SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Prosthesis, Spinous Process Spacer/Plate
Device Trade Name:	DIAM™ Spinal Stabilization System
Device Product Code	NQO
Applicant's Name and Address:	Companion Spine Etage 5 – 4 Allée des Acacias Mérignac 33 700 France
Date of Panel Recommendation:	None
Premarket Approval Application: (PMA Number)	P240043
Date Of FDA Notice of Approval:	December 10, 2025

Breakthrough Device: Granted breakthrough device status on October 5, 2021, because the device and proposed indication for use met the program criteria.

II. INDICATIONS FOR USE

The DIAM™ Spinal Stabilization System is indicated for skeletally mature patients that have moderate to severe primary low back pain (greater than leg pain) secondary to lumbar degenerative disc disease (DDD), at a single level from L2-L5 with current episode refractory to at least 6 months non-operative care.

Symptomatic disc disease is confirmed by patient history, physical examination, and radiographic evaluation with one or more of the following factors:

- Greater than 2mm of decreased disc height (average disc height) compared to the adjacent level
- Scarring/thickening of the ligamentum flavum, annulus fibrosus, or facet joint capsule
- Non-extruded herniated nucleus pulposus

The DIAM™ device is implanted via a minimally invasive posterior approach.

III. CONTRAINDICATIONS

The DIAM™ Spinal Stabilization System is contraindicated in patients with:

- An allergy to silicone, polyethylene terephthalate, or titanium;
- Spinal anatomy or disease that would prevent implantation of the device or cause the device to be unstable in situ, such as: Instability of the lumbar spine, e.g., isthmic spondylolisthesis or degenerative spondylolisthesis (anterolisthesis with more than 2mm of translation) or retrolisthesis at the involved level;
- Disc height loss greater than 67% (average disc height) at the involved level compared to the next adjacent spinal level;
- Scoliosis (Cobb angle greater than 10 degrees), flat back, or kyphotic spine at the operative level;
- Severe anatomical alterations at the operative levels including congenital abnormalities, spinal tumor, or evidence of prior or existing lumbar spine trauma;
- Prior surgery at operative level;
- Cauda equina syndrome defined as neural compression causing neurogenic bladder or bowel dysfunction;
- Disc degeneration requiring treatment at more than one lumbar level;
- Extruded or sequestered disc herniations;
- Large osteophytes and/ or severe hypertrophy between the vertebral bodies and/ or the facet articular process with or without severe subarticular bone erosions and/ or subchondral cysts;
- Diagnosis of osteoporosis, defined as a DEXA bone mineral density T-score equal to or less than -2.5;
- Pregnancy;
- Active systemic infection, or infection localized to the site of implantation;
- Morbid obesity defined as body mass index (BMI) greater than 40.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the DIAM™ Spinal Stabilization System Physician labeling.

V. DEVICE DESCRIPTION

DIAM™ Spinal Stabilization System is an interspinous spacer implanted between adjacent spinous processes using a posterior surgical approach. The DIAM™ device is designed to load-share with the posterior disc and facet joints that are overloaded due to disc degeneration, thereby relieving low back pain while preserving motion at the treated spinal level.

The DIAM™ Spinal Stabilization System implant consists of 3 main components: the H-shaped interspinous process spacer, the spinous process tethers, and the crimps. The spacer

is implanted between two adjacent spinous processes, each tether is looped around a spinous process, and the crimps are used to secure the ends of the tethers. Each spacer is packaged with two tethers and two crimps. The DIAM™ Spinal Stabilization System is packaged with the tethers preloaded into the spacer. The spacer component is manufactured from a core of silicone (NuSil MED 4765) and is covered by a fabric knitted jacket of high tenacity polyester (Polyethylene Terephthalate, or PET). The spacer is in an "H"-shaped configuration with the wings of the "H" extending on each side of the spinous processes between which it is placed.

The tethers are manufactured from PET fibers that are the same material as the woven spacer jacket. A small, open "eye" is spliced into one end of each tether, and a curved needle is crimped onto the other end. The curved needle is used for passage of the tether around the spinous process. It is then passed through the eye-end of the tether to form a complete loop and secure the construct to the spinous process. The crimp is used to secure the tether loop. The crimp is manufactured from Grade 2 commercially pure titanium. The crimp is locked in place by compressing its diameter using a crimper tool similar to a pair of pliers. A visual representation of the DIAM™ Spinal Stabilization System and its components are shown below in **Figure 1**.

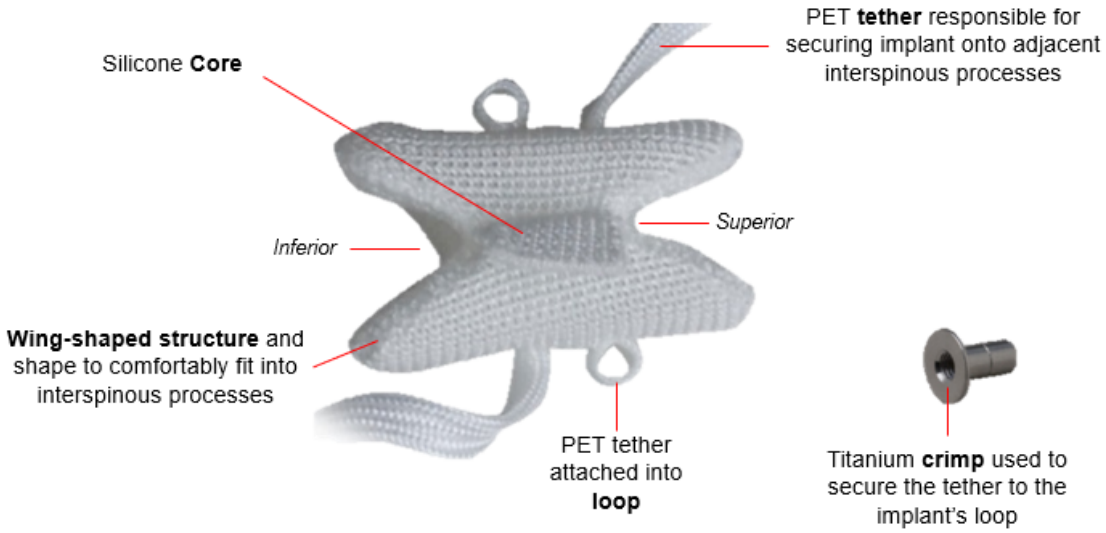

Figure 1: Components of the DIAM™ Spinal Stabilization System Implant

The DIAM™ Spinal Stabilization System is offered in 4 sizes: 8, 10, 12, and 14 mm. These sizes correspond to the height of the spacer portion of the device that is placed between the spinous processes. The tethers and crimps remain the same regardless of the spacer size. The available catalog sizes for the DIAM™ Spinal Stabilization System are listed in **Table 1**.

Table 1: DIAM™ Spinal Stabilization System Device Sizes

Catalog Number	Description
CS001A0008	8 mm DIAM™ Spinal Stabilization Device
CS001A0010	10 mm DIAM™ Spinal Stabilization Device
CS001A0012	12 mm DIAM™ Spinal Stabilization Device
CS001A0014	14 mm DIAM™ Spinal Stabilization Device

VI. ALTERNATE PRACTICES AND PROCEDURES

There are several other alternatives for the treatment of primary low back pain secondary to lumbar DDD, which is a multi-factorial and often nonreversible pathologic condition. Non-surgical alternatives include, but are not limited to, patient education, prescribed medications, physical therapy, spinal injections, braces, exercise programs, or rest. Surgical alternatives include, but are not limited to, fusion using various bone grafting techniques and devices (including but not limited to interbody fusion devices and posterior pedicle screw/rod systems), or non-fusion surgeries such as lumbar total disc replacement devices. The DIAM™ Spinal Stabilization System is intended to treat subjects with primary discogenic low back pain requiring treatment at a single level (L2-L5) who are not yet suitable candidates for more invasive treatments including lumbar total disc replacement (TDR) or lumbar fusion. Each treatment option has advantages and disadvantages. Patients should fully discuss the available alternatives with his or her physician to select the option that best meets their clinical condition, lifestyle and expectations.

VII. MARKETING HISTORY

The DIAM™ Spinal Stabilization System has been marketed outside the United States since 1998. The device is currently distributed on five continents, in countries/regions including but not limited to, Brazil, Canada, European Union, Korea, and Mexico. The DIAM™ Spinal Stabilization System has not been withdrawn from distribution/ marketing in any country for safety or effectiveness reasons.

VIII. POTENTIAL ADVERSE EVENTS

Below is a list of the potential adverse events (i.e., complications) identified from the DIAM™ Spinal Stabilization System clinical study results, approved device labeling for other interspinous devices, published literature, and international post-marketing data including: 1) those associated with any surgical procedure; 2) those potentially associated with lumbar spinal surgery using a posterior approach; and, 3) those potentially associated with lumbar spinal implants and, in particular, with interspinous devices including the DIAM™ Spinal Stabilization System. In addition to the risks listed below, there is also the risk that the procedure may not be effective in relieving symptoms and may cause

worsening of symptoms. Additional surgery may be required to correct some of the adverse effects.

Risks Associated with any Surgical Procedure

General surgical risks include, but are not limited to:

- Anesthesia complications including allergic reaction, anaphylaxis, or other reactions to anesthesia
- Anemia
- Blood loss/hemorrhage possibly requiring a blood transfusion with possible transfusion reaction
- Myocardial infarction
- Blood clots including pulmonary emboli
- Phlebitis
- Injury to blood vessels
- Septicemia
- Cerebral Vascular Accident (i.e., stroke)
- Pulmonary complications including atelectasis, pneumothorax or pneumonia, pulmonary edema and respiratory distress
- False aneurysm
- Infection (wound, local, and/or systemic) abscess, or cellulitis, localized or systemic, fever
- Soft tissue damage or fluid collections, including edema, hematoma or seroma, which may require drainage, aspiration, or debridement or other intervention
- Surgical wound dehiscence, necrosis, or scarring of tissue around the wound
- Impairment of the gastrointestinal system including ileus or bowel obstruction, nausea or vomiting
- Impairment of the genitourinary system including incontinence, bladder dysfunction, urinary tract infection, or reproductive system complications
- Neurological complications including nerve damage, paralysis, seizures or convulsions, changes to mental status, or reflex sympathetic dystrophy
- Numbness
- Complications of pregnancy including miscarriage or congenital defects
- Pain at surgical site
- Death

Risks Associated with Lumbar Spine Surgery

Risks associated with lumbar spine surgery include, but are not limited to:

- Risks to neurological structures:
    - Dural tear, dural leak and/or dural injury with or without CSF leakage
    - Arachnoiditis
    - Neurologic deterioration - injury to nerves or nerve roots associated with the spinal cord (resulting in pain, weakness, paralysis (partial or complete), paresthesia, altered reflexes, numbness, tingling, or other changes in sensation)
    - Gait disturbance

    - Cerebrospinal fluid leakage
    - Cerebrospinal fistula
    - Reflex Sympathetic Dystrophy (RSD)
- New or worsened back or leg pain
- Damage to nerves, blood vessels, and nearby tissues
- Impaired muscle or nerve function
- Epidural bleeding, hematoma, or fibrosis
- Surgery at incorrect levels
- Osteolysis
- Loss of bowel or bladder function
- Fracture of the vertebrae, spinous process, or other damage to bony structures during or after surgery
- Postoperative muscle and tissue pain
- Development of degenerative changes at adjacent levels
- Scarring or soft tissue damage
- Spinal instability
- Post-surgical spondylolisthesis (vertebral slippage)
- Retrolisthesis
- Spinal stenosis (narrowing of the spinal canal)
- Spondylosis
- Infection of the bone, or surrounding soft tissue
- Perineural fibrosis
- Pain and discomfort associated with the presence of implants
- Pain and discomfort associated with the surgical procedure (e.g., cutting of muscles, ligaments, and tissue) and healing
- The spine may undergo adverse changes or deterioration including loss of proper spinal curvature, correction, height, and/or reduction, or malalignment, and another surgery may be required
- Adverse bone/implant interface reaction
- Instruments breaking or malfunctioning which may cause damage to the operative site or adjacent structures

<u>Risks Associated with Lumbar Spine Implants (including the DIAM™ Spinal Stabilization System)</u>

Risks associated with lumbar spine implants such as DIAM™ Spinal Stabilization System include, but are not limited to:

- Sensitivity or allergy to the implant material [Polyethylene Terephthalate (PET), silicone, and titanium]
- 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

- Sizing issues with components
- Uncrimping of the needle instrument leading to increased operation time
- Anatomical or technical difficulties implanting the device
- Spinous process fracture
- Spinous process bone resorption
- Bone loss or decrease in bone density, possibly caused by stress shielding
- Production of wear debris which may damage surrounding soft tissues including muscle or nerve
- Foreign body reaction to implant material or material debris and/or autoimmune disease
- Deep infection
- Formation of scar tissue at implant site
- Implantation at the wrong spinal level
- 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
- Reoperation including revision, removal, or supplemental fixation
- Loosening, fatigue, deformation, breakage or disassembly of the implant, which may require another operation to remove the implant and may require another treatment method.

For the specific adverse events (AEs) that occurred in the clinical study, please see **Section X** below.

IX. SUMMARY OF NON-CLINICAL STUDIES

Several non-clinical tests were conducted to characterize the performance of the DIAM™ Spinal Stabilization System. Where relevant, all tests were performed using finished components, devices, or representative test specimens manufactured in accordance with current specifications. The non-clinical tests are outlined below.

A. Laboratory Studies

The laboratory studies conducted are listed below. Table 2 provides further details on methods, acceptance criteria, and results.

- Static Axial Compression
- Static Compressive Creep
- Axial Compression Fatigue
- Static Tension
- Tension Fatigue
- Static and Fatigue Testing of Accelerated Aged DIAM™ Devices
- Rotational Fatigue
- Axial Grip
- Wear Debris Analysis

- Biomechanical Evaluation

Table 2: Laboratory Studies on DIAM™ Spinal Stabilization System

Test	Methods	Acceptance Criteria	Results
Static Axial Compression	Six samples of the smallest (8 mm) DIAM™ implant were tested under static axial compression loading between metallic test fixtures intended to mimic the geometry of spinous processes. Testing was performed under a displacement rate of 25 mm/min until just before fixture-to-fixture contact was reached at which time the peak load required to achieve this displacement was recorded.	Maximum compressive strength should exceed expected *in vivo* spinous process fracture load of 339 N[1].	Average peak load achieved was 2199 ± 82.6 N, which was greater than the acceptance criterion. No damage to the devices was observed during testing. Average device stiffness observed between 0 N and 500 N (clinically relevant loading range) was 76.3 ± 9.8 N/mm. There was no acceptance criterion associated with device stiffness.
Static Compressive Creep	Compressive creep was measured by applying a range of physiological compressive loads (270 N, 360 N, 450 N) were applied to the worst-case (8 mm) DIAM™ device to quantify the strain observed on the device. Three DIAM™ devices were tested under the static loads listed above (n=1 for each load) in phosphate buffered saline at 37°C. Static loads were applied for 1000 hours.	The max % strain for each static load level shall be below the failure limit of 90%. The % strain vs. time should exhibit a projection toward an asymptotic strain steady state. The % strain at the projected steady state should be below the failure limit of 90%.	The maximum % strains and steady state strains for all three (n=3) static load levels were below the acceptance criteria of 90%. 270 N – 16.2% strain 360 N – 15.0% strain 450 N – 16.1% strain
Axial Compressive Fatigue	Six samples of the smallest (8 mm) and thirteen samples of the largest (14 mm) DIAM™ device were subjected to dynamic axial compression loading between metallic test fixtures intended to mimic the geometry of the spinous processes. Testing	Two samples of each device size should run out to 10 MC at a load level equal to or above the expected *in vivo* spinous process fracture load of 339 N[1] without failure.	Two 8 mm devices ran out to 10 MC at 480N Two 14 mm devices ran out to 10 MC at 500 N. The acceptance criterion was exceeded for both device sizes.

Test	Methods	Acceptance Criteria	Results
	was conducted in phosphate buffered saline at 37°C at 8 Hz with R=10 to 10 million cycles (MC) or device failure.		Wear of the outer PET sheath at the fixture contact point was observed for non-runouts.
Gravimetric Wear Debris Analysis	Gravimetric wear analysis was performed on devices that achieved dynamic axial compression loading to 10 MC.	This evaluation was performed for characterization purposes only.	For the largest runout loads at each size, the average decrease in weight was 0.18% for the small (8 mm) and 0.26% for the large (14 mm) implants.
Wear Debris Analysis (Axial Compression Fatigue Samples)	A particle analysis per ASTM F1877 was performed on wear debris from the DIAM™ device collected in the saline bath after axial compression fatigue testing.	This test was performed in order to characterize the particulate wear debris generated by the DIAM™ device. No specific acceptance criteria are associated with this evaluation.	The compositions of the particles were polymeric-based, consistent with PET, and Silicone. The average size of particles in the sample was 1.24 microns in diameter using SEM analysis. The particles were generally oval in shape with an average aspect ratio of 1.9.
Static Tension	Six samples of the smallest (8 mm) DIAM™ device were subjected to static tension loading after attachment to metallic test blocks intended to mimic the geometry of the spinous processes. Tensile loading was applied in displacement control at a rate of 25 mm/min until failure. Testing was conducted in phosphate buffered saline at 37°C.	Maximum compressive strength should exceed expected *in vivo* spinous process fracture load of 339 N[1].	Average peak load achieved was 401 ± 50 N. All samples exceeded the acceptance criterion. Failure mode for all devices was slippage of one or both tethers.
Tension Fatigue	Six samples of the smallest (8 mm) DIAM™ device were subjected to dynamic tension loading after attachment to metallic test fixtures intended to mimic the geometry of the spinous processes. Testing was	The DIAM™ device must be able to withstand a tensile fatigue load of 100 N to 10 MC.	Two devices ran out to 10 MC at 155 N without any visual failures. Tether detachment from the spacer was the failure mode for non-runouts.

