, and risks associated with the Superion® ISS should use this device. A lack of adequate experience and/or training may lead to a higher incidence of adverse events.

The effects of multiple deployments upon implant strength have not been determined. In the event that a Superion® Interspinous Spacer must be deployed, closed, and redeployed for repositioning more than three times during a procedure, the Spacer should be discarded, and a new device used.

Data have demonstrated that spinous process fractures can occur with Superion® ISS implantation. Potential predictors for spinous process fractures include:

- thin, or “gracile” spinous processes
- kissing” spinous processes
- shallow” or more dorsal placement of the device

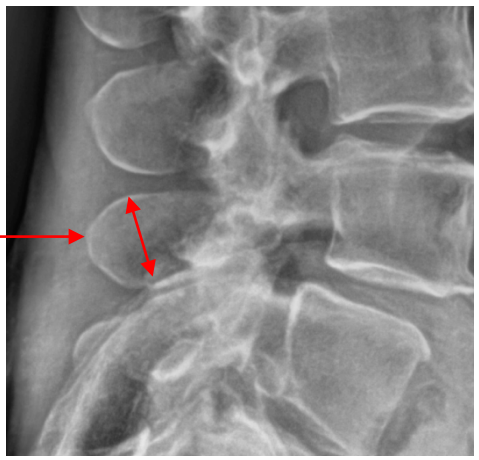
Anatomical Considerations

Certain anatomical characteristics have been associated with an increased risk of spinous process fractures, while others may increase the difficulty of cannula and Implant placement.

Thin, or “gracile” Spinous Processes

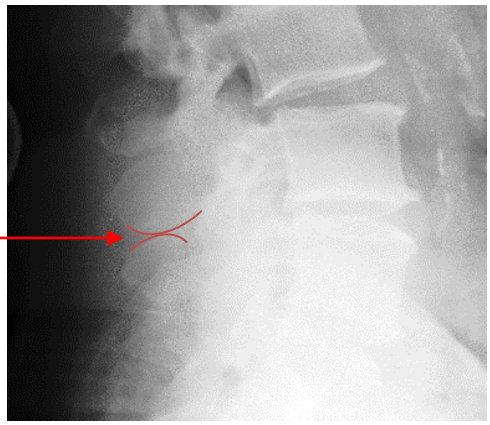
Where a spinous process is unusually thin, or measures less than 20mm in superior-inferior dimension, the likelihood of a post-operative spinous process fracture may be increased.

Thin Spinous Process



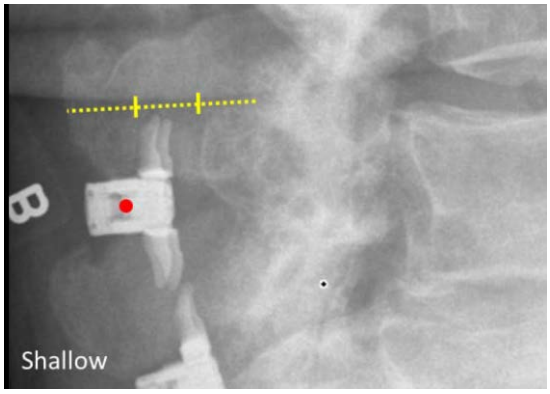
"Kissing Spine"

Where spinous processes are in very close approximation, or are in contact (i.e., "kissing"), increased difficulty may be experienced in placement of the cannula. Where spinous processes do not "open up" in flexion, the likelihood of a spinous process fracture may be increased.

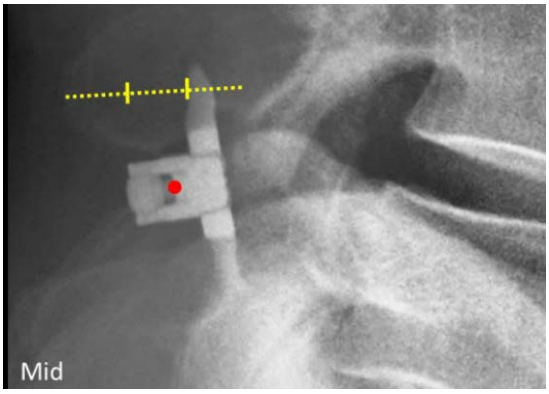


Implant Placement Location

Where the Superion® Implant is placed in a "shallow" or more dorsal position, the likelihood of a post-operative spinous process fracture may increase by a factor >4. To reduce the potential for post-operative fracture, be certain to locate the implant body sufficiently anterior, and confirm implant position fluoroscopically.