Test	Methods	Acceptance Criteria	Results
	conducted in phosphate buffered saline at 37°C at 8 Hz with R=10 to 10 MC or device failure.		
Static Axial Compression (10Yr Accelerated Aged Implants)	Five accelerated aged samples of the smallest (8 mm) DIAM™ implant were tested under static axial compression loading between metallic test fixtures intended to mimic the geometry of spinous processes. Testing was performed in phosphate buffered saline at 37°C under a displacement rate of 25 mm/min until just before fixture-to-fixture contact was reached at which time the peak load required to achieve this displacement was recorded.	The mean static compression stiffness must be sufficiently equivalent to previous testing of unaged DIAM™ samples.	The average static axial compression stiffness was 77.6 ± 3.8 N/mm which was considered sufficiently equivalent to previous testing of unaged DIAM™ devices.
Axial Compression Fatigue (10Yr Accelerated Aged Implants)	Seven accelerated aged samples of the smallest (8 mm) DIAM™ device were subjected to dynamic axial compression loading between metallic test fixtures intended to mimic the geometry of the spinous processes. Testing was conducted in phosphate buffered saline at 37°C at 8 Hz with R=10 to 10 MC or device failure.	Two samples should run out to 10 MC at a load level equal to or above the expected *in vivo* spinous process fracture load of 339 N[1] without failure.	Two compressive fatigue runouts were achieved at 360 N which exceeds the acceptance criterion. Tearing of the outer sheath was the failure mode for non-runouts.
Tension Fatigue (10Yr Accelerated Aged Implants)	Three accelerated aged samples of the smallest (8 mm) DIAM™ device were subjected to dynamic tension loading after attachment to metallic fixtures intended to mimic the geometry of the spinous processes. Testing was conducted in	The tensile fatigue runout load must be equal to or exceed a load of 100 N.	Two tensile fatigue runouts were achieved at the required load of 100 N. Tether breakage was the failure mode for the non-runout.

Test	Methods	Acceptance Criteria	Results
	phosphate buffered saline at 37°C at 8 Hz with R=10 to 10 MC or device failure.		
Rotational Fatigue	Two samples of the smallest (8 mm) DIAM™ device were tested in rotational fatigue testing which was adapted from ASTM F2077. Testing was conducted in phosphate buffered saline at 37°C. A 150 N compressive load was applied to each sample while the superior fixture was rotated ± 3° at a rate of 8 Hz until 10 MC were reached or failure of the device occurred.	The devices shall achieve runouts to 10 MC of axial rotation ± 3° and a compressive load of 150 N without exhibiting gross implant failure.	The two samples reached 10 MC under the conditions described without experiencing gross failure. Minor damage was observed on the device sheath at the fixture contact point.
Axial Grip (Tether and Crimp)	Five flat tethers and crimps of the DIAM™ device were tested in isolation from the core under tensile loading to determine the force necessary for the tether to slip in the crimp. Testing was conducted in displacement control at 0.25 mm/sec in ambient lab conditions.	The static axial grip strength of the crimp on the flat tether must be sufficiently equivalent or greater than the axial grip strength of the crimp on round tethers of the previous DIAM™ design.	The average static axial grip strength of the crimp on the flat tethers was 91.6 ± 35.5 N. This result was sufficiently equivalent to the static axial grip strength of the crimp on the round tether.
Static Tension (Tether Only)	Five flat tethers of the DIAM™ device were tested under static tension loading in isolation from the core. Testing was conducted in displacement control at 0.25 mm/sec in ambient lab conditions.	The static tensile strength of the flat tether must be sufficiently equivalent or greater than the strength of the round tethers of the previous DIAM™ design.	The average static tensile strength of the flat tethers was 526.86 ± 48.47 N. This result exceeded the static tensile strength of the round tether.
Wear Debris Analysis (Explants)	Wear debris from the explanted DIAM™ devices was characterized in accordance with ASTM F1877.	This test was performed in order to characterize the particulate wear debris generated by the DIAM™ device. No specific	Wear particulate characterization was consistent with prior in vitro and in vivo evaluations.

Test	Methods	Acceptance Criteria	Results
		acceptance criteria are associated with this evaluation.	
Biomechanics	Six male cadaveric lumbar spine specimens (L1 – sacrum) were implanted with a DIAM™ device at L4-L5. Range of motion (ROM) data were collected at L3/L4, L4/L5 and L5/S1 (index and adjacent levels) in flexion-extension (±6 Nm) with and without a 450 N static pre-load (follower load), lateral bending (±5 Nm) without a follower load, and axial rotation (±4 Nm) without a follower load. The above ROM measurements were made in four conditions: intact spine, after facetectomy at L4-L5, after discectomy at L4-L5, and after DIAM™ implantation at L4-L5 (after facetectomy and discectomy).	This study was performed to characterize the stabilizing effects of the DIAM™ implant in each of the three standard directions of rotation (flexion-extension, lateral bending, and axial rotation). No specific acceptance criteria were associated with this evaluation.	The study showed reduction of flexion-extension ROM (with and without follower load) at L4-L5 after DIAM™ implantation as compared to the intact and destabilized conditions. Lateral bending and axial rotation ROM were not significantly impacted by implantation of the DIAM as compared to the intact and destabilized conditions. Implantation of DIAM™ appeared to have minimal impact on ROM measurements at adjacent levels.

[1] Shepherd, Duncan ET, et al. "Spinous process strength." Spine 25.3 (2000): 319-323.

B. Animal Studies

The following animal studies were conducted:

- Rabbit Wear Debris Study
- Sheep Implantation Study

Details on the studies are provided below.

Evaluation of Local and Systemic Effects of Wear Debris Particulate from DIAM™ Following Implantation in Rabbits

An *in vivo* study was performed to evaluate local and systemic responses to implantation of particulate wear debris from the DIAM™ Spinal Stabilization System in the lumbar spine of New Zealand White Rabbits. The animals were sacrificed at 3- and 6-month timepoints. The test article utilized was wear particles composed of the PET woven fabric jacket and silicone core of the DIAM™ implant. Evaluations included clinical and

neurological observations, hematology, serum chemistry, and gross pathology and histopathology of the implantation sites and organs.

The test article wear debris was classified as a slight irritant as compared to the sham control at each timepoint. Interspinous implantation of the test article for three (3) and six (6) months resulted in inflammation that reached a steady state of biological response by the 6-month timepoint. There were no indications of systemic toxicity, and no systemic presence of test article wear debris.

Biocompatibility Evaluation of DIAM™ Spinal Stabilization System Using Sheep Model

An *in vivo* study was performed to evaluate the long-term interactions between the materials of the DIAM™ implant and the interspinous process tissues. The DIAM™ test article was implanted in the lumbar spine of adult sheep. The animals were sacrificed at 6- and 12-month timepoints. Evaluations included clinical observations and gross pathology and histopathology of the implantation sites and organs.

There were no wound infections and there were no neurological symptoms associated with the surgery. At necropsy, there were no signs of gross tissue reaction surrounding the implants. Histopathology showed chronic reactive fibrosis around the implant and vertebral spinous processes, as well as reactive changes in the sub-lumbar lymph nodes with no foreign implant material found. There were no changes in major organs that were associated with the implant.

C. Additional Studies

Additional studies conducted are listed below. Table 3 provides further details on the methods and results.

- MR Compatibility
- Biocompatibility/Toxicity
- Device Sterilization
- Packaging/Shelf-Life Validation

Table 3: Additional Non-Clinical Studies on the DIAM™ Device

Test	Methods and Results
Biocompatibility	Biocompatibility evaluations for the DIAM™ Spinal Stabilization System were conducted based on the FDA guidance, "Use of International Standard ISO 10993-1, 'Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process.'" Testing was designed to evaluate the device's cytotoxicity, irritation, sensitization, acute systemic toxicity, sub-chronic toxicity, chronic toxicity, material mediated pyrogenicity, genotoxicity (bacterial reverse mutation, mammalian chromosomal aberration, and mouse bone marrow micronucleus), implantation, and carcinogenicity. Alternative assessments or testing methods (per ISO 10993) were utilized where appropriate.

Test	Methods and Results
	Results of testing in combination with toxicological risk evaluation demonstrated biocompatibility in line with the requirements of ISO 10993-1 for a permanent implant in contact with tissue/bone. Biocompatibility assessments were also performed on the needle leader instrument utilized during the DIAM™ implantation procedure, and adequate biocompatibility was demonstrated
Sterilization Validation	Full sterilization validation has been conducted for the DIAM™ implant, including the needle leader, per ISO 11137-1 and ISO 11737-2 to establish 25kGy as the sterilization dose to achieve a Sterility Assurance Level (SAL) of at least 10^{-6}.
Packaging and Shelf-Life Validations	Shelf life and transit validation studies, including assessments of packaging seal integrity, real time and accelerated aging testing, were conducted to demonstrate that the device packaging can maintain a sterile barrier over a 1-year shelf life.
MR Compatibility	Non-clinical testing was performed to evaluate the safety and compatibility of the DIAM™ Spinal Stabilization System in the MR environment. Testing completed included: Magnetically Induced Displacement Force (ASTM F2052-06), Magnetically Induced Torque (ASTM F2213-06), Extent of Imaging Artifact (ASTM F2119-07), and RF-Induced Heating (ASTM F2182-11a). The non-clinical testing demonstrated that the DIAM™ device is MR Conditional. A person with the DIAM™ device may be safely scanned under the conditions shown below in **Table 4**.

Table 4: MR Compatibility Conditions

Static Magnetic Field Strength (B_0)	1.5T or 3T
Maximum Spatial Field Gradient	30 T/m (3000 Gauss/cm)
RF Excitation	Circularly polarized (CP)
RF Transmit Coil Type	Integrated whole body transmit/ Receive coil
Operating Mode	Normal or first level controlled operating mode
Maximum Whole-Body SAR	4 W/kg
Scan Duration	4 W/kg whole-body average SAR for 60 minutes of continuous RF (a sequence or back-to-back series/ scan without breaks).
Scan Region	Any landmark is acceptable
MR Image Artifact	The maximum artifact beyond the implant was 5 mm for the spin echo sequence and 9 mm for the gradient echo sequence in a 3-Tesla MR system (GE Signa HDxt MR System). Therefore, optimization of MR imaging parameters to compensate for the presence of this device may be necessary. The presence of other implants or the health state of the patient may require a modification of the MR conditions.
During an MRI, the patient may notice a warming sensation around the implant or feel a tingling sensation. If the warming or tingling sensation is uncomfortable the patient should communicate this to the MR technologist, the MRI should be stopped, and the settings adjusted to reduce or eliminate the sensation. The highest temperature change above the background observed in non-clinical testing was +3.2°C (associated with specific conditions listed above).	

If information about a specific parameter is not included, there are no conditions associated with that parameter.

X. SUMMARY OF PRIMARY CLINICAL STUDY

A clinical study was conducted to establish a reasonable assurance of safety and effectiveness of the DIAM™ Spinal Stabilization System for treatment of primary low back pain at a symptomatic, single level (L2-L5) in the US under Investigational Device Exemption (IDE) G050025. Data from this clinical study were the basis for the PMA approval decision. This primary dataset was supplemented with data provided from a long-term follow-up (LTFU) study, 'DIAM™ Spinal Stabilization System Long Term Follow Up Clinical Plan' (NCT 05201573). The goal of this additional study was to collect LTFU data on subjects who participated in the DIAM™ Spinal Stabilization System IDE Study and received the investigational device. A large cohort of subjects treated with the investigational device during the IDE study were evaluated at a mean final follow-up of 11.5 years. A summary of the clinical study conducted under G050025 is presented directly below. A summary of data collected in the LTFU study is presented in Section XII.

A. Study Design

Subjects were treated between 2007 and 2014. The database for this PMA reflected data collected through 2018 and included 283 subjects. The study was a prospective, multi-center, open label, randomized, controlled clinical trial comparing the DIAM™ Spinal Stabilization System to a control group of subjects treated with non-operative care. Subjects were randomized in a ratio of 2:1 to receive either surgical implantation of the investigational DIAM™ Spinal Stabilization System or non-operative care (control group). The control group received an individualized non-operative regimen of standard of care treatments tailored specifically to each individual subject's needs. Non-operative care included patient education, as well as physical therapy, spinal injections, and medications. Control subjects were permitted to cross over to surgical treatment with the DIAM™ Spinal Stabilization System after 6-months of follow-up if their Oswestry Disability Index (ODI) score remained above 30, and a 15-point improvement in ODI was not achieved from baseline.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in this clinical study was limited to subjects that met the following inclusion criteria:

- Has moderate low back pain secondary to lumbar degenerative disc disease at a single level from L2-L5. Low back pain is defined as persistent back pain, with or without radicular pain, with current episode of less than one year duration. Degenerative disc disease is confirmed by patient history, physical examination, and radiographic studies

with one or more of the following factors (as measured radiographically by MRI scans or x- rays):
  - Decreased disc height >2mm, compared to the disc space at the next adjacent (superior or inferior, whichever has greater disc height) spinal level;
  - Scarring/thickening of the ligamentum flavum, annulus fibrosis, or facet joint capsule;
  - Herniated nucleus pulposus.
- Is 18-70 years of age, inclusive, and is skeletally mature.
- Has pre-treatment ODI score ≥ 30.
- Has pre-treatment back Numerical Rating Scale (NRS) pain score of ≥ 8 based on the Pre-Treatment Back and Leg Pain Questionnaire (Back Pain Intensity + Back Pain Frequency).
- Has been treated non-operatively (e.g., bed rest, physical therapy, medications, TENS, manipulation, and/or spinal injections) within a period of at least 6 weeks and not more than 6 months prior to enrollment in the clinical study.
- If of child-bearing potential, patient is not pregnant or nursing and agrees not to become pregnant during the study period.
- Is willing and able to participate in either of the randomized treatments for the duration of the study follow-up period. If the patient is randomized to the investigational group, he/she is willing to undergo surgery and receive the DIAM™ device. If the patient is randomized to the control group, he/she is willing to undergo all four non-operative treatments.
- Is willing and able to comply with the study plan and able to understand and sign the Patient Informed Consent Form.

Subjects were <u>not</u> permitted to enroll in this clinical study if they met any of the following exclusion criteria:

- Has disc height loss > 67% at the involved level, compared to the next adjacent (superior or inferior, whichever has greater disc height) spinal level.
- Has arachnoiditis.
- Has a primary diagnosis of a spinal disorder other than degenerative disc disease at the involved level.
- Requires treatment of degenerative disc disease at more than one lumbar level.
- Has had all of the following non-operative treatments (prescribed medications, active physical therapy, spinal injections, and patient education) within the past 6weeks.
- Has a sequestered herniated nucleus pulposus.
- Has had any previous surgery at the involved or adjacent spinal levels (including procedures such as a rhizotomy).
- Has received any intradiscal ablation therapy, such as intradiscal electrothermal therapy (IDET).
- Has congenital or iatrogenic posterior element insufficiency (e.g., facet resection, spondylolysis, pars fracture, or spinal bifida occulta).

- Has back pain (with or without leg, buttock, or groin pain) that is not alleviated in any spinal position.
- Has a motor deficit of the lower extremity.
- Has cauda equina syndrome.
- Has compression of nerve roots with neurogenic bowel (fecal incontinence) or bladder (urinary retention or incontinence) dysfunction.
- Has been previously diagnosed with clinically significant peripheral neuropathy.
- Has significant vascular disease causing vascular claudication.
- Has a medical contraindication that prevents the patient from receiving spinal injections (i.e., allergy to contrast media used to aid in placement of the needle in the epidural space).
- Has anterolisthesis with more than 2mm of translation at the involved level.
- Has evidence of prior fracture or trauma to the L1, L2, L3, L4, or L5 levels in either compression or burst.
- Has lumbar scoliosis with a Cobb angle of greater than 15°.
- Has lumbar kyphosis or flat back syndrome.
- Has sustained a hip fracture within the last year.
- Has any of the following (if "Yes" to any of the below risk factors, a lumbar spine DEXA Scan will be required to determine eligibility):
    - Previous diagnosis of osteoporosis, osteopenia, or osteomalacia.
    - Postmenopausal non-black female over 60 years of age who weighs less than 140 pounds.
    - Postmenopausal female who has sustained a non-traumatic hip, spine, or wrist fracture.
    - Male over the age of 60 who has sustained a non-traumatic hip or spine fracture.
    - If the level of DEXA T-score is -1.0 or lower (i.e., - 1.5, -2.0, etc.), the patient is excluded from the study.
- Has obesity defined by BMI greater than or equal to 40.
- Has a documented allergy to silicone, polyethylene, titanium or latex.
- Has overt or active bacterial infection, either local or systemic, and/or potential for bacteremia.
- Has a suppressed immune system or has taken steroids daily for more than one month within the last year (excluding low dose inhalers for the treatment of asthma).
- Has a history of autoimmune disease.
- Has presence of active malignancy or prior history of malignancy within the last 5 years (except for basal cell carcinoma of the skin).
- Has presence or prior history of a spinal malignancy.
- Has chronic or acute renal and/or hepatic failure or prior history of renal and/or hepatic parenchymal disease.
- Has any disease (e.g., neuromuscular disease) that would preclude accurate clinical evaluation of the safety and effectiveness of the treatment regimens in this study.

- Has received treatment with an investigational therapy (device and/or pharmaceutical) within 30 days prior to entering the study or such treatment is planned during the 24 months following enrollment in the study.
- Has an implantable metal device (e.g., stimulator, pacemaker) and is unable to have an MRI.
- Is an alcohol and/or drug abuser, as defined by currently undergoing treatment for alcohol and/or drug abuse.
- Is mentally incompetent. If questionable, obtain psychiatric consult.
- Has a Waddell Signs of Inorganic Behavior score of 3 or greater.
- Is a prisoner.

2. Follow-up Schedule

All subjects were scheduled to return for follow-up examination at 6 weeks, 3 months, 6 months, 12 months, 24 months post-operatively. Pre-operatively, subjects were confirmed to meet the enrollment criteria, to have given Informed Consent, along with other pre-treatment evaluations. Post-operatively, the objective parameters measured during the study included ODI, back and leg pain assessment, neurological assessment, and radiological evaluation. AEs and complications were recorded at all visits. **Table 5** includes detailed information regarding the schedule of study assessments and data collected at each timepoint. The key timepoints are shown below in the tables summarizing safety and effectiveness. Crossover subjects were assessed at the same follow-up timepoints, after being implanted with the DIAM™ Spinal Stabilization System, as investigational and control subjects originally enrolled in the study. Therefore, all presentations of safety and effectiveness results for crossover subjects below represent data collected from the point the subject received the crossover treatment. For example, 6-month crossover data represent results 6 months after subjects received the crossover treatment and not 6 months after crossover subjects were originally enrolled in the control arm of the study.

Table 5: Schedule of Study Assessments

Procedure	**Study Time Period**							
	Pre-Operative/ On Treatment	**Surgery / Hospital / Discharge#**	**6Wks ± 2Wks**	**3M ± 2Wks**	**6M ± 1M**	**12M ± 2M**	**24M ± 2M & Annually Until Required Follow-Up Complete**	**Additional Evaluation*** **
Pre-Treatment Information								
Confirm subject eligibility	X							

Procedure	Study Time Period							
	Pre-Operative/ On Treatment	**Surgery / Hospital / Discharge#**	**6Wks ± 2Wks**	**3M ± 2Wks**	**6M ± 1M**	**12M ± 2M**	**24M ± 2M & Annually Until Required Follow-Up Complete**	**Additional Evaluation*** **
Obtain informed consent	X							
Case Report Forms								
Medical history	X							
Pre-treatment concomitant medications	X							
Neurological status	X	X	X	X	X	X	X	X
Surgery data# and hospital discharge		X						
Non-operative treatment data (control only)	X		X	X	X	X	X	
Patient data	X		X	X	X	X	X	X
Additional medications / injections (if applicable)			X	X	X	X	X	X
Patient survey	X		X	X	X	X	X	X
ODI	X		X	X	X	X	X	X
Back & leg pain (NRS)	X		X	X	X	X	X	X
SF-36	X		X	X	X	X	X	X
Adverse event assessment (as needed)		X	X	X	X	X	X	X
Study deviation-patient or site (if applicable)	X	X	X	X	X	X	X	
Patient disposition**	X	X	X	X	X	X	X	
Radiologic Procedures								
Anterior/posterior	X	X	X	X	X	X	X	
Lateral	X	X	X	X	X	X	X	
Lateral Flexion/extension	X		X	X	X	X	X	
MRI	X					X	X*	
Lumbar spine DEXA scan+	X							

* Only collected through 24 months

** Filled out only once at time of subject completion or withdrawal

*** Additional Evaluation CRF's were required for subjects who were scheduled for surgery based on the unsatisfactory outcome of their original Treatment if the subject had not had an evaluation within the last 2 months prior to surgery.

applies to investigational subjects and crossover subjects
+ as required by exclusion criteria #22.

3. Clinical Endpoints

With regards to safety, the DIAM™ Spinal Stabilization System was assessed by comparison to the non-operative care control group with respect to the nature and frequency of adverse events (overall and in terms of severity and relationship to the implant), subsequent index level surgical procedures, and maintenance or improvement in neurological status. Given the ability of control subjects to cross over to the investigational group, all data available for subjects treated with the investigational device were also assessed.

With regards to effectiveness, the DIAM™ Spinal Stabilization System was assessed by comparison to the non-operative care control group with respect to a primary composite endpoint, as described below. Effectiveness was further assessed by assessing improvement in ODI, absence of Serious AEs (SAEs) that were treatment associated, and absence of subsequent surgical procedures at the index level.

Primary Endpoint
The primary composite endpoint was defined as follows:

- Pain/disability success measured as greater than or equal to 15-point improvement in ODI score relative to baseline
- No SAE classified as "implant associated," "implant-/surgical procedure associated," or non-operative treatment associated, and
- No additional surgical procedure at the involved level classified as a failure.

Subject success was evaluated using the primary composite endpoint above at 24 months post-operatively (Month 24).

Secondary Endpoints
Additional secondary endpoints were evaluated to further define the safety and effectiveness of the DIAM™ Spinal Stabilization System. Secondary effectiveness variables include, but were not limited to:

- ODI
- Medical Outcomes Study 36-Item Short Form Health Survey (SF-36) Physical Component Summary (PCS)
- NRS Back Pain Intensity
- Radiographic Evaluations
  - Disc Height
  - Intervertebral Angle and Angular Motion
  - Implant Location

    - Integrity of Spinous Process
- Subject Satisfaction with Study Treatment
- Subject Global Perceived Effect
- Work Status

B. Accountability of PMA Cohort

At the time of database lock, 311 subjects were enrolled in the PMA study, with n=207 randomized to the investigational group, and n=104 randomized to the non-operative control group (Intent-to-Treat (ITT) population). 90.7% (253/279) of subjects were available for analysis at Month 24.

A total of 59 subjects randomized to the non-operative control group met the pre-defined conditions and elected to crossover and receive the investigational device. This subset of subjects was then followed for at least 24 months post-operatively, using the same follow-up timepoints as the originally enrolled subjects, and assessed for primary overall success separately from the investigational cohort. At Month 24, 98.3% (58/59) of the crossover subjects were available for analysis of the Composite Clinical Success (CCS).

A summary of the subject accounting and follow-up compliance (**Table 6**) and subject accounting tree (**Figure 2**) are presented below, followed by a description of the analysis populations.

Table 6: Subject Accounting and Follow-up Compliance for Investigational, Control, and Crossover mITT-Followed

	Month 12			Month 24		
	I	C	Crossover	I	C	Crossover
Accounting						
(1) Theoretical follow-up*	182	97	59	182	97	59
(2) Cumulative Death	0	0	0	0	1	0
(3a) Crossover	0	48	0	0	55	0
(3b) Cumulative Non-Crossover SSI Failures	6	7	1	12	9	3
(4) Not Yet Overdue	0	0	0	0	0	0
(5) Deaths + SSI Failures + Crossover among Theoretically Due	6	55	1	12	65	3
(6) Expected Due [(6)=(1)-(4)-(5)][A]	176	42	58	170	32	56
(7) SSI Failures + Crossover among Theoretically Due	6	55	1	12	64	3
(8) Expected Due + SSI Failures + Crossover among Theoretically Due [(8)=(6)+(7)]	182	97	59	182	96	59
All Evaluated Accounting (Actual[B])						
(9) Procedures with any clinical data in interval[C]	170	33	55	156	20	54
(10) Visit Compliance (%)[D]	97%	79%	95%	92%	63%	96%
(11) ODI Evaluation (censored for SSI)	170	33	55	156	20	54
(12) Back Pain Evaluation (censored for SSI)	169	33	55	155	20	53
(13) Leg Pain Evaluation (censored for SSI)	170	33	55	156	19	53
(14) Neurological Evaluation (not censored for SSI)	174	39	56	166	26	57
(15) Composite Clinical Success (CCS)	176	88	57	169	84	58
(16) Actual[B] % Follow-up for CCS[E]	97%	91%	97%	93%	88%	98%
Within Window Accounting (Actual[F])						
(17) Procedures with any clinical data in interval[C]	163	27	53	146	18	50
(18) Visit Compliance (%)[D]	93%	64%	91%	86%	56%	89%
(19) ODI Evaluation (censored for SSI)	163	27	53	146	18	50
(20) Back Pain Evaluation (censored for SSI)	162	27	53	145	18	49
(21) Leg Pain Evaluation (censored for SSI)	163	27	53	146	17	49
(22) Neurological Evaluation (not censored for SSI)	167	33	54	156	24	53
(23) Composite Clinical Success (CCS)	169	83	55	160	82	54
(24) Actual[F] % Follow-up for CCS[E]	93%	86%	93%	88%	85%	92%

* Note, 56 control subjects crossed over prior to Month 24 (n=1 had a treatment surgery first, and is captured in row (3b)). Three (3) additional subjects crossed over after Month 24 (Day 790); therefore, all 59 crossover subjects are included above.

[A] Includes subjects with no SSI prior to the visit specified.

[B] Patients with any follow-up data reviewed or evaluated by investigator ("all evaluated" accounting).

[C] Defined as ODI, back pain, or leg pain data after censoring for SSI.

[D] Denominator is row (6).

[E] Denominator is row (8).

[F] Patients with complete data for each endpoint, within window.

(1) Theoretical follow-up: The theoretical follow-up is the number of subjects that would be theoretically due for Month 12 and Month 24 follow-up before database closure. All subjects in the mITT-Followed population were theoretically due.
(2) Cumulative deaths: Cumulative deaths up to the date of the exact anniversary defining the current interval.
(3a) Crossover: Subjects who had crossover surgery prior to specified visit and the end of visit window.
(3b) Cumulative Non-Crossover SSI Failures: Subjects who had any non-crossover SSI prior to specified visit and the end of visit window. This includes revisions, removals, re-operations, supplemental fixations, and treatment surgeries.
(4) Not Yet Overdue: Includes subjects whose clinical data has not been collected, but they are in between surgical/treatment anniversary and protocol specified follow-up window. Such subjects may not yet be observed, and follow-up compliance estimates account for this by removing such subjects from the denominator when determining compliance ratios. There are no subjects Not Yet Overdue at the time of this database lock.
(5) Deaths + SSI Failures + Crossover among Theoretically Due: This row records the sum of deaths and all SSI failures, including crossovers. The SSIs, including crossovers, must have occurred prior to the specified visit and before the end of the visit window to be counted in this row. This row is subtracted from theoretically due to determine the number expected due for clinical evaluation.

(6) Expected Due: This row is the number of subjects expected for a given time interval. This includes the theoretical number of subjects due to be evaluated minus the number who died, were SSI/Crossover failures, or were not yet overdue. **Expected = Theoretical – [Death + Failures + Not yet overdue]**. This row serves as the denominator for Visit Compliance and includes subjects lost to follow-up.
(7) SSI Failures + Crossover among Theoretically Due: SSI Failures, including crossovers, that need to be "added back" to the number of expected due to serve as the denominator for CCS counts when determining CCS follow-up compliance.
(8) Expected Due + SSI Failures + Crossover among Theoretically Due: Expected due plus theoretical due failures is computed by adding rows (6) and (7). This row serves as the denominator for CCS outcomes because CCS status is known for subjects with an SSI.
(9) and (17) Procedures with any clinical data in interval: These rows indicate the number of subjects with any ODI, back pain, or leg pain data after SSI censoring for all evaluated subjects **(9)** and for all subjects that are within window **(17)** among expected due subjects.
(10) and (18) Visit Compliance (%): These rows indicate the percentage of subjects compliant with the specified visit scheduled. **(10)** is the percentage of all evaluated among expected due subjects [**(9)** out of **(6)**], and **(18)** is the percentage of subjects within window among expected due subjects [**(17)** out of **(6)**].
(11) and (19) ODI Evaluation (censored for SSI): These rows indicate the number of subjects with any ODI data after SSI censoring for all evaluated subjects **(11)** and for all subjects that are within window **(19)** among expected due subjects.
(12) and (20) Back Pain Evaluation (censored for SSI): These rows indicate the number of subjects with any back pain data after SSI censoring for all evaluated subjects **(12)** and for all subjects that are within window **(20)** among expected due subjects.
(13) and (21) Leg Pain Evaluation (censored for SSI): These rows indicate the number of subjects with any leg pain data after SSI censoring for all evaluated subjects **(13)** and for all subjects that are within window **(21)** among expected due subjects.
(14) and (22) Neurological Evaluation (not censored for SSI): These rows indicate the number of subjects with any neurological evaluations for all evaluated subjects **(14)** and for all subjects that are within window **(22)** among expected due subjects.
(15) and (23) Composite Clinical Success (CCS): These rows indicate the number of subjects evaluable for CCS at specified visit for all evaluated subjects **(15)** and for all subjects that are within window **(23)**. Subjects are evaluable for CCS if they had any SSI or treatment-associated AE before the end of the visit window or if they had an ODI evaluation at the specified visit.
(16) and (24) Actual % Follow-up for CCS: These rows indicate the percentage of subjects evaluable for CCS at specified visit for all evaluated subjects **(16)** and for all subjects that are within window **(24)**. Subjects are evaluable for CCS if they had any SSI or treatment-associated AE before the end of the visit window or if they had an ODI evaluation at the specified visit. The denominator for percentages is expected due plus SSI failures, including crossovers **(8)**.

The subject accounting tree for the DIAM™ IDE study is depicted below in **Figure 2**.

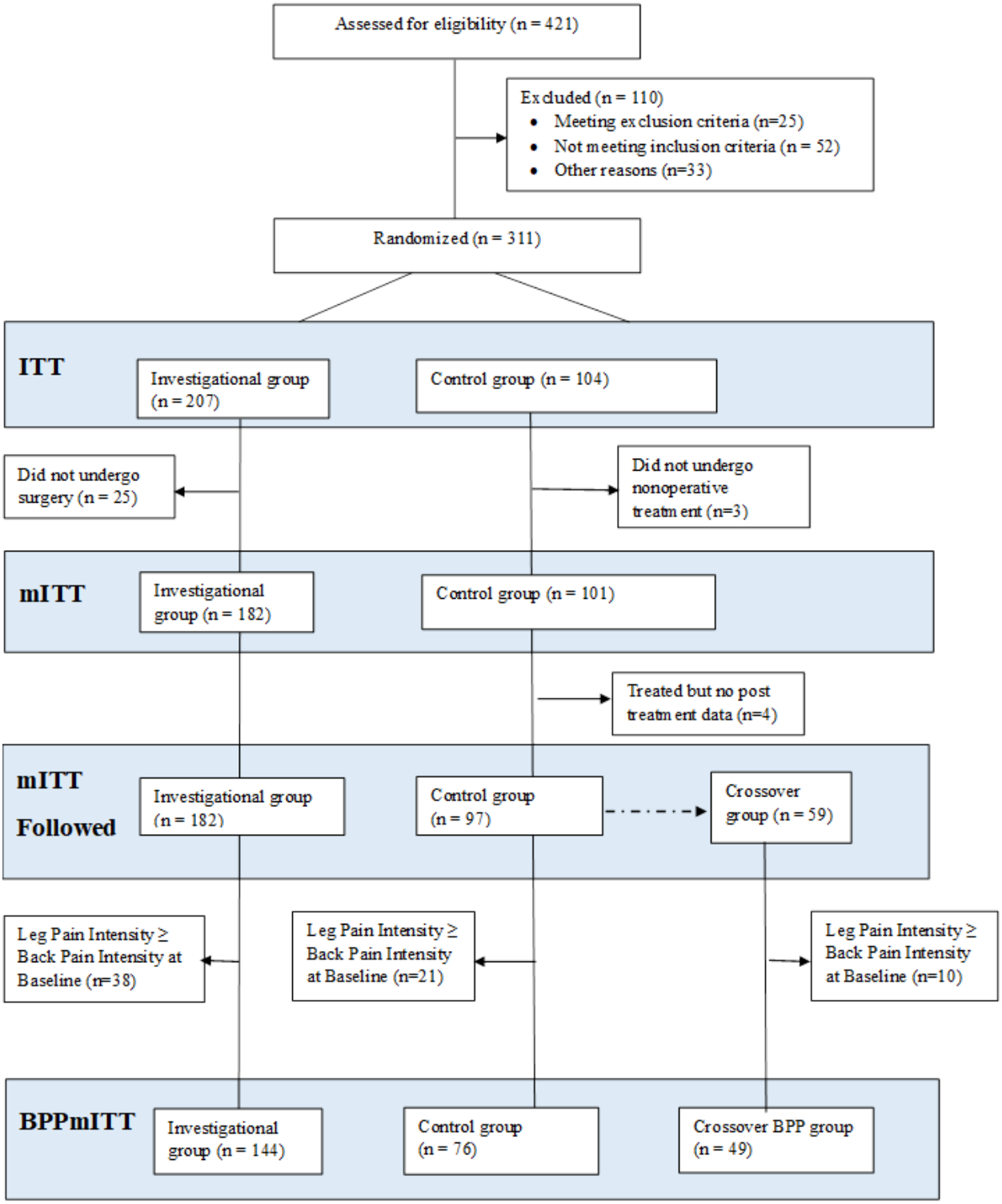

Figure 2: Subject Accounting Tree

Analysis Populations

For the purpose of assessing safety and effectiveness, the following analysis populations were used:

- ***ITT Analysis Set – 311 Subjects:*** The ITT analysis set included all subjects randomized to either the DIAM™ Spinal Stabilization System or non-operative care. This included 207 subjects randomized to DIAM™ Spinal Stabilization System and 104 subjects randomized to non-operative care.

- ***Modified Intent-to-Treat (mITT) Analysis Set – 283 Subjects:*** The mITT analysis set includes all subjects in the ITT analysis set for which treatment was attempted. This includes 182 DIAM™ Spinal Stabilization System subjects and 101 non-operative care subjects. The DIAM™ Spinal Stabilization System mITT analysis set includes one subject in which treatment was initiated and but not completed due to an intraoperative adverse event. This subject was defined as a composite endpoint failure. The non-operative care mITT analysis set includes 4 subjects that initiated non-operative care but for whom there was no follow-up.

- ***Modified Intent-to-Treat Followed (mITT-Followed) Analysis Set – 279 Subjects:*** The mITT-Followed analysis set includes all subjects in the mITT analysis set with any follow-up. Therefore, this is the mITT analysis set excluding the 4 controls that completed treatment but who had no post treatment follow-up. The sample sizes are 182 DIAM™ Spinal Stabilization System subjects and 97 non-operative care controls.

Safety data are presented for the mITT-Followed analysis set.

- ***Back Pain Predominate Modified Intent-to-Treat (BPPmITT) Analysis Set – 220 Subjects:*** The BPPmITT analysis set is a subset of the mITT-Followed dataset which excludes subjects with leg pain intensity scores ≥ back pain intensity scores at baseline. This analysis set comprises 144 DIAM™ Spinal Stabilization System subjects and 76 non-operative care controls. The BPPmITT analysis set was designated the primary endpoint analysis population.

Effectiveness data are presented for the BPPmITT analysis set due to the retrospective modification to the Indications for Use Statement for the DIAM™ Spinal Stabilization System.

- ***Crossover Analysis Set – 59 Subjects:*** This analysis set includes all subjects who were randomized to the control group and elected to receive the DIAM™ Spine Stabilization System as a treatment surgery. A total of 59 control subjects ultimately crossed over to receive the DIAM™ Spinal Stabilization System treatment: 56 within 24-months and 3 additional after the 24-month visit. For crossover subjects, outcome measurements

after implanting the investigational device were summarized as crossover cohort and compared to measurements obtained immediately prior to surgery.

Effectiveness data are also presented for a subset of crossover subjects (Crossover BPP), including 49 crossover subjects with back pain intensity scores > leg pain intensity scores.