Incorrect: Shallow Implant Position



Optimal: Implant Position

PRECAUTIONS

- Radiological evidence of stenosis must be correlated with the patient's symptoms before the diagnosis can be confirmed.
- If the spinous processes at the affected levels are not distracted in flexion, the Superion® Interspinous Spacer may not be indicated.
- The safety and effectiveness of the Superion® Interspinous Spacer has not been studied in patients with the following conditions: axial back pain without leg, buttock, or groin pain; symptomatic lumbar spinal stenosis at more than two levels; prior lumbar spine surgery; significant peripheral neuropathy; acute denervation secondary to radiculopathy; Paget's disease; vertebral metastases; morbid obesity; pregnancy; a fixed motor deficit; angina; active rheumatoid arthritis; peripheral vascular disease; advanced diabetes; or other systemic disease that may affect the patient's ability to walk.
- Implantation of the Superion® Interspinous Spacer should be performed only by qualified and experienced spinal physicians having specific training in the implantation of the device, because this is a technically demanding procedure presenting risk of serious injury to the patient.
- Clinicians should not implant the Superion® Interspinous Spacer until receiving adequate training in surgical technique. Inadequate training may result in poor outcomes and/or increased rates of adverse events.
- Spinous process fractures have been reported with this device type. Avoiding strenuous activity in the immediate postoperative period may be advisable.

Potential Adverse Events:

The following potential adverse events may occur as a result of interspinous process decompression with the Superion® ISS:

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.

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 $\geq$ 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 $\geq$ 3mm translation or $\geq$ 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 $\leq$ -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 1. Adverse events were recorded at all visits.

Table 1: 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.

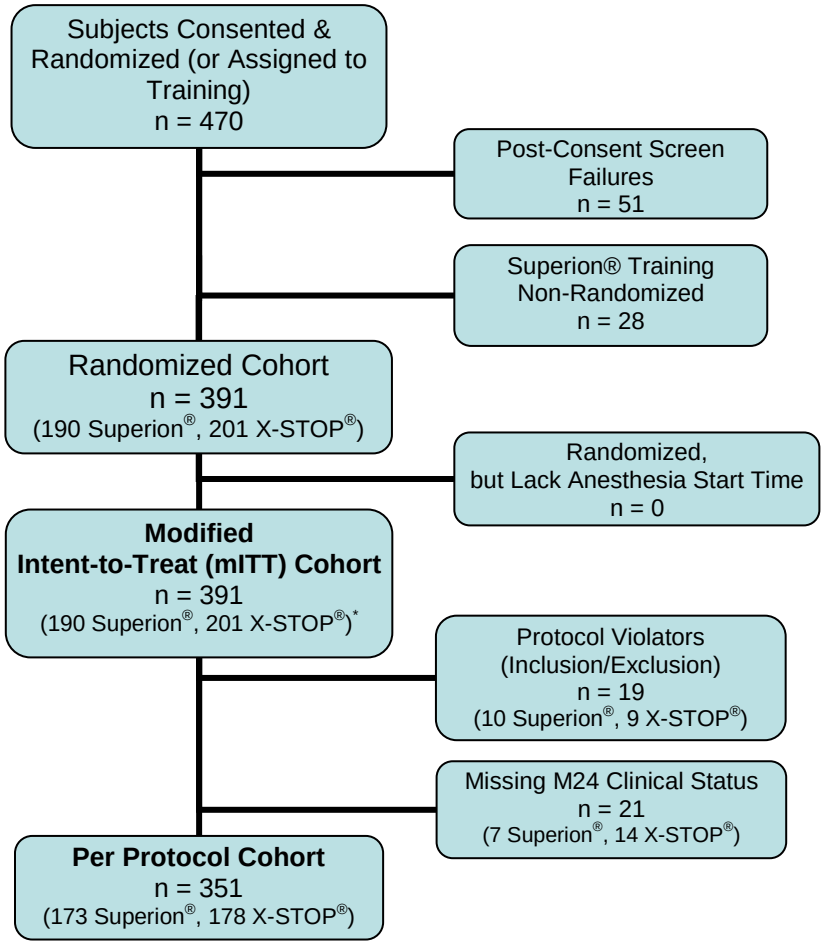
Patient accounting and follow-up (Table 2), a patient accounting tree (Figure 1), and a summary of patient and data accounting at 24 months (Table 3) are provided below.