C. Study Population Demographics and Baseline Parameters

Demographics and baseline parameters are provided for the mITT analysis set (182 investigational; 101 non-operative care) (all randomized subjects in whom study treatment was attempted) and all 59 subjects included in the crossover sub-group. All available demographics and baseline data are presented. As shown below, overall, the treatment groups had similar mean age, height, weight, and BMI, gender distribution, race distribution, education level distribution, proportion of subjects with ongoing spinal litigation, history of prior back surgery, and smoking history. In addition to the similarities in demographics, the investigational and non-operative care control groups had similar baseline scores, including mean ODI scores, NRS back pain, SF-36 mental scores and SF-36 physical scores. In summary, randomization was effective in providing a well-balanced study population, with similar demographic, baseline, and clinical characteristics between the investigational and non-operative care control groups.

The baseline and demographics for the mITT analysis population are summarized in **Table 7**, **Table 8**, **Table 9**, and **Table 10** for continuous variables, categorical variables, clinical endpoints, and neurological status, respectively. The data demonstrate the two treatment groups have no major difference in terms of characteristics of enrolled subjects. The demographics of the study population are typical for a spine study performed in the US.

Table 7: Summary of Baseline and Demographic Continuous Variables – Investigational, Control, and Crossover mITT

	Investigational						Control						Crossover					
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max
Age (years)	182	42.5	11.0	43.5	18.0	69.0	101	44.6	10.4	44.0	23.0	70.0	59	45.8	10.2	45.0	23.0	70.0
Height (in)	182	67.5	3.6	67.0	59.0	78.0	101	67.8	4.3	68.0	60.0	77.0	59	67.9	4.4	68.0	60.0	77.0
Weight (lbs)	182	183.7	39.6	181.0	108.0	320.0	101	188.2	44.5	185.0	108.0	318.0	59	186.9	47.8	185.0	108.0	311.0
BMI (kg/m^2)	182	28.3	5.2	27.4	18.5	41.1	101	28.6	5.6	27.8	17.4	39.7	59	28.3	5.9	27.3	17.4	39.3

Table 8: Summary of Baseline and Demographic Categorical Variables – Investigational, Control, and Crossover mITT

	Investigational			Control			Crossover		
	N	n	%	N	n	%	N	n	%
Sex									
Female	182	105	57.7%	101	50	49.5%	59	29	49.2%
Male	182	77	42.3%	101	51	50.5%	59	30	50.8%
Race									
Caucasian	182	167	91.8%	101	92	91.1%	59	55	93.2%
Black	182	3	1.6%	101	5	5.0%	59	1	1.7%
Asian	182	1	0.5%	101	0	0.0%	59	0	0.0%
Hispanic	182	11	6.0%	101	1	1.0%	59	1	1.7%
Other	182	0	0.0%	101	3	3.0%	59	2	3.4%
Education Level									
< High School	182	13	7.1%	101	7	6.9%	59	3	5.1%
High School	182	50	27.5%	101	22	21.8%	59	11	18.6%
> High School	182	117	64.3%	101	72	71.3%	59	45	76.3%
Not Reported	182	2	1.1%	101	0	0.0%	59	0	0.0%
Spinal Litigation									
Yes	182	25	13.7%	101	11	10.9%	59	7	11.9%
No	182	157	86.3%	101	90	89.1%	59	52	88.1%
Back Surgery Hx									
Yes	182	1	0.5%	101	4	4.0%	59	2	3.4%
No	182	181	99.5%	101	97	96.0%	59	57	96.6%
Tobacco									
Yes	182	46	25.3%	101	34	33.7%	59	18	30.5%
No	182	134	73.6%	101	65	64.4%	59	40	67.8%
Not Reported	182	0	0.0%	101	0	0.0%	59	1	1.7%

Table 9: Comparison of Baseline Clinical Endpoints – Investigational, Control, and Crossover mITT

	Investigational						Control						Crossover					
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max
Back Pain*	182	16.8	2.3	17.0	9.0	20.0	101	16.2	2.8	17.0	8.0	20.0	59	16.4	2.7	17.0	8.0	20.0
Leg Pain*	182	10.3	6.2	12.0	0.0	20.0	101	9.1	6.5	10.0	0.0	20.0	59	10.3	6.9	12.0	0.0	20.0
ODI	182	50.4	13.9	48.0	30.0	94.0	101	50.4	13.2	50.0	30.0	82.0	59	55.4	13.1	54.0	32.0	96.0
SF36: MCS	181	36.0	9.0	36.6	13.4	54.0	101	35.9	9.7	37.0	11.0	56.0	59	35.2	10.1	35.8	16.3	51.9
SF36: PCS	181	31.5	6.3	30.5	16.4	47.8	101	30.5	5.7	29.8	19.8	46.5	59	29.7	5.3	28.5	21.7	43.1

*Baseline Back Pain and Leg Pain Scores were each evaluated on a 0-20 scale comprising pain intensity (0-10) and pain frequency (0-10) components.

Table 10: Summary of Baseline Neurological Status – Investigational, Control, and Crossover mITT

	Investigational			Control			Crossover		
	N	n	%	N	n	%	N	n	%
Normal Motor Function	182	182	100.0%	101	101	100.0%	59	58	98.3%
Normal Sensory Function	182	164	90.1%	101	95	94.1%	59	56	94.9%
Normal Reflexes	182	164	90.1%	101	92	91.1%	59	54	91.5%
Normal Straight Leg Raise	182	151	83.0%	101	79	78.2%	59	49	83.1%

Data was collected on the type of non-operative care received by control subjects in the mITT population. Treatments received by control subjects at the initial treatment included: education (99% - 100/101); medication (82.2% - 83/101); physical therapy (68.3% - 69/101); and spinal injection (36.6% - 37/101).

The continuous operative variables are summarized in **Table 11** for subjects randomized to the investigational group and subjects who were randomized to the non-operative care control group and subsequently elected to crossover**.** The average operative times were 62.6 minutes and 59.5 minutes with mean blood loss of 31.4 mL and 35.6 mL in the investigational and crossover groups, respectively. Most subjects were discharged from the hospital in less than a day with a mean length of stay of 0.8 days reported in both the investigational and crossover cohorts. General anesthesia was utilized for all investigational and crossover subjects with a reported anesthesia type. In both the investigational and crossover cohorts, the majority of subjects were treated at L4-L5. In the investigational cohort, 4.9% (9/182) subjects were treated at L2-L3, 7.1% (13/182) were treated at L3-L4, and 87.9% (160/182) were treated at L4-L5. The distribution of levels treated was similar in the crossover subjects: 3.4% (2/59) at L2-L3, 5.1% (3/59) at L3-L4, 89.8% (53/59) at L4-L5, and 1.7% (1/59) at L5-L6 (anatomic variant). Regarding surgery site, 62.1% (113/182) and 59.3% (35/59) of subjects were treated in outpatient procedures, and 37.9% (69/182) and 40.7% (24/59) were inpatient procedures in the investigational and crossover groups, respectively.

Table 11: Summary of Operative Details – Continuous Variables Investigational mITT-Followed and Crossover

	Investigational						Crossover					
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max
Surgery Time (min)	182	62.6	18.7	60.0	21.0	123.0	59	59.5	20.3	56.0	25.0	138.0
Blood Loss (mL)	182	31.4	26.9	25.0	0.0	100.0	59	35.6	29.9	23.0	9.0	100.0
Length of Stay (days)	182	0.8	0.7	1.0	0.0	3.0	59	0.8	0.9	1.0	0.0	6.0

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the mITT-Followed Analysis population of 279 subjects available beyond the Month 24 evaluation (day 790). Note that the listings of days related to adverse event results (e.g., "day 790") represents the upper bound of the follow-up window (e.g., 24 months + 2 months). The key safety outcomes for this study are presented below in **Table 12** to **Table 24**.

Adverse Event Summary

The safety endpoint evaluated the rate of AEs, categorized by severity (mild, moderate or severe), relationship to the implant, surgical procedure, or non-operative care, and SAEs. AEs were reviewed by an independent Clinical Events Committee (CEC) and adjudicated for severity and relationship to the non-operative care, implant, and/or surgical procedure in accordance with the definitions provided below.

Severity

AEs were assessed for severity using the following definitions:

- **Mild (Grade 1)** – Noticeable to the subject but did not interfere with routine activity, and for subjects in the investigational group, the AE did not require removal of the implant;
- **Moderate (Grade 2)** – Interfered with routine activity but responded to symptomatic therapy or rest, and for subjects in the investigational group, the AE did not require removal of the implant;
- **Severe (Grade 3)** – Significantly limited the subject's ability to perform routine activities despite symptomatic therapy, and for subjects in the investigational group, the AE may require removal of the implant; and,
- **Life-threatening (Grade 4)** – The subject is at immediate risk of death, and for subjects in the investigational group, the AE may require removal of the implant.

Serious Adverse Events

An SAE was defined as an AE that: led to a death; led to fetal distress, fetal death, or a congenital abnormality or birth defect; or, led to a serious deterioration in health of the subject that:

- Resulted in a life-threating illness or injury;
- Resulted in permanent impairment of a body structure or function;
- Required in-patient hospitalization or prolongation of existing hospitalization; or
- Resulted in medical or surgical intervention to prevent permanent impairment to body structure or a body function.

Association with Study Treatment

For investigational and crossover subjects (i.e., subjects randomized to non-operative care who elected to undergo implantation with the DIAM^{TM} Spinal Stabilization System), association of an AE with the investigational treatment was assessed according to the following definitions:

- **Implant-Associated AE:** An AE for which there was a reasonable possibility that the event may have been caused primarily by the implant/implant component.
- **Surgical Procedure-Associated AE:** An AE for which there was a reasonable possibility that the event may have been caused primarily by the surgical procedure.
- **Implant/Surgical Procedure-Associated AE:** An AE for which there was a reasonable possibility that the event may have been caused primarily by the implant/implant component and/or the surgical procedure but cannot be definitively associated exclusively with the implant or exclusively with the surgical procedure.
- **Undetermined AE:** An AE for which sufficient information to determine the causality of the event was not available.
- **Not Related AE:** An AE for which sufficient information existed to indicate that the etiology of the event was unrelated to the study treatment.

For non-operative care control subjects, association of an AE with non-operative care treatments was assessed according to the following definitions:

- **Non-operative Treatment Associated AE:** An AE for which there was a reasonable possibility that the event may have been caused primarily by the non-operative treatment.
- **Undetermined AE:** An AE for which sufficient information was not available to determine its causality.
- **Not Related AE:** An AE for which sufficient information existed to indicate that the etiology of the event was unrelated to the study treatment.

For any event categorized by CEC as implant-associated, surgical procedure-associated, implant/surgical procedure-associated, or non-operative care associated, the CEC assigned the following relationship categories.

- **Definitely Associated:** An AE that has a strong causal relationship. An AE that follows a strong temporal relationship, follows a known response pattern, and cannot reasonably be explained by known characteristics of the subject's clinical state or other therapies.
- **Probably Associated:** An AE that potentially has a causal relationship. The AE has a reasonable temporal relationship and alternative etiology is less likely compared to the potential relationship to the use of the investigational device/procedure or non-operative treatment (control only).
- **Possibly Associated:** An AE that potentially has a causal relationship. The AE has a reasonable temporal relationship to the use of the investigational device/procedure, but alternative etiology is equally likely compared to the potential relationship to the use of the investigational device/procedure or non-operative treatment (control only).

Please note, the Month 24 and Month 60 safety tables below present all AEs that occurred within that interval following initial randomized treatment to the investigational or control arms, regardless of whether the subject received additional treatment. Accordingly, AEs presented for the control group include AEs that occurred after crossover treatment. However, AEs presented for the crossover group do not include AEs that occurred prior to subjects receiving the crossover treatment. The tables displaying treatment-associated events provide context on whether events that occurred over the 24-month (day 790) or 60-month (day 1,885) intervals were associated to the implant and/or surgical procedure.

Further, a separate set of select safety tables that list AEs through six months (day 210) are provided since the comparison between the investigational and non-operative care control treatments through 6 months is not impacted by AEs occurring after crossover in the control group at later timepoints.

AEs through Month 6 for the investigational, crossover, and control groups are reported in **Table 12**. The results indicate that through Month 6, 76.9% (140/182) of investigational subjects, 66.0% (64/97) of control subjects, and 76.3% (45/59) of crossover subjects

experienced at least one AE. The percentage of subjects who reported at least one SAE was 13.7% (25/182) in the investigational group, 22.7% (22/97) in the control group, and 15.3% (9/59) in the crossover group. While more subjects in the investigational and crossover groups experienced an AE, this is not unexpected for an implant relative to non-operative care.

Table 12: Comparison of Summary of Safety Events up to 6 Months – Investigational and Control mITT-Followed and Crossover

	Investigational (N=182)			Control (N=97)			Crossover (N=59)		
	Events	n	%	Events	n	%	Events	n	%
Any adverse event	319	140	76.9%	117	64	66.0%	92	45	76.3%
Any implant/surgical procedure associated AE	6	6	3.3%	0	0	0.0%	2	2	3.4%
Any implant only associated AE	1	1	0.5%	0	0	0.0%	1	1	1.7%
Any surgical procedure only associated AE	46	44	24.2%	0	0	0.0%	25	22	37.3%
Any nonoperative treatment associated AE	0	0	0.0%	1	1	1.0%	0	0	0.0%
Any serious AE	27	25	13.7%	23	22	22.7%	9	9	15.3%
Any implant/surgical procedure associated SAE	3	3	1.6%	0	0	0.0%	0	0	0.0%
Any implant only associated SAE	0	0	0.0%	0	0	0.0%	0	0	0.0%
Any surgical procedure only associated SAE	10	10	5.5%	0	0	0.0%	6	6	10.2%
Any nonoperative treatment associated SAE	0	0	0.0%	1	1	1.0%	0	0	0.0%
Spinous Process Fracture	13	13	7.1%	0	0	0.0%	5	5	8.5%
Deaths	0	0	0.0%	0	0	0.0%	0	0	0.0%

Only adverse events through the first 210 days are included.

AEs through Month 24 for the investigational, crossover, and control groups are reported in **Table 13**. The results indicate that through Month 24, 92.9% (169/182) of investigational subjects, 89.7% (87/97) of control subjects, and 91.5% (54/59) of crossover subjects experienced at least one AE. It should be noted that some AEs captured under the control group through Month 24 may be related to subjects that crossed over. Nevertheless, the investigational and crossover subjects experienced an AE rate within only a few percent higher than the control group, and this again is to be expected with an implant relative to non-operative care.

Table 13: Comparison of Summary of Safety Events up to 24 Months – Investigational and Control mITT-Followed and Crossover

	Investigational (N=182)			Control (N=97)			Crossover (N=59)		
	Events	n	%	Events	n	%	Events	n	%
Any adverse event	638	169	92.9%	314	87	89.7%	173	54	91.5%
Any implant/surgical procedure associated AE	6	6	3.3%	0	0	0.0%	2	2	3.4%
Any implant only associated AE	4	4	2.2%	0	0	0.0%	1	1	1.7%
Any surgical procedure only associated AE	46	44	24.2%	0	0	0.0%	27	24	40.7%
Any nonoperative treatment associated AE	0	0	0.0%	2	2	2.1%	0	0	0.0%
Any serious AE	69	59	32.4%	47	42	43.3%	19	16	27.1%
Any implant/surgical procedure associated SAE	3	3	1.6%	0	0	0.0%	1	1	1.7%
Any implant only associated SAE	2	2	1.1%	0	0	0.0%	0	0	0.0%
Any surgical procedure only associated SAE	10	10	5.5%	0	0	0.0%	6	6	10.2%
Any nonoperative treatment associated SAE	0	0	0.0%	2	2	2.1%	0	0	0.0%
Spinous Process Fracture	14	14	7.7%	0	0	0.0%	6	6	10.2%
SSI	13	12	6.6%	68	65	67.0%	4	3	5.1%
Deaths	1*	1	0.5%	1**	1	1.0%	0	0	0.0%

Only adverse events through the first 790 days are included.
*Cause of death was acidosis and septic shock at approximately 24 months post-operatively.
**Cause of death was hypertensive cardiomegaly at 23 months post-treatment.

The mITT-Followed population (investigational and non-operative care) and the crossover population also reported comparable rates of AEs through the 60-month follow-up, as shown below. The overall adverse event rate was 96.2% (175/182) in the investigational group, 93.8% (91/97) in the control group, and 94.9% (56/59) in the crossover group. Similar proportions of subjects in the investigational, control, and crossover treatment groups experienced any SAE during the 60-month follow-up. The percentage of subjects who reported at least one SAE was 42.3% (77/182) in the investigational group, 52.6% (51/97) in the control group, and 40.7% (24/59) in the crossover group. Compared to Month 24, there were no significant differences in the rates of implant-associated, surgical procedure-associated, or implant/surgical procedure-associated SAEs reported in the investigational and crossover subjects at Month 60. A similar trend was observed in the SSI rates reported across all three treatment groups.

Table 14: Comparison of Summary of Safety Events up to 60 Months – Investigational and Control mITT-Followed and Crossover

	Investigational (N=182)			Control (N=97)			Crossover (N=59)		
	Events	n	%	Events	n	%	Events	n	%
Any adverse event	1033	175	96.2%	507	91	93.8%	269	56	94.9%
Any implant/surgical procedure associated AE	6	6	3.3%	0	0	0.0%	2	2	3.4%
Any implant only associated AE	4	4	2.2%	0	0	0.0%	2	2	3.4%
Any surgical procedure only associated AE	46	44	24.2%	0	0	0.0%	27	24	40.7%
Any nonoperative treatment associated AE	0	0	0.0%	2	2	2.1%	0	0	0.0%
Any serious AE	110	75	41.2%	58	47	48.5%	32	24	40.7%
Any implant/surgical procedure associated SAE	3	3	1.6%	0	0	0.0%	1	1	1.7%
Any implant only associated SAE	2	2	1.1%	0	0	0.0%	0	0	0.0%
Any surgical procedure only associated SAE	10	10	5.5%	0	0	0.0%	6	6	10.2%
Any nonoperative treatment associated SAE	0	0	0.0%	2	2	2.1%	0	0	0.0%
Spinous Process Fracture	14	14	7.7%	0	0	0.0%	6	6	10.2%
SSI	20	18	9.9%	71	68	70.1%	7	5	8.5%
Deaths	2*	2	1.1%	1**	1	1.0%	0	0	0.0%

Only adverse events through the first 1,885 days are included.
*Cause of death was acidosis and septic shock at approximately 24 months post-operatively.
**Cause of death was hypertensive cardiomegaly at 23 months post-treatment.