Table 2: 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 1.



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 1: 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 3: 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 4, Table 5, and Table 6.

Table 4: 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 5: 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 6: 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

4. 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 7 through Table 28.

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 7.

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 7: 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 8.

Table 8: 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 9. 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 9), 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 9: 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
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

Table 9: 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**
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

Table 9: 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**
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
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	2	2	1.1	10	8	4	2.9	-7	12.8

Table 9: 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**
tissue									
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 10 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 10: 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

Table 10: 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
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 control	**0**	0	**0**	0	**0**	0	**0**	0	**0**	1	**0**	0	**0**	**1**
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	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0	**0**	**0**

Table 10: 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
placement														
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
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	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0	**0**	0

Table 10: 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
associated with non-index condition														
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 11 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 11: 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 12 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 12: 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 11 and 12 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 13.

Table 13: 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 14 below.

Table 14: 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

Table 14: 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 infection at the operative site	0	0	0	3	2	1	1	-8.9	10.9
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	21	20	10.5	16	15	7.5	-3.1	-13	6.9

Table 14: 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**
symptoms at index level									
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 15: 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 16 (Superion® ISS) and Table 17 (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 16: 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 17: 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 18, 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 18: 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 19 and Table 20. 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 19 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 19: Perioperative Results from Superion® ISS IDE (mean ± SD)

Operative Detail	**Superion® ISS**	**X-STOP® IPD®**
	(n=190)	**(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 20, 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 20: 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
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 21.

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 21. 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 21: 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 22. The results from independent radiographic review were used in the final Clinical Composite Success (CCS) analysis and are also shown in Table 22 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 26 below). The core laboratory determined that 21 investigational and 10 control fractures remained unhealed at 24 months.

Table 22: 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 23. As demonstrated in Table 23 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 23: 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 24 and Table 25 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 24) 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 24: 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 25). 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 25: 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 26 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 26 below.

Table 26: 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)
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 27). 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 26, suggest that some of these spinous process fractures may have been asymptomatic.

Table 27: 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 28 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 28: 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

5. 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 29 to 35.

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 29, 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 29: 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 30 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 30, the Superion® ISS demonstrates greater than 80% success in each individual sub-component of the CCS.

Table 30: 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 31 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 31: 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 32). 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 32: 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 33 and Table 34 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 33: 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 34: 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 35). 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 35: 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 36. 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 36: 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 37. 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 37: 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 38. 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 38: 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 39. 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 39: 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 40 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 40: 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 41. 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 41: 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 42. 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 42: 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 43. 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 43: 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 44 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 45 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 44: 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 45: 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

6. 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.

7. Conclusions Drawn

The clinical results from the use of the investigational device, the Superion® InterSpinous Spacer, were shown to be statistically non-inferior to the control group results. The scientific evidence that has been presented here supports the safety and effectiveness of the Superion® InterSpinous Spacer in the treatment of moderate degenerative lumbar spinal stenosis at one or two levels from L1 to L5. The study demonstrated that treatment of moderate degenerative lumbar spinal stenosis with the Superion® InterSpinous Spacer was as effective as the control treatment (X-STOP® IPD®). The results for the

primary effectiveness outcome parameters for the investigational group were non-inferior to the control group.

PACKAGING

All packages containing implants should be intact upon receipt. Damaged packaging may indicate the presence of unsafe product. If the product packaging is damaged, the product should not be used and should be returned.

The Superion® Interspinous Spacer components must be stored, opened and handled in such a way that they are protected from inadvertent damage or contamination.

STERILITY

The Superion® Interspinous Spacer is sterilized with gamma radiation (25 kGy minimum), and is supplied **"STERILE"** and intended for single patient use only. DO NOT RESTERILIZE THIS PRODUCT. The sterility can only be assured if the packaging is intact. Do not use this device if the STERILE packaging has been opened or damaged. Contact your VertiFlex® representative for replacement. Remove all packaging material prior to use. Only sterile implants should be used in surgery.

STERILE	R	**Radiation Sterilized**

FOR SINGLE USE ONLY

STORAGE

The Superion® Interspinous Spacer and instruments should be stored in a clean and dry area until ready for use.

INSTRUCTIONS FOR USE

The physician implanting the Superion® Interspinous Spacer is expected to be fully educated and trained in the techniques necessary to implant the device.