Counts and percentages of subjects with specific AEs through Month 6 are presented in the table below. No control subjects received crossover treatment prior to 6 months; therefore, data presented in the table below is a more representative comparison of AE rates between treatment with the investigational subjects and non-operative care subjects as compared to AE rates collected after 6 months (which include crossover and other surgical treatments in the control group). At Month 6, the most commonly reported AEs were: back and/or leg pain (of back etiology) (22.0% - 40/182) and accidental injury/muscle strain (14.3% - 26/182) in the investigational group; spinal event at target level (21.6% - 21/97) and back and/or leg pain (of back etiology) (15.5% - 15/97) in the non-operative care control group; and, back and/or leg pain (of back etiology) (23.7% - 14/59), lower extremity pain (not of back etiology) (11.9% - 7/59) and spinal event at target level (11.9% - 7/59) in the crossover group.

Table 15: Counts and Percentages of Subjects with Specific Safety Events up to 6 Months – Investigational and Control mITT-Followed and Crossover

	Investigational (N=182)			Control (N=97)			Crossover (N=59)		
	Events	n	%	Events	n	%	Events	n	%
All AEs	319	140	76.9%	117	64	66.0%	92	45	76.3%
Accidental Injury/Muscle Strain	26	26	14.3%	4	4	4.1%	5	4	6.8%
Allergic Reaction	1	1	0.5%	0	0	0.0%	1	1	1.7%
Back and/or Leg Pain (of back etiology)	43	40	22.0%	16	15	15.5%	14	14	23.7%
Cancer[1]	1	1	0.5%	0	0	0.0%	0	0	0.0%
Cardiovascular (i.e., M.I., Stroke)	2	2	1.1%	2	2	2.1%	3	3	5.1%
Cervical Spine Event	5	5	2.7%	4	4	4.1%	5	5	8.5%
Depression	7	7	3.8%	1	1	1.0%	1	1	1.7%
Electrolyte Imbalance	4	4	2.2%	0	0	0.0%	0	0	0.0%
Endocrine (i.e., Hypothyroid, etc.)	0	0	0.0%	1	1	1.0%	0	0	0.0%
Gastrointestinal-Other[2]	17	10	5.5%	6	6	6.2%	1	1	1.7%
Hematological	1	1	0.5%	0	0	0.0%	0	0	0.0%
Incision-Related[3]	12	12	6.7%	0	0	0.0%	6	6	10.2%
Infection[4]	13	12	6.6%	8	7	7.2%	3	3	5.1%
Infection UTI	2	2	1.1%	0	0	0.0%	1	1	1.7%
Lower Extremity (not of back etiology, i.e., knee, ankle)	24	20	11.0%	10	7	7.2%	8	7	11.9%
Malpositioned Implant	0	0	0.0%	1	1	1.0%	1	1	1.7%
Neck and Arm Pain	2	2	1.1%	1	1	1.0%	0	0	0.0%
Neurological	9	9	4.9%	4	2	2.1%	1	1	1.7%
Other[5]	20	16	8.8%	10	9	9.3%	1	1	1.7%
Other Pain[6]	11	9	4.9%	2	2	2.1%	0	0	0.0%
Prolonged postoperative sequalae	9	9	4.9%	4	3	3.1%	7	6	10.2%
Psychological	1	1	0.5%	2	2	2.1%	1	1	1.7%
Radiculopathy/Sciatica without back pain	10	9	4.9%	0	0	0.0%	5	5	8.5%
Respiratory	6	6	3.3%	1	1	1.0%	3	3	5.1%
Retrograde Ejaculation	1	1	0.5%	0	0	0.0%	0	0	0.0%
Skin Disorder	1	1	0.5%	1	1	1.0%	0	0	0.0%
Spinal Event at Other Lumbar Level	9	8	4.4%	4	4	4.1%	2	2	3.4%
Spinal Event at Target Level[7]	18	18	9.9%	21	21	21.6%	7	7	11.9%
Subsidence	0	0	0.0%	0	0	0.0%	1	1	1.7%
Superficial Incision Infection	15	15	8.2%	0	0	0.0%	2	2	3.4%
Systemic[8]	1	1	0.5%	1	1	1.0%	6	5	8.5%
Trauma[9]	27	16	8.8%	5	3	3.1%	3	3	5.1%
Upper Extremity Pain (not of neck etiology, i.e., shoulder, arm)	15	12	6.6%	7	6	6.2%	3	3	5.1%
Urogenital	8	6	3.3%	1	1	1.0%	0	0	0.0%
Vascular Event Post-Op Peripheral/DVT	0	0	0.0%	0	0	0.0%	1	1	1.7%

Only adverse events through the first 210 days are included.

[1]Cancer: cervical cancer

[2]Gastrointestinal-Other: nausea, epigastric pain

[3]Incision-Related: pain on the incision site, delayed wound healing, erthema, bruising, hematoma, rash

[4]Infection: viral illness, sinus infection, pneumonia, common cold, otitis, flu, pharyngitis, cough, zona, cold symptoms, respiratroy infection, systemic

[5]Other: needle issue, eye disorder, miscarriage, gynecological disorder, breast surgery, dental surgery

[6]Other Pain: migraine headache, ankylosing spondylitis, extreme low back pain

[7]Spinal Event at Targey Level - bilateral hip pain radiating from surgical site, low back pain with or without leg pain, discogenic pain, disc herniation/stenosis/slip, facet joint changes, spinous process fracture, numbness/paresthesia

[8]Systemic: mental confusion, lupus, hypercholesterolemia, polycythemia, insomnia, hypertension, weight gain, allergies

[9]Trauma: fall or motor vehicle accident or other trauma resulting in a broken or sprained foot, ankle, hand; meniscal tear, or temporary increase in back pain

Counts and percentages of subjects with specific AEs through Month 24 are presented in **Table 16**. Importantly, control group AE counts in **Table 16** include AEs for subjects that received crossover treatment or other surgical interventions after Month 6 and should not be considered representative of AEs associated with non-operative care alone. At Month 24, the most commonly reported AEs were: back and/or leg pain (of back etiology) (36.8% - 67/182) and lower extremity pain (not of back etiology) (21.4% - 39/182) in the investigational group; spinal event at target level (36.1% - 35/97) and back and/or leg pain (of back etiology) (33.0% - 32/97) in the non-operative care control group; and, back and/or leg pain (of back etiology) (37.3% - 22/59) and lower extremity pain (not of back etiology) (23.7% - 14/59) in the crossover group.

Table 16: Counts and Percentages of Subjects with Specific Safety Events up to 24 Months – Investigational and Control mITT-Followed and Crossover

	Investigational (N=182)			Control (N=97)			Crossover (N=59)		
	Events	n	%	Events	n	%	Events	n	%
All AEs	638	169	92.9%	314	87	89.7%	173	54	91.5%
Accidental Injury/Muscle Strain	42	35	19.2%	16	15	15.5%	11	10	16.9%
Allergic Reaction	5	5	2.7%	3	3	3.1%	2	2	3.4%
Back and/or Leg Pain (of back etiology)	76	67	36.8%	37	32	33.0%	24	22	37.3%
Cancer[1]	3	3	1.6%	0	0	0.0%	0	0	0.0%
Cardiovascular (i.e., M.I., Stroke)	12	12	6.6%	7	7	7.2%	5	5	8.5%
Cervical Spine Event	10	9	4.9%	7	7	7.2%	7	7	11.9%
Death[2]	0	0	0.0%	1	1	1.0%	0	0	0.0%
Depression	12	12	6.6%	3	3	3.1%	3	3	5.1%
Dysphagia	0	0	0.0%	1	1	1.0%	1	1	1.7%
Electrolyte Imbalance	4	4	2.2%	0	0	0.0%	0	0	0.0%
Endocrine (i.e., Hypothyroid, etc.)	4	4	2.2%	3	3	3.1%	1	1	1.7%
Gastrointestinal-Other[3]	46	26	14.3%	7	6	6.2%	6	5	8.5%
Hematological	4	4	2.2%	1	1	1.0%	0	0	0.0%
Incision-Related[4]	10	10	5.5%	8	8	8.2%	7	7	11.9%
Infection[5]	45	29	15.9%	23	16	16.5%	3	3	5.1%
Infection UTI	5	4	2.2%	1	1	1.0%	2	2	3.4%
Lower Extremity (not of back etiology, i.e., knee, ankle)	46	39	21.4%	26	19	19.6%	19	14	23.7%
Malpositioned Implant	0	0	0.0%	1	1	1.0%	1	1	1.7%
Neck and Arm Pain	9	7	3.8%	6	5	5.2%	0	0	0.0%
Neurological	16	15	8.2%	12	10	10.3%	3	3	5.1%
Other[6]	46	33	18.1%	24	17	17.5%	9	8	13.6%
Other Pain[7]	28	22	12.1%	6	6	6.2%	0	0	0.0%
Prolonged postoperative sequelae	9	9	4.9%	5	4	4.1%	7	6	10.2%
Psychological	7	7	3.8%	8	7	7.2%	4	4	6.8%
Radiculopathy/Sciatica without back pain	13	12	6.6%	2	2	2.1%	6	6	10.2%
Respiratory	10	10	5.5%	6	6	6.2%	8	7	11.9%
Retrograde Ejaculation	1	1	0.5%	0	0	0.0%	0	0	0.0%
Skin Disorder	3	3	1.6%	2	2	2.1%	0	0	0.0%
Spinal Event at Other Lumbar Level	14	12	6.6%	6	6	6.2%	4	4	6.8%
Spinal Event at Target Level[8]	33	33	18.1%	36	35	36.1%	9	9	15.3%
Subsidence	0	0	0.0%	0	0	0.0%	1	1	1.7%
Superficial Incision Infection	15	15	8.2%	0	0	0.0%	2	2	3.4%
Systemic[9]	2	2	1.1%	2	2	2.1%	9	7	11.9%
Trauma[10]	54	31	17.0%	29	20	20.6%	6	4	6.8%
Upper Extremity Pain (not of neck etiology, i.e., shoulder, arm)	23	19	10.4%	17	14	14.4%	11	9	15.3%
Urogenital	30	20	11.0%	7	7	7.2%	0	0	0.0%
Vascular Event Post-Op Peripheral/DVT	1	1	0.5%	1	1	1.0%	2	2	3.4%

Only adverse events through the first 790 days are included.
[1]Cancer: cervical cancer
[2]Death: cardiac arrest
[3]Gastrointestinal Other: gastrointestinal illness such as epigastric or abdominal pain, nausea and vomiting, stomach virus, constipation, abdominal cramping, hernia, cholecystitis, pancreatitis
[4]Incision-Related: pain on the incision site, delayed wound healing, erythema, bruising, hematoma, rash
[5]Infection: viral illness, sinus infection, pneumonia, common cold, otitis, flu, pharyngitis, cough, zona, cold symptoms, respiratory infection, mononucleosis, varicella-zoster, systemic
[6]Other: needle issue, eye disorder, miscarriage, gynecological disorder, sinusitis, ENT disorder, breast surgery, opioid dependence
[7]Other Pain: (migraine) headache, ankklyosing spondylitis, extreme low back pain, fibromyalgia, panic attack, eye injury, pain post childbirth
[8]Spinal Event at Target Level: bilateral hip pain radiating from surgical site, low back pain with or without leg pain, discogenic pain, disc herniation/stenosis/slip, facet joint changes, spnious process fracture, spinous process bony erosion, numbness/paresthesia
[9]Systemic: mental confusion, luppus, hypercholesterolemia, polycythemia, insomnia, hypertension, weight gain, allergies
[10]Trauma: fall or motor vehicle accident or other trauma resulting in a broken or sprained foot, ankle, nose, hand, or tooth; meniscal tear, rotator cuff tear, bruising, contusion or temporary increase in back pain

Table 17 provides a comparison of all AEs through Month 24 (day 790) reported in the investigational, non-operative care control, and crossover groups, classified as mild,

moderate, severe, or life-threatening. At Month 24, 17.7% (113/182) of investigational subjects, 22.6% (71/97) of non-operative care control subjects, and 11.6% (20/59) of crossover subjects experienced AEs categorized as severe. However, it should be noted that control group AE counts after Month 6 included AEs for subjects that received crossover treatment or other surgical interventions, and should not be considered representative of AEs associated with non-operative treatment alone.

Table 17: Comparison of All Safety Events by Severity Through 24 Months – Investigational and Control mITT-Followed and Crossover

	Mild		Moderate		Severe		Life-Threatening		Total
	Events	%*	Events	%*	Events	%*	Events	%*	Events
Investigational (n=182)	152	23.8%	372	58.3%	113	17.7%	1	0.2%	638
Non-Operative Care (n=97)	81	25.8%	160	51.0%	71	22.6%	2	0.6%	354
Crossover (n=59)	113	65.3%	40	23.1%	20	11.6%	0	0.0%	173
*Percentage of total events									

Treatment-Associated Adverse Events

Below, the counts and percentages of all implant- and surgical procedure-associated AEs, in the investigational and crossover groups are shown in **Table 18.** There were 2 AEs (both SAEs) in 2 subjects (2.1%) that were non-operative care-associated, which were both classified as worsening back pain.

Table 18: Counts and Percentages of Implant- and Surgical Procedure-Associated Adverse Events Through 24 Months - Investigational mITT-Followed and Crossover

	Investigational (N=182)			Crossover (N=59)		
	Events	n	%	Events	n	%
All AEs	56	52	28.6%	30	25	42.4%
Accidental Injury/Muscle Strain	1	1	0.5%	0	0	0.0%
Allergic Reaction	0	0	0.0%	1	1	1.7%
Back and/or Leg Pain (of back etiology)	3	3	1.6%	0	0	0.0%
Cardiovascular (i.e., M.I., Stroke)	0	0	0.0%	1	1	1.7%
Gastrointestinal-Other[1]	1	1	0.5%	0	0	0.0%
Incision-Related[2]	11	11	6.0%	7	7	11.9%
Infection[3]	0	0	0.0%	1	1	1.7%
Lower Extremity (not of back etiology, i.e., knee, ankle)	1	1	0.5%	0	0	0.0%
Malpositioned Implant	0	0	0.0%	1	1	1.7%
Other[4]	1	1	0.5%	1	1	1.7%
Prolonged postoperative sequelae[5]	9	9	4.9%	7	6	10.2%
Radiculopathy/Sciatica without back pain	4	4	2.2%	3	3	5.1%
Respiratory	1	1	0.5%	0	0	0.0%
Skin Disorder	1	1	0.5%	0	0	0.0%
Spinal Event at Other Lumbar Level	1	1	0.5%	0	0	0.0%
Degeneration of Adjacent Level	1	1	0.5%	0	0	0.0%
Spinal Event at Target Level[6]	8	8	4.4%	4	4	6.8%
Back Pain	0	0	0.0%	1	1	1.7%
Disc Herniation/Stenosis/Slip	4	4	2.2%	0	0	0.0%
Spinous Process Bony Erosion	1	1	0.5%	0	0	0.0%
Spinous Process Fracture	1	1	0.5%	0	0	0.0%
Worsening Back Pain	1	1	0.5%	2	2	3.4%
Superficial Incision Infection	14	14	7.7%	2	2	3.4%
Systemic[7]	0	0	0.0%	1	1	1.7%
Vascular Event Post-Op Peripheral/DVT	0	0	0.0%	1	1	1.7%

Only adverse events through the first 790 days are included.
[1]Gastrointestinal-Other: abdominal pain
[2]Incision-Related: infection, pain on the incision site, delayed wound healing, erythema, bruising, hematoma, rash
[3]Infection:Varicella-zoster
[4]Other: needle issue, opioid dependence
[5]Prolonged postoperative sequelae: post-operative low back pain, tightness in chest, constipation, fever, ENT issue, headache, tachycardia, low potassium, hyperglycemia
[6]Spinal Event at Target Level: bilateral hip pain radiating from surgical site, low back pain with or without leg pain
[7]Systemic: insomnia

Serious Adverse Events

A listing of all specific serious adverse events (SAEs) that occurred through Month 6 is presented in **Table 19**. In total, 27 SAEs occurred in 13.7% (25/182) of investigational subjects, 23 SAEs occurred in 22.7% (22/97) of non-operative care control subjects, and 9 SAEs occurred in 15.3% (9/59) of crossover subjects.

Table 19: Counts and Percentages of Subjects with Specific Serious Adverse Events at 6 Months – Investigational and Control mITT-Followed and Crossover

	Investigational (N=182)			Control (N=97)			Crossover (N=59)		
	Events	n	%	Events	n	%	Events	n	%
All AEs	27	25	13.7%	23	22	22.7%	9	9	15.3%
Back and/or Leg Pain (of back etiology)	1	1	0.5%	7	7	7.2%	0	0	0.0%
Cancer[1]	1	1	0.5%	0	0	0.0%	0	0	0.0%
Cardiovascular (i.e., M.I., Stroke)	0	0	0.0%	0	0	0.0%	1	1	1.7%
Cervical Spine Event	1	1	0.5%	0	0	0.0%	0	0	0.0%
Depression	1	1	0.5%	0	0	0.0%	0	0	0.0%
Gastrointestinal-Other[2]	2	2	1.1%	0	0	0.0%	0	0	0.0%
Infection[3]	0	0	0.0%	0	0	0.0%	1	1	1.7%
Lower Extremity (not of back etiology, i.e., knee, ankle)	1	1	0.5%	1	1	1.0%	0	0	0.0%
Malpositioned Implant	0	0	0.0%	0	0	0.0%	1	1	1.7%
Neurological	1	1	0.5%	0	0	0.0%	0	0	0.0%
Other[4]	1	1	0.5%	3	3	3.1%	0	0	0.0%
Prolonged postoperative sequelae[5]	5	5	2.7%	3	3	3.1%	4	4	6.8%
Radiculopathy/Sciatica without back pain	1	1	0.5%	0	0	0.0%	0	0	0.0%
Respiratory	2	2	1.1%	0	0	0.0%	0	0	0.0%
Superficial Incision Infection	4	4	2.2%	0	0	0.0%	0	0	0.0%
Spinal Event at Target Level[6]	3	3	1.6%	8	8	8.2%	1	1	1.7%
Trauma[7]	2	2	1.1%	0	0	0.0%	0	0	0.0%
Upper Extremity Pain (not of neck etiology, i.e., shoulder, arm)	0	0	0.0%	1	1	1.0%	0	0	0.0%
Urogenital	1	1	0.5%	0	0	0.0%	0	0	0.0%
Vascular Event Post-Op Peripheral/DVT	0	0	0.0%	0	0	0.0%	1	1	1.7%

Only adverse events through the first 210 days are included.
[1]Cancer: cervical cancer
[2]Gastrointestinal-Other: epigastric pain, abdominal pain
[3]Infection: systemic
[4]Other: gynecological issue, dental surgery
[5]Prolonged postoperative sequelae: post operative low back pain, tightness in chest, fever, ENT issue, hyperglycemia
[6]Spinal Event at Target Level: back pain with or without leg pain, discogenic back pain, disc herniation/stenosis/slip, numbness/paresthesia
[7]Trauma: fall or motor vehicle accident or other trauma resulting in a broken or sprained foot or hand

A listing of all specific serious adverse events (SAEs) that occurred through Month 24 is identified in **Table 20** below. In total, sixty-nine (69) SAEs occurred in 32.4% (59/182) of investigational subjects, 47 SAEs were reported in 43.3% (42/97) of non-operative control subjects, and 19 SAEs occurred in 27.1% (16/59) of crossover subjects.

Table 20: Counts and Percentages of Subjects with Specific Serious Adverse Events at 24 Months – Investigational and Control mITT-Followed and Crossover

	Investigational (N=182)			Control (N=97)			Crossover (N=59)		
	Events	n	%	Events	n	%	Events	n	%
All AEs	69	59	32.4%	47	42	43.3%	19	16	27.1%
Back and/or Leg Pain (of back etiology)	3	3	1.6%	12	12	12.4%	1	1	1.7%
Cancer[1]	3	3	1.6%	0	0	0.0%	0	0	0.0%
Cardiovascular (i.e., M.I., Stroke)	1	1	0.5%	1	1	1.0%	1	1	1.7%
Cervical Spine Event	2	2	1.1%	0	0	0.0%	2	2	3.4%
Death[2]	0	0	0.0%	1	1	1.0%	0	0	0.0%
Depression	1	1	0.5%	0	0	0.0%	0	0	0.0%
Gastrointestinal-Other[3]	9	9	4.9%	0	0	0.0%	0	0	0.0%
Infection[4]	1	1	0.5%	1	1	1.0%	1	1	1.7%
Infection UTI	1	1	0.5%	0	0	0.0%	0	0	0.0%
Lower Extremity (not of back etiology, i.e., knee, ankle)	7	7	3.8%	1	1	1.0%	0	0	0.0%
Malpositioned Implant	0	0	0.0%	0	0	0.0%	1	1	1.7%
Neurological	2	2	1.1%	0	0	0.0%	0	0	0.0%
Other[5]	4	4	2.2%	4	4	4.1%	1	1	1.7%
Other Pain[6]	1	1	0.5%	0	0	0.0%	0	0	0.0%
Prolonged postoperative sequelae[7]	5	5	2.7%	4	4	4.1%	4	4	6.8%
Radiculopathy/Sciatica without back pain	1	1	0.5%	0	0	0.0%	0	0	0.0%
Respiratory	2	2	1.1%	1	1	1.0%	0	0	0.0%
Spinal Event at Target Level[8]	11	11	6.0%	19	18	18.6%	5	5	8.5%
Superficial Incision Infection	4	4	2.2%	0	0	0.0%	0	0	0.0%
Trauma[9]	3	3	1.6%	1	1	1.0%	1	1	1.7%
Upper Extremity Pain (not of neck etiology, i.e., shoulder, arm)	3	3	1.6%	1	1	1.0%	0	0	0.0%
Urogenital	5	5	2.7%	0	0	0.0%	0	0	0.0%
Vascular Event Post-Op Peripheral/DVT	0	0	0.0%	1	1	1.0%	2	2	3.4%

Only adverse events through the first 790 days are included.
[1]Cancer: cervical cancer
[2]Death: cardiac arrest
[3]Gastrointestinal Other: epigastric pain, hernia, abdominal pain, pancreatitis
[4]Infection: systemic, cough
[5]Other: breast surgery, dental surgery, gynecological disorder
[6]Other Pain: headache
7Prolonged postoperative sequelae: post operative low back pain, tightness in chest, fever, ENT issue, hyperglycemia
[8]Spinal Event at Target Level: low back pain with or without leg pain, disc herniation/stenosis/slip, spinous process bony erosion, facet joint changes
[9]Trauma: Trauma: fall or motor vehicle accident or other trauma resulting in a broken or sprained foot, ankle, hand; compression fracture, rotator cuff tear, or temporary increase in back pain

Treatment-Associated Serious Adverse Events

Table 21 shows the counts and percentages of all implant-associated and surgical procedure-associated SAEs, in the investigational and crossover groups. The counts and percentages of all non-operative treatment-associated SAEs in the non-operative care control group are discussed below. In the control group, there were 2 SAEs in 2 subjects (2.1%) that were non-operative treatment-associated, which were both classified as Worsening Back Pain.

Table 21: Counts and Percentages of Subjects with Serious Implant- and Surgical Procedure-Associated Adverse Events Through 24 Months - Investigational mITT-Followed and Crossover

	Investigational (N=182)			Crossover (N=59)		
	Events	n	%	Events	n	%
All AEs	15	14	7.7%	7	6	10.2%
Malpositioned Implant	0	0	0.0%	1	1	1.7%
Prolonged postoperative sequelae[1]	5	5	2.7%	4	4	6.8%
Radiculopathy/Sciatica without back pain	1	1	0.5%	0	0	0.0%
Respiratory	1	1	0.5%	0	0	0.0%
Spinal Event at Target Level	4	4	2.2%	1	1	1.7%
Back Pain	3	3	1.6%	0	0	0.0%
Disc Herniation/Stenosis/Slip	0	0	0.0%	1	1	1.7%
Spinous Process Bony Erosion	1	1	0.5%	0	0	0.0%
Superficial Incision Infection	4	4	2.2%	0	0	0.0%
Vascular Event Post-Op Peripheral/DVT	0	0	0.0%	1	1	1.7%

Only adverse events through the first 790 days are included.
[1]Prolonged postoperative sequelae: postoperative back pain, ENT disorder, hyperglycemia, tightness in chest, fever

Unanticipated Device Adverse Effects

Adverse events were reviewed by the CEC to confirm or reclassify the severity, seriousness, relationship to the device or procedure, and whether it was anticipated or unanticipated. No unanticipated adverse device effects were reported during the course of this study or adjudicated as such by the CEC.

Secondary Surgical Interventions

In the investigational group, procedures performed at the index level at or before Month 24 were considered secondary surgical intervention (SSI) failures in the clinical study. For the control group, SSI failure was defined as receiving an index level surgery (subsequent to poor response to the non-operative care provided) to treat the subject's original condition. After 6 months of non-operative care treatment, control subjects were permitted to cross over and undergo surgical treatment if their ODI score remained above 30 and their ODI score failed to improve by 15 points from baseline. It is important to note that while surgical interventions in the control group were technically classified as SSIs, these procedures represent *primary* surgical interventions for control subjects.

In the mITT-Followed analysis cohorts, there were a total of 13 SSIs in 12/182 (6.6%) of investigational subjects compared to 68 SSIs in 65/97 (67.0%) in non-operative care control subjects. Importantly, 56 of the 68 SSIs in the control group were crossover surgeries. Time course listings of secondary surgical interventions (SSIs) reported in the investigational and non-operative care control groups are provided in the tables below.

In the investigational group, 12/182 (6.6%) subjects had 13 additional surgeries at the index level, including 5 removals in 5/182 (2.7%) subjects, and 6 reoperations in 6/182 (3.3%) subjects, and 2/182 (1.1%) subjects had lumbar supplemental fixation procedures.

Table 22: SSI by Time of Occurrence – DIAM™ Spinal Stabilization System Investigational mITT-Followed

SSI Type	Event Time Course (Months)				Total (Events)
	0-3	3-6	6-12	12-24	
Removal and Decompression	1	1	0	1	3
Debridement and Wound Care	3	0	0	0	3
Decompression	1	1	0	1	3
TDR Placement (No Device Removal)	0	0	1	0	1
Removal	0	0	0	1	1
Removal, TDR Placement	0	0	0	1	1
Fusion	0	0	0	1	1
TOTAL	**5**	**2**	**1**	**5**	**13**

*To be consistent with the inclusion period for each time visit, events occurring with 104 days, 210 days, 425 days, 790 days are captured within the 0-3 months, 3-6 months, 6-12 months, and 12-24 months follow-up timepoints, respectively.

In the non-operative care control group, 68 SSIs were performed in 65/97 (67.0%) subjects through 24 months. Fifty-six (56/97, 57.7%) of these subjects received crossover surgery to the investigational device with 29 subjects receiving crossover surgery at the 6-month follow-up, 23 subjects between 6- and 12-months follow-up, and 9 subjects between 12 and 24 months. An additional 12 SSIs were considered treatment surgeries at the index level. Importantly, although classified as SSIs in the study, the 68 surgical procedures listed in the control group are *primary* surgical interventions.

Table 23: SSI by Time of Occurrence – Control mITT-Followed

SSI Type	Event Time Course (Months)				Total (Events)
	0-3	3-6	6-12	12-24	
Crossover Surgery	0	29	23	4	56
Instrumentation (Pedicle Screws) Removal and Decompression	0	0	0	1	1
Decompression	1	0	0	1	2
Fusion	1	0	1	2	4
Fusion and Decompression	0	1	2	1	4
Fusion and Arthroplasty**	0	0	1	0	1
TOTAL	**2**	**30**	**27**	**9**	**68**

* To be consistent with the inclusion period for each time visit, events occurring with 104 days, 210 days, 425 days, 790 days are captured within the 0-3 months, 3-6 months, 6-12 months, and 12-24 months follow-up timepoints, respectively.
** Subject experienced worsening severe discogenic low back pain and MRI showed L4-L5 advanced DDD with vascular fibrosis of adjacent vertebral bodies and a new disc herniation at L5-S1. The SSI included L4-L5 ALIF and L5-S1 arthroplasty.

Crossover subjects were followed for at least 24 months, and all secondary surgical interventions (SSIs) throughout the 24-month follow-up period from the time of crossover surgery were documented and adjudicated in accordance with the same criteria applied to the investigational cohort.

There were 4 SSIs in 3 crossover subjects (3/59, 5.1%). Two SSIs were classified as supplemental fixation procedures (fusion), and two were classified as removal procedures (Device Removal and Fusion; Device Removal, Fusion and decompression). One subject (1/59, 1.7%) underwent both supplemental fixation and removal procedures.

Neurological Status

Neurological status was evaluated prior to study treatment and at each follow-up visit (surgery/discharge assessment conducted for investigational and crossover subjects only). Neurological status was based on four types of measurements: motor, sensory, reflexes, and straight leg raising. Below, **Table 24** presents a summary of the proportion of investigational, control, and crossover subjects determined to have maintained or improved neurological functional status in the respective neurological domains at baseline and Month 24.

At Month 24, the overall assessment of neurologic function indicates that there are similar rates of maintenance or improvement of neurologic function in each of the treatment groups at all timepoints. The results demonstrate no acute or longer-term neurological deterioration (particularly in terms of motor function) after implantation of the DIAM™ Spinal Stabilization System.

Table 24: Neurological Functional Status – Investigational and Control mITT-Followed and Crossover

	Pre-Op									Month 24								
	Investigational			Control			Crossover			Investigational			Control			Crossover		
	N	n	%	N	n	%	N	n	%	N	n	%	N	n	%	N	n	%
Motor Functions	182	182	100.0%	97	97	100.0%	59	58	98.3%	166	162	97.6%	26	26	100.0%	57	55	96.5%
Sensory Functions	182	164	90.1%	97	91	93.8%	59	56	94.9%	166	152	91.6%	26	24	92.3%	57	52	91.2%
Reflexes	182	164	90.1%	97	88	90.7%	59	54	91.5%	166	160	96.4%	26	25	96.2%	57	54	94.7%
Straight Leg Raise	182	151	83.0%	97	75	77.3%	59	49	83.1%	166	161	97.0%	26	23	88.5%	57	55	96.5%

Implant Migration

Implant location of the investigational device and the positions of the left and right crimps were evaluated on anterior-posterior (AP) and lateral radiographs at each post-operative visit starting at 6 weeks, and were compared with radiographs obtained at surgery discharge to determine if migration of any component had occurred. No subjects treated with the DIAM™ Spinal Stabilization System device experienced a migration of any component through 24 months.

Spinous Process Fractures
In the investigational group, spinous process fractures were observed in 0 subjects pre-operatively, 5 subjects (2.9%; 5/171) at discharge, 8 subjects (4.5%; 8/179) at 6 weeks, 9 subjects (5.1%; 9/177) at 3 months, 8 subjects (4.6%; 8/173) at 6 months, 7 subjects at (4.0%; 7/157) at 12 months, and 3 subjects (1.9%; 3/157) at 24 months. Cumulatively, there were 14 (7.7%; 14/182) subjects with spinous process fractures within 24 months. Most spinous process fractures occurred by 6 weeks (64.3%; 9/14), and most were healed by Month 24 (78.6%; 11/14). No spinous process fractures were reported in the non-operative care control group at any point during the 24-month follow-up duration.

2. Effectiveness Results

Primary Endpoint
The primary endpoint analysis reported the CCS event rate at Month 24 in the mITT-Followed cohort (182 DIAM™ Spinal Stabilization System and 97 Non-operative Care subjects). At Month 24, the CCS rate was 63.9% (108/169) for the investigational group, and 11.9% (10/84) for the non-operative care control group based on evaluable subjects.

All subsequent effectiveness analyses are shown for the Back Pain Predominate Modified Intent-to-Treat (BPPmITT) analysis set (144 DIAM™ Spinal Stabilization System and 76 Non-operative Care subjects).

The BPPmITT analysis population was utilized due to a retrospective modification to the Indications for Use Statement for the DIAM™ Spinal Stabilization System, which limits use of the device to subjects with pre-operative back pain intensity greater than leg pain intensity. This change better defines the target population intended to be treated by the DIAM™ Spinal Stabilization System and helps to exclude subjects with predominate leg pain with radiculopathy. In line with this change, it was determined that presentation of effectiveness data from the BPP subset, which included a majority of study subjects, was most appropriate. It is important to note, however, that the effectiveness results for the BPPmITT analysis population were not substantially different from the mITT analysis population.

Similarly, the subsequent effectiveness analyses for the crossover subjects are shown for the Crossover Back Pain Predominant (Crossover BPP) analysis set, including 49 crossover subjects.

Table 25 and **Table 26** present the overall effectiveness evaluation for the BPPmITT and Crossover BPP analysis populations at Month 24 and Month 60, respectively.

Table 25: Overall Success Rates at 24 Months – Investigational and Control BPPmITT and Crossover BPP

	Investigational			Control			Crossover		
	N	n	%	N	n	%	N	n	%
Composite Clinical Success	135	91	67.4%	67	8	11.9%	48	33	68.8%
(1) No Secondary Surgical Intervention	144	136	94.4%	76	23	30.3%	49	46	93.9%
No Revision	144	144	100.0%	76	76	100.0%	49	49	100.0%
No Removal	144	139	96.5%	76	76	100.0%	49	48	98.0%
No Re-operation	144	139	96.5%	76	76	100.0%	49	49	100.0%
No Supplemental Fixation	144	140	97.2%	76	76	100.0%	49	46	93.9%
No Crossover/Treatment Surgery	144	144	100.0%	76	23	30.3%	49	49	100.0%
(2) ODI Responder	126	97	77.0%	15	8	53.3%	45	36	80.0%
(3) No Related Serious AEs	144	134	93.1%	76	75	98.7%	49	44	89.8%
No Implant Associated	144	143	99.3%	76	76	100.0%	49	49	100.0%
No Implant/Surgical Procedure Associated	144	143	99.3%	76	76	100.0%	49	49	100.0%
No Surgical Procedure Associated	144	136	94.4%	76	76	100.0%	49	44	89.8%
No Nonoperative Treatment Associated	144	144	100.0%	76	75	98.7%	49	49	100.0%

Table 26: Overall Success Rates at 60 Months – Investigational and Control BPPmITT and Crossover BPP

	Investigational			Control			Crossover		
	N	n	%	N	n	%	N	n	%
Composite Clinical Success	101	64	63.4%	64	7	10.9%	30	21	70.0%
(1) No Secondary Surgical Intervention	144	131	91.0%	76	20	26.3%	49	45	91.8%
(2) ODI Responder	84	66	78.6%	8	7	87.5%	24	22	91.7%
(3) No Related Serious AEs	144	133	92.4%	76	75	98.7%	49	44	89.8%

At 24 months, the CCS rate for the BPPmITT cohort was 67.4% (91/135) for investigational subjects, 11.9% (8/67) for non-operative care control subjects, and 68.8% (33/48) for crossover subjects. At 60 months, the CCS rates were largely maintained with a 63.4% (64/101) success rate for investigational subjects, 10.9% (7/64) for non-operative care control subjects, and 70.0% (21/30) for crossover subjects. The low CCS success rates in the control group at Month 24 and Month 60 is largely driven by the high number of crossover subjects, and other surgical procedures that occurred after 6 months.

Secondary Endpoints

This section focuses on secondary clinical endpoints from a number of relevant domains including ODI, back pain intensity (NRS), general health status (SF-36), subject work status and satisfaction assessments which were assessed preoperatively (baseline) and at prescribed clinical intervals throughout the follow-up period. Note that the high crossover rate in the control group makes interpretation of secondary endpoint success rates difficult after 6 months.

For each continuous clinical endpoint, summary tables were designed to present clinical outcomes for the investigational, control, and crossover groups over time. These tables include the individual sample sizes for each group at each timepoint as well as the mean, standard deviation (SD), and percentage of subjects meeting the pre-specified responder

criteria at each timepoint. Overall, subjects treated with the investigational device exhibited improvement across a spectrum of secondary analyses.

Table 27 below presents the responder rates for ODI, Back Pain Intensity, and SF-36 PCS at 24 and 60 months for both treatment groups in the BPPmITT analysis set (144 DIAM™ Spinal Stabilization System and 76 Non-operative Care subjects) and the Crossover BPP analysis set (n=49).

Table 27: Secondary Effectiveness Subject Outcomes at Month 24 and Month 60 Compared to Baseline - Investigational and Control BPPmITT and Crossover BPP

Secondary Effectiveness Endpoint	Investigational (N=144)		Control (N=76)		Crossover (N=49)	
	Month 24	Month 60	Month 24	Month 60	Month 24	Month 60
ODI Improvement ≥ 15-point Responder Rate (out of 100)	77.0% (97/126)	78.6% (66/84)	53.3% (8/15)	87.5% (7/8)	80.0% (36/45)	91.7% (22/24)
Back Pain Intensity ≥ 2-point Responder Rate (out of 10)	83.2% (104/125)	85.7% (72/84)	46.7% (7/15)	75.0% (6/8)	90.9% (40/44)	87.5% (21/24)
SF-36 PCS ≥ 5-point Responder Rate (out of 100)	75.6% (93/123)	71.1% (59/83)	40.0% (6/15)	75.0% (6/8)	86.4% (38/44)	79.2% (19/24)

ODI Results

Table 28 presents the mean ODI scores and the ODI responder rates through the Month 60 follow-up for both treatment groups comprising the BPPmITT analysis set (144 DIAM™ Spinal Stabilization System and 76 non-operative care), as well as the Crossover BPP analysis set (n=49).

ODI is scored on a 50-point scale (10 questions with a score of 0-5 for each) and is then normalized to a scale of 100 percentage points. Higher ODI is representative of greater disability. In the investigational and crossover groups, mean ODI scores were improved at all time-points compared to baseline. The ODI responder rates (defined as a ≥ 15-point decrease in ODI) at all follow-up timepoints up through Month 48 were higher in the investigational group than the control group. At Month 60 the control group had a higher responder rate (87.5%) than the investigational group (78.6%); however, significant attrition in the control group limits interpretation of longer-term outcomes. The responder rate for the crossover group was similar to the investigational group through Month 60.

Table 28: Mean ODI Score and ODI Responder Rates Over 60 Months – Investigational and Control BPPmITT and Crossover BPP

	Investigational					Control					Crossover				
	N	Mean	SD	Responder		N	Mean	SD	Responder		N	Mean	SD	Responder	
				n	%				n	%				n	%
Pre-Op	144	49.9	14.1	N/A	N/A	76	50.8	13.4	N/A	N/A	49	55.2	13.3	N/A	N/A
Week 06	140	26.4	16.6	92	65.7%	73	43.3	15.1	17	23.3%	49	25.7	15.7	35	71.4%
Month 03	139	22.1	16.4	111	79.9%	73	42.6	15.9	21	28.8%	49	22.2	17.3	36	73.5%
Month 06	140	20.7	16.9	110	78.6%	71	50.5	16.3	12	16.9%	49	22.2	17.3	39	79.6%
Month 12	137	21.6	19.7	105	76.6%	24	41.1	18.1	9	37.5%	47	21.1	16.9	38	80.9%
Month 24	126	20.2	17.0	97	77.0%	15	35.9	20.1	8	53.3%	45	20.5	17.9	36	80.0%
Month 36	120	20.1	18.9	91	75.8%	12	33.2	18.1	6	50.0%	40	18.8	16.0	33	82.5%
Month 48	103	18.0	17.4	85	82.5%	8	32.0	18.2	6	75.0%	35	19.7	13.7	31	88.6%
Month 60	84	19.3	18.8	66	78.6%	8	32.3	21.6	7	87.5%	24	17.5	12.6	22	91.7%

Back Pain Results

Table 29 shows mean back pain intensity scores and back pain intensity responder rates over 60 months. Subjects rated their back pain intensity on the Numerical Rating Scale (NRS) from 0-10, with a score of 0 representing "no pain" and a score of 10 representing "pain as bad as it could be."

In the investigational and crossover groups, mean back pain intensity scores decreased at all follow-up timepoints as compared to baseline. Back pain intensity responder rates (defined as a ≥ 2-point decrease on NRS) were above 75% at all follow-up timepoints in the investigational and crossover groups.

Table 29: Mean Back Pain Intensity Scores and Back Pain Intensity Responder Rates Over 60 Months – Investigational and Control BPPmITT and Crossover BPP

	Investigational					Control					Crossover				
	N	Mean	SD	Responder		N	Mean	SD	Responder		N	Mean	SD	Responder	
				n	%				n	%				n	%
Pre-Op	144	8.1	1.6	N/A	N/A	76	7.9	1.7	N/A	N/A	49	7.5	1.7	N/A	N/A
Week 06	140	3.3	2.5	126	90.0%	73	6.3	2.4	33	45.2%	49	2.8	2.3	43	87.8%
Month 03	139	3.4	2.7	117	84.2%	73	6.1	2.6	29	39.7%	48	2.9	2.5	43	89.6%
Month 06	139	3.3	2.7	117	84.2%	71	6.8	2.3	28	39.4%	49	3.0	2.9	39	79.6%
Month 12	137	3.6	3.2	107	78.1%	24	5.9	2.8	11	45.8%	47	3.0	2.9	36	76.6%
Month 24	125	3.4	3.1	104	83.2%	15	5.5	3.3	7	46.7%	44	2.5	2.4	40	90.9%
Month 36	119	3.4	3.2	99	83.2%	12	5.1	3.2	7	58.3%	40	2.8	2.7	31	77.5%
Month 48	103	2.8	3.0	84	81.6%	8	5.1	2.9	6	75.0%	35	3.2	2.7	28	80.0%
Month 60	84	2.9	2.9	72	85.7%	8	4.4	3.0	6	75.0%	24	2.7	2.4	21	87.5%

SF-36 PCS Results

Table 30 shows mean SF-36 Physical Component Score (PCS) scores and SF-36 PCS responder rates over 60 months for the BPPmITT analysis set (144 DIAM™ Spinal Stabilization System and 76 non-operative care), and Crossover BPP analysis set (n=49). In the investigational and crossover groups, mean SF-36 PCS scores increased at all follow-up timepoints from baseline. SF-36 PCS responder rates (defined as an improvement of ≥ 5 points in SF-36 PCS) were above 70% at all follow-up timepoints 3 months and after for the investigational and crossover subjects.

Table 30: Mean SF-36 PCS Scores and SF-36 PCS Responder Rates Over 60 Months – Investigational and Control BPPmITT and Crossover BPP

	Investigational					Control					Crossover				
	N	Mean	SD	Responder		N	Mean	SD	Responder		N	Mean	SD	Responder	
				n	%				n	%				n	%
Pre-Op	143	31.9	6.3	N/A	N/A	76	30.4	5.8	N/A	N/A	49	29.5	5.0	N/A	N/A
Week 06	137	39.5	7.4	76	55.5%	73	32.8	6.4	26	35.6%	49	39.7	7.6	35	71.4%
Month 03	138	41.5	8.3	97	70.3%	72	32.6	6.6	20	27.8%	48	41.1	8.5	35	72.9%
Month 06	139	42.8	8.6	103	74.1%	71	30.8	6.4	18	25.4%	48	41.3	8.7	37	77.1%
Month 12	135	43.0	9.3	102	75.6%	24	33.5	8.0	6	25.0%	47	42.4	8.0	39	83.0%
Month 24	123	43.2	9.4	93	75.6%	15	36.4	9.0	6	40.0%	44	42.9	9.1	38	86.4%
Month 36	117	43.4	9.4	86	73.5%	12	36.3	10.2	6	50.0%	39	42.0	9.0	30	76.9%
Month 48	102	44.0	9.3	76	74.5%	8	36.9	9.9	5	62.5%	35	41.1	8.1	28	80.0%
Month 60	83	43.5	9.3	59	71.1%	8	38.7	10.0	6	75.0%	24	41.8	7.1	19	79.2%

Subject Satisfaction with Treatment

At the 24 month follow-up timepoint, 81.2% (108/133) of investigational subjects and 57.9% (11/19) of control subjects were satisfied with the results of their non-operative care or surgical intervention; 76.7% (102/133) of investigational subjects and 57.9% (11/19) of control subjects said that it was "definitely true" or "mostly true" that they were helped as much as they expected; and 81.2% (108/133) of investigational subjects said that they would have the treatment again for the same condition, as compared to 42.1% (8/19) of control subjects. Based on these results, investigational subjects were more satisfied with their treatment than the subjects in the control group.

Global Subject Perception of Treatment Effectiveness

At 24 months, the success rate of subject global perception of treatment effect was 86.2% (112/130) for the investigational subjects and 57.9% (11/19) for the control subjects.

Work Status

Subjects were asked to provide work status at preoperative and each postoperative follow-up through 24 months. Preoperatively, 68.8% (99/144) of investigational subjects and 69.7% (53/76) of control subjects reported working. At 24 months following surgery, 72.5% (95/131) of investigational subjects and 52.6% (10/19) of control subjects reported working.

Pain Medication Usage

At baseline, the number of subjects who were taking narcotic pain medications in some capacity was 49.3% (69/143) among investigational subjects and 58.7% (44/75) among non-operative care subjects. At Month 24, these rates dropped to 28.6% (38/133) among investigational subjects and 36.8% (7/19) among non-operative care subjects. Furthermore, the number of investigational subjects who were taking narcotic pain medications daily decreased from 23.1% (33/143) at baseline to 15.0% (20/133) at 24 months while the percentage of control subjects also decreased (baseline: 30.7% (23/75); 24 months: 21.1% (4/19)). The decreasing trend in daily narcotic pain medication usage compared to baseline

in investigational subjects was consistent at later timepoints where 18.9% (24/127), 17.0% (19/112), and 14.1% (13/92) of investigational subjects reported daily use at the 36-, 48-, and 60-month follow-up visits.

Disc Height and Angular Range of Motion

Radiographic analyses are presented in the following tables. Note that significant attrition in the control group limits the ability to compare results across groups.

Posterior disc height was measured between the posterior-inferior corner of the superior vertebra and the posterior-superior corner of the inferior vertebra. Average disc height was calculated as the simple mean of the posterior and anterior disc heights.

Mean posterior disc height as shown in **Table 31** was numerically higher through Month 12 in subjects treated with the DIAM™ Spinal Stabilization System as compared to the non-operative care control. Mean average disc height was maintained across all groups through 24 months.

Table 31: Mean Posterior Disc Height (mm) at Target Level up to 24 Months – Investigational and Control BPPmITT and Crossover BPP

	Investigational			Control			Crossover		
	N	Mean	SD	N	Mean	SD	N	Mean	SD
Pre-Op	141	7.0	1.7	76	7.0	2.0	49	7.0	2.0
Week 06	139	7.8	1.9	70	6.9	1.9	49	7.9	2.2
Month 03	141	7.8	2.0	74	6.7	2.0	48	7.8	2.4
Month 06	136	7.6	1.9	71	6.8	1.9	49	7.6	2.1
Month 12	138	7.5	2.0	27	6.6	2.0	46	7.3	2.0
Month 24	122	7.3	1.9	16	7.5	2.1	46	7.0	2.2

Mean intervertebral angle in extension was reduced in subjects treated with DIAM™ Spinal Stabilization System as compared to non-operative care at Week 6 through Month 24.

Table 32: **Mean Intervertebral Angle (degrees) at Extension Position up to 24 Months – Investigational and Control BPPmITT and Crossover BPP**

	Investigational			Control			Crossover		
	N	Mean	SD	N	Mean	SD	N	Mean	SD
Pre-Op	141	9.5	3.8	73	9.4	4.2	49.0	9.7	3.9
Week 06	136	6.0	3.7	70	9.5	4.2	49.0	7.1	3.9
Month 03	139	6.5	3.9	73	9.5	4.1	47.0	6.6	3.7
Month 06	136	7.3	4.3	69	9.9	4.1	49.0	7.5	3.7
Month 12	136	7.6	4.3	27	10.0	5.0	46.0	8.6	3.7
Month 24	122	7.4	4.4	15	8.6	4.2	45.0	8.3	3.8

No meaningful difference in mean intervertebral angle in flexion was seen through Month 24 between groups.

Table 33: Mean Intervertebral Angle (degrees) at Flexion Position up to 24 Months – Investigational and Control BPPmITT and Crossover BPP

	Investigational			Control			Crossover		
	N	Mean	SD	N	Mean	SD	N	Mean	SD
Pre-Op	141	2.0	5.7	73	1.2	5.2	49	2.3	5.6
Week 06	135	0.6	4.3	70	1.6	5.4	49	1.7	3.8
Month 03	139	0.8	4.6	73	1.8	5.3	47	1.2	4.0
Month 06	136	0.9	5.1	70	1.9	5.3	49	1.7	4.9
Month 12	136	1.1	5.1	27	2.6	5.3	46	2.5	5.7
Month 24	122	1.1	5.4	16	0.4	5.9	45	1.4	5.3

3. Subgroup Analyses

The study was not specifically powered for any subgroup analyses.

4. Pediatric Extrapolation

In this premarket application, existing clinical data were not leveraged to support approval for a pediatric patient population.

XI. FINANCIAL DISCLOSURE

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 24 principal investigators and 50 sub-investigators who were associated with sites that enrolled and treated subjects of which none were full-time or part-time employees of the sponsor and 15 (seven principal investigators and eight sub-investigators) had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c), and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: None
- Significant payment of other sorts: 15
- Proprietary interest in the product tested held by the investigator: None
- Significant equity interest held by investigator in sponsor of covered study: None

Companion Spine has adequately disclosed the financial interest/arrangements with clinical investigators in both the IDE study (G050025) and the Long-term Follow-Up (LTFU) study. Statistical analyses were conducted by FDA to determine whether the

financial interests/arrangements had any impact on the clinical study outcomes. Findings from these analyses did not raise any questions about the reliability of the data.

XII. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

A long-term follow-up (LTFU) Study, sponsored by Companion Spine, was conducted to evaluate the long-term outcomes of treatment with the DIAM™ Spinal Stabilization System in the extended follow-up of the pivotal IDE study subjects.

- Study Design

There was no randomization for this study. The design was a hybrid prospective/retrospective, multicenter, single-arm, data collection study. The goal was to collect long-term follow-up data on patients who participated in the DIAM™ Spinal Stabilization System IDE Study and received the investigational device. Therefore, eligible subjects included those who were randomized to the investigational arm or were randomized to the control arm and crossed over to receive DIAM™ Spinal Stabilization System treatment. The enrolled subjects comprising the LTFU population (n=116) were evaluated for device safety and effectiveness at the LTFU timepoint, which was an average of 11.5 years (min 8.3 years, max 15.3 years). The enrolled subjects comprising the long-term follow-up back pain predominant population (LTFU BPP, n=92) were evaluated for device effectiveness at the LTFU timepoint.

- Subject Accountability

All investigational sites participating in the original IDE study (G050025) were invited to participate in the LTFU Study. Nine (9) investigational sites agreed to participate in the LTFU Study. Fourteen (14) sites did not participate in the LTFU Study; five (5) were excluded as no subjects were treated with the DIAM™ Spinal Stabilization System , the principal investigator (PI) and/or sub-investigator(s) (Sub-I) from four (4) sites had moved practices and were unable to be reached, the PIs from three (3) sites had moved practices and the remaining Sub-Is declined to participate, and the remaining two (2) sites were unresponsive.

A total of 241 subjects were treated with the DIAM^{TM} Spinal Stabilization System in the IDE study; 182 subjects were randomized to the investigational group and a total of 59 subjects originally randomized to non-operative care ultimately crossed over to receive treatment with the DIAM^{TM} Spinal Stabilization System device. Of these 241 subjects potentially eligible for enrollment in the LTFU Study, 60 were excluded due to their corresponding site electing to not enroll in the study. Of the 181 subjects treated at participating sites, a total of 116 patients were enrolled and evaluated for long-term follow-up. Of the 116 enrolled subjects, 83 were originally randomized to treatment with the

DIAM™ Spinal Stabilization System, and 33 were subjects who crossed over to receive treatment with the DIAM™ Spinal Stabilization System.

The LTFU Back Pain Predominant (LTFU BPP) analysis set consisted of 92 patients. Of those 92 patients, 62 were originally randomized to treatment with the investigational device and 30 were subjects who crossed over to receive treatment with the investigational device.

A subject accounting tree is provided in **Figure 3**.

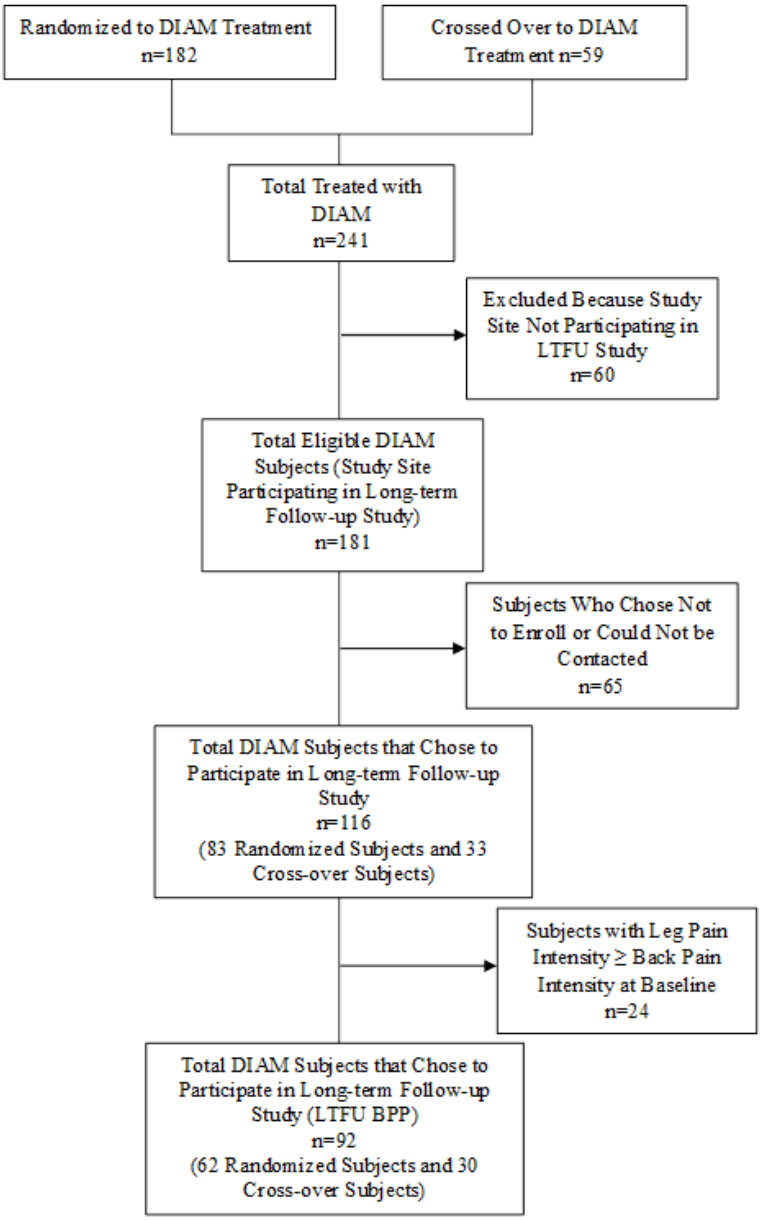

Figure 3: Subject Accounting Tree – LTFU Study

- Study Population Demographics and Baseline Parameters

Table 34 summarizes the demographic and baseline continuous variables for the LTFU population. The mean age and BMI of these subjects (n=116) were 44.6 years and 28.8 kg/m^2, respectively.

Table 34: Summary of Baseline and Demographic Continuous Variables - LTFU Subjects

	LTFU					
	N	Mean	SD	Med	Min	Max
Age (years)	116	44.6	10.0	46.0	18.0	63.0
Height (in)	116	67.6	3.9	67.0	60.0	76.0
Weight (lbs)	116	188.2	41.7	187.5	110.0	310.0
BMI (kg/m^2)	116	28.8	5.1	28.4	18.9	39.8

Table 35 shows the demographic and baseline categorical variables. Overall, the enrolled study population consisted of 65 females (56.0%) and 51 males (44.0%).

Table 35: Summary of Baseline and Demographic Categorical Variables – LTFU Subjects

	LTFU		
	N	n	%
Sex			
Female	116	65	56.0%
Male	116	51	44.0%
Race			
Caucasian	116	110	94.8%
Black	116	4	3.4%
Asian	116	0	0.0%
Hispanic	116	1	0.9%
Other	116	1	0.9%
Education Level			
< High School	116	7	6.0%
High School	116	35	30.2%
> High School	116	73	62.9%
Not Reported	116	1	0.9%
Spinal Litigation			
Yes	116	24	20.7%
No	116	92	79.3%
Back Surgery Hx			
Yes	116	2	1.7%
No	116	114	98.3%
Marital Status			
Single	116	19	16.4%
Married	116	70	60.3%
Divorced	116	23	19.8%
Separated	116	2	1.7%
Widowed	116	2	1.7%

Table 36 shows the baseline clinical endpoints. Back pain intensity and leg pain intensity were both captured via Numerical Rating Scales (NRS) (0 – 10 scale).

Table 36: Baseline Clinical Endpoints – LTFU Subjects

	LTFU					
	N	Mean	SD	Med	Min	Max
Back Pain	116	8.1	1.6	8.0	4.0	10.0
Leg Pain	116	5.0	3.2	6.0	0.0	10.0
ODI	116	51.0	14.5	50.0	30.0	96.0
SF36: MCS	116	36.0	9.0	37.4	13.4	52.1
SF36: PCS	116	31.8	6.0	30.9	19.8	47.8

- Operative Data

Table 37 summarizes the continuous variables for the operative details of the LTFU population. In the LTFU population, 6.0% (7/116) of subjects were treated at L2-L3, 10.3% (12/116) were treated at L3-L4, and 83.6% (97/116) were treated at L4-L5.

Table 37: Summary of Operative Continuous Variables – LTFU Subjects

	LTFU					
	N	Mean	SD	Med	Min	Max
Surgery Time (min)	116	58.6	14.7	55.0	24.0	95.0
Blood Loss (mL)	116	31.9	29.6	20.0	0.0	100.0
Length of Stay (days)	116	0.7	0.7	1.0	0.0	6.0

- Safety and Effectiveness Results

All safety outcomes are presented for the 116 total subjects who were treated with the investigational device and participated in the LTFU Study. All effectiveness outcomes are presented for the LTFU BPP analysis set comprising 92 patients treated with the DIAM™ Spinal Stabilization System.

Secondary Surgical Interventions

Sixteen (16) SSIs were reported in 12 subjects (10.3%, 12/116) over the total duration of the LTFU period (with a mean final follow-up of 11.5 years). A timecourse summary of all SSIs, as classified by the CEC is presented in **Table 38.** The mean time to secondary surgery was 44.5 months post-op (range, 3-122 months). The Kaplan-Meier survival rate of freedom from secondary surgery through final follow-up is 88.9%.

Table 38: Secondary Surgical Intervention Timecourse – LTFU Subjects

SSI Type	Procedure Description*	Event Timecourse (Months)								Total (Events)
		0-3	3-6	6-12	12-24	24-36	36-84	84-120	>120	
Removal	2 DIAM™ Removal 1 DIAM™ Removal and Decompression + Fusion 1 DIAM™ Removal and Decompression	-	-	-	2	-	1	-	1	**4**
Revision	N/A	-	-	-	-	-	-	-	-	**0**
Reoperation	2 Decompression 1 Decompression w/ temporary device elevation	1	1	-	1	-	-	-	-	**3**
Supplemental Fixation	1 TDR (No DIAM™ Removal) 1 Decompression + TDR 1 Fusion w/ DIAM™ Removal 1 Decompression + Fusion 2 Fusions	-	-	2	-	2	1	1	-	**6**
Other	2 Spinal cord stimulators 1 Spinal cord stimulator revision	-	-	-	-	-	-	2	1	**3**
Total		**1**	**1**	**2**	**3**	**2**	**2**	**3**	**2**	**16**

*Note that subjects may have simultaneously undergone multiple procedures; type of procedure is shown separately in this column

Osteolysis and Spinous Process Fracture

Radiographs were collected by trained technicians to evaluate spinous process fractures (SPF), bony erosions, and bony changes. Subjects with previously confirmed symptomatic spinous process fractures were evaluated with CT.

At the final LTFU visit, no subjects exhibited radiographic evidence of osteolysis at either the superior or inferior spinous processes at the index level. Of the 52 subjects with evaluable images at both the Month 24 and final LTFU visit, 5.8% (3/52) of subjects and 1.9% (1/52) of subjects were observed to exhibit contour change of the superior and inferior

spinous processes, respectively, between Month 24 and final follow-up (occurring at a mean 11.5 years).

Of the 116 subjects who enrolled in the LTFU Study, 12 subjects had experienced an SPF during the mean 11.5-year follow-up period. Notably, five (5) of these 12 subjects had fractures which were observed and confirmed to heal prior to month 24 and were not observed to have any subsequent fractures throughout the remainder of the duration of the LTFU Study.

Seven (n=7) of the 96 subjects (7.3%) who had evaluable images at the final LTFU visit exhibited SPFs. Five (n=5) of these were present in the superior spinous process compared to two (n=2) in the inferior spinous process. Of the seven (7) patients with SPFs observed at the LTFU visit, only three (3) had SPFs which had not been previously observed at any earlier time point. Notably, of the seven (7) subjects that had an SPF present at the final LTFU visit, only one (1) was a CCS secondary endpoint failure. The subject was a CCS failure due to not being an ODI responder. The subject did not undergo an SSI.

Neurologic Changes

Neurological status (including motor and sensory measurements) was evaluated and compared to baseline evaluations. All subjects (100%, 113/113) that presented with normal motor function at baseline also had normal motor function at LTFU. Of the patients who presented with normal sensory at baseline, 82.3% (93/113) remained normal at LTFU, and 100.0% (13/13) of the subjects with abnormal sensory function at baseline improved to normal at LTFU. Conversely, seven subjects (6.2%, 7/113) that presented with normal sensory function at baseline were observed to have abnormal sensory function at LTFU.

LTFU ODI Results

ODI responder success is defined as greater than or equal to a 15-point improvement (negative change) from baseline.

Below, **Table 39** presents the mean ODI scores and responder rates (censored at DIAM™ removal SSI) over time for LTFU BPP subjects in the LTFU Study at baseline, 24 months, and the LTFU visit. The mean, standard deviations from the mean value, and proportion of subjects achieving the responder criteria are presented for each time point. The mean ODI continually decreased from 51.7 at baseline to 18.0 and 16.6 at 24 months and LTFU, respectively. The ODI responder rate was shown to improve through LTFU from the Month 24 visit, improving from 82.4% to 86.4%.

Table 39: ODI Mean Scores and ODI Responder Rates Over Time (Baseline, 24 Month, LTFU) – LTFU BPP Subjects

	LTFU				
	N	Mean	SD	Responder	
				n	%
Pre-Op	92	51.7	15.2	N/A	N/A
Month 24	91	18.0	15.3	75	82.4%
Long-term Follow -up Visit	88	16.6	17.3	76	86.4%
Note: Censored at DIAM ™ Spinal Stabilization System Removal SSI					

Back Pain Intensity Results

The NRS results were used to evaluate back pain intensity. Subjects rated their back pain intensity on a scale from 0-10, with a score of 0 representing "no pain" and a score of 10 representing "pain as bad as it could be."

Table 40 presents the mean NRS back pain intensity and responder rates (censored at DIAM™ removal SSI) over time for LTFU BPP subjects in the LTFU Study at baseline, 24 months, and the LTFU visit. The mean, standard deviations from the mean, and proportion of subjects achieving the responder criteria are presented for each time point. The mean NRS back pain continually decreased from 8.1 at baseline to 3.0 at month 24 and 2.7 at LTFU. The defined criteria for a subject to be considered a responder was greater than or equal to a 2-point decrease in back pain intensity score. 89.0% (81/91) and 86.4% (76/88) of the LTFU BPP subjects were considered responders at 24 months and at the LTFU visit, respectively.

Table 40: Back Pain Mean Scores and Responder Rates Over Time (Baseline, Month 24, LTFU) – LTFU BPP Subjects (Censored at DIAM™ Removal SSI)

	LTFU				
				Responder	
	N	Mean	SD	n	%
Pre-Op	92	8.1	1.6	N/A	N/A
Month 24	91	3.0	2.9	81	89.0%
Long-term Follow -up Visit	88	2.7	2.9	76	86.4%
Note: Censored at DIAM ™ Spinal Stabilization System Removal SSI					

Additional Effectiveness Results

In addition to durable improvements in back pain and back pain-related disability, subjects in the LTFU Study reported clinically meaningful outcomes across additional secondary effectiveness endpoints related to general physical function (SF-36 PCS) and subject satisfaction. **Table 41** presents the outcomes at the final LTFU visit, occurring at a mean

of 11.5 years. Notably, the rates of subjects' perceived effect with the treatment and subject global perception of treatment effect demonstrate that the majority of subjects in the LTFU cohort experienced clinically meaningful quality of life improvements which were maintained through LTFU.

Table 41: Secondary Effectiveness Subject Outcomes at LTFU Compared to Baseline – LTFU BPP Subjects

Secondary Effectiveness Endpoint	LTFU BPP (N=92)
SF-36 PCS ≥ 5-point Responder Rate (out of 100)*	63/87 (72.4%)
Subject Satisfaction with Treatment:	
1) I am satisfied with the results of my surgery	79/92 (85.9%)
2) I was helped as much as I thought I would be with my surgery	75/92 (81.5%)
3) All things considered I would have the surgery again for the same condition	80/92 (87.0%)
4) I would recommend the procedure to a friend	75/92 (81.5%)
Global Subject Perception of Treatment Effectiveness Success	
1) DIAM provided relief of my symptoms at some point after surgery	82/92 (89.1%)
2) Following DIAM treatment, I was able to return to normal quality of life	81/92 (88.0%)

* Note: Censored at DIAM™ Spinal Stabilization System Removal SSI

Additionally, the number of LTFU BPP patients taking narcotic pain medications decreased from 45.1% of patients (41/91) using narcotics at baseline to 15.6% (14/90) at LTFU. The usage of non-narcotic pain medications, non-steroidal anti-inflammatory drugs (NSAIDs), and muscle relaxants all decreased as well.

XIII. PANEL MEETING RECOMMENDATION AND POST-PANEL ACTION

A. Panel Meeting Recommendation

A meeting of the Orthopaedic and Rehabilitation Devices (OR) Panel of the Medical Devices Advisory Committee was held on February 19, 2016. At this meeting, the OR Panel was presented with 12-month interim analysis of 150 subjects collected under IDE G050025. The OR Panel voted 4 "yes", 7 "no", and 0 "abstain" that the data showed reasonable assurance that the device is safe for use in patients who meet the criteria specified in the proposed indications for use. The OR Panel voted 2 "yes", 8 "no" and 1 "abstain" that there is reasonable assurance that the device is effective for use in patients who meet the criteria specified in the proposed indications for use. The OR Panel voted 0 "yes", 7 "no", and 4 "abstain", that the benefits of the device do outweigh the risks in patients who meet the criteria specified in the proposed indications for use. Concerns communicated by the OR Panel included the timepoint of the *a priori* primary endpoint evaluation (12 months), heterogeneity of the study population, control group selection and crossover design, observations during index DIAM™ Spinal Stabilization System treatment, severity of the enrolled population at baseline, interpretability of safety data attributed to classifications used, and need to better understand the long-term safety of the subject device.

B. FDA's Post Panel Meeting Action

The current applicant provided an updated clinical evaluation report with complete follow-up through Month 24 on all available subjects and provided supplemental LTFU study results on a subset of the G050025 IDE patients with an average of 11.5 years of follow-up. The previous concerns raised by the OR Panel were addressed as follows:

- The primary endpoint was revised to evaluate the pre-specified CCS at Month 24 rather than Month 12.
- The Indications for Use and Contraindications were refined to further target appropriate candidates for the DIAM™ Spinal Stabilization System. Analyses were further updated to reflect the indicated population.
- Additional analyses were provided in an attempt to account for confounding factors introduced by the availability of a crossover option.
- Concerns with spinous process fracture and osteolysis were addressed with outcomes in the presented full 24-month follow-up data and LTFU data.
- The IDE safety data were re-adjudicated by an independent CEC to ensure consistent classification of adverse events and to enhance the interpretability of safety outcomes.

The applicant has adequately addressed the outstanding issues raised by the Panel through the totality of scientific evidence presented in the subject PMA, both from the IDE clinical study and supplemental LTFU data.

XIV. CONCLUSIONS DRAWN FROM THE PRECLINICAL AND CLINICAL STUDIES

The scientific evidence that has been presented herein provides reasonable assurance of the safety and effectiveness of the DIAM™ Spinal Stabilization System in the treatment of moderate to severe primary low back pain (greater than leg pain) secondary to lumbar degenerative disc disease (DDD), at a single level from L2-L5 with current episode refractory to at least 6 months non-operative care.

A. Effectiveness Conclusions

One-hundred eighty-two (N=182) subjects were randomized and received the DIAM™ Spinal Stabilization System device, and N=101 subjects were randomized and provided with non-operative care (collectively, the mITT analysis set). Assessment of effectiveness was performed using the BPPmITT analysis set (N=144 DIAM™ Spinal Stabilization System and N=76 non-operative care subjects).

In subjects evaluable at Month 24, the investigational group demonstrated a clinically meaningful and substantial advantage over the non-operative care control group. Overall, the CCS rate at Month 24 for the BPPmITT analysis set was 67.4% (91/135) for the DIAM™ Spinal Stabilization System cohort, and 11.9% (8/67) for the non-operative care cohort.

It is acknowledged that there are limitations with the study design, due in part with the non-operative care being tailored to each subject, and therefore, not standardized. Furthermore, the availability of a crossover treatment for subjects in the control group may have biased study outcomes against the control group. As crossover subjects were defined in the study protocol as individual subject failures in the control group, and a substantial proportion of subjects underwent crossover treatment in the control group by Month 24 (58%, 56/97), the impact of the crossover on the success rate in the control group was substantial. Additional retrospective analyses were performed in attempts to remove the impact of the crossover design on the control group success rate. The analysis in **Table 42** below shows the CCS rates for the investigational and control groups at Month 24 with: (1) crossover subjects removed from the analysis, (2) control subjects that underwent surgical interventions (other than crossover) not considered failures, (3) control subjects with missing ODI data were removed. These analyses substantially reduce the sample size in the control group. However, even with this exaggerated, best-case evaluation of the control group data, the CCS rates are still numerically in favor of the investigational cohort as compared to the control cohort.

Table 42: Month 24 CCS with Missing ODI Removed; Crossover Subjects Removed; Control Subjects with Treatment Surgery Not Considered SSI Failures

	Investigational			Control		
	N	n	%	N	n	%
Composite Clinical Success	135	91	67.4%	18	10	55.6%
(1) No Secondary Surgical Intervention	144	136	94.4%	30	30	100.0%
(2) ODI Responder	126	97	77.0%	18	10	55.6%
(3) No Related Serious AEs	144	134	93.1%	30	29	96.7%

Additionally, secondary effectiveness endpoints assessing pain, function, and overall subject quality of life further demonstrated that a large percentage of investigational subjects achieved a clinically meaningful improvement at first follow-up at Week 6 that persists through Month 24. Subjects in the investigational group achieved an ODI responder success rate of 77.0% (97/126), and a back pain intensity responder success rate of 83.2% (104/125). Similarly, in the subsequent LTFU study, DIAM™ Spinal Stabilization System subjects achieved an ODI responder success rate of 86.4% (76/88), and a back pain intensity responder success rate of 86.4% (76/88), with average follow-up out to 11.5 years.

B. Safety Conclusions

The risks of the DIAM™ Spinal Stabilization System are based on non-clinical testing as well as data collected under IDE G050025 and the subsequent LTFU study. Non-clinical testing performed on the device demonstrated that the DIAM™ Spinal Stabilization System is designed to withstand the expected physiologic loads in the lumbar spine. The clinical data from the mITT-Followed analysis set were used in the primary safety analysis. Data considered were AEs, index-level SSIs, and neurological status at Month 24. These same safety endpoints were further evaluated through a mean final follow-up of 11.5 years under the subsequent LTFU study.

The results of the IDE clinical study demonstrate reasonable assurance that the DIAM™ Spinal Stabilization System is safe as compared to the control group. At 24 months, the rate of subjects reporting an AE was 92.9% (169/182) for the investigational subjects and 89.7% (87/97) for the control subjects, and the rate of subjects reporting an SAE was 32.4% (59/182) in the investigational group and 43.3% (42/97) in the control group. Of these SAEs, 7.7% (14/182) of investigational