The Superion® Interspinous Spacer may be implanted only using the applicable Superion® manual instrumentation provided by VertiFlex®. For care, cleaning, and sterilization instructions, please refer to the package insert accompanying the instruments.

Refer to the Superion® Interspinous Spacer **Surgical Technique Manual** for recommended implantation procedures.

The techniques for implanting the Superion® Interspinous Spacer should be reviewed by the physician prior to use of the system.

Proper selection of patients, and good compliance of patients with instructions for postoperative care and behavior, are critical to the realization of a successful procedure. All patients contemplating implantation of this device should be apprised of the risks associated with the procedure, as well as the limitation of activities the patient will face following surgery. The physician is expected to provide detailed instructions to the patient regarding postoperative activities.

The physician should inspect the components and instruments of the Superion® Interspinous Spacer system before surgery to assure that all necessary components are present.

MR

MRI COMPATIBILITY

Non-clinical testing has demonstrated that the VertiFlex Superion® Interspinous Spacer is MR Conditional. It can be scanned safely under the following conditions:

- Static magnetic field of 1.5-Tesla (1.5 T) or 3.0-Tesla (3.0 T).
- Spatial gradient field of up to:
  - 7,480 G/cm (74.80 T/m) for 1.5 T systems.
  - 3,740 G/cm (37.40 T/m) for 3.0 T systems.
- Maximum whole body averaged specific absorption rate (SAR) of:
  - 2.0 W/kg for 15 minutes of scanning in Normal Operating Mode at 1.5T.

- 2.0 W/kg for 15 minutes of scanning in Normal Operating Mode at 3.0T.

1.5T RF heating

In non-clinical testing with body coil excitation, the VertiFlex Superion® Interspinous Spacer produced a temperature rise of less than 4.0 ºC at a maximum whole body averaged specific absorption rate (SAR) of 2.0 W/kg, as assessed by calorimetry for 15 minutes of scanning in a 1.5 T Siemens Espree (MRC30732) MR scanner with SYNGO MR B17 software.

3.0T RF heating

In non-clinical testing with body coil excitation, the VertiFlex Superion® Interspinous Spacer produced a temperature rise of less than 5.0 ºC at a maximum whole body averaged specific absorption rate (SAR) of 2.0 W/kg, as assessed by calorimetry for 15 minutes of scanning in a 3.0 T Siemens Trio (MRC20587) MR scanner with SYNGO MR A30 4VA30A software.

Caution: The RF heating behavior does not scale with static field strength. Devices that do not exhibit detectable heating at one field strength may exhibit high values of localized heating at another field strength.

MR Artifact

In testing with gradient-echo sequencing, the shape of the image artifact follows the approximate contour of the device and extends radially up to 2.6 cm from the implant.

DEVICE RETRIEVAL EFFORTS

Should it be necessary to remove the VertiFlex Superion® Interspinous Spacer, call VertiFlex®, Incorporated, prior to the scheduled surgery for product/tissue retrieval information. Return all explanted devices to VertiFlex®, Incorporated, attention Regulatory Affairs.

PRODUCT COMPLAINTS

Any health care professional (e.g, customer or user of this system of products) who has any complaints or who has experienced any dissatisfaction in the product quality, identity, durability, reliability, safety, effectiveness, and/or performance, should notify the distributor or VertiFlex®, Incorporated. Further, if any of the implanted spinal system component(s) ever “malfunctions” (i.e., does not meet any of its performance specifications or otherwise does not perform as intended), or is suspected of doing so, the distributor should be notified immediately. If any VertiFlex®, Incorporated, product ever malfunctions and may have caused or contributed to the death or serious injury of a patient, the distributor should be notified immediately by telephone, fax, or written correspondence. When filing a complaint, provide the component(s) name and number, lot number(s), your name and address, the nature of the complaint, and notification of whether or not a written report from the distributor is requested.

DESCRIPTION OF DEVICE SYMBOLS

	Batch code
REF	Catalogue number
	CAUTION: Federal law (U.S.A.) restricts this device to sale by or on the order of a physician
	Consult instructions for use

	Do not re-use
	CE mark approval
	Manufacturer
	MR conditional
	Non-sterile
	Sterilized using irradiation
	Use-by date
	Important safety information follows

FOR FURTHER INFORMATION

Please contact VertiFlex®, Incorporated, if further information pertaining to the Superion® Interspinous Spacer is required.

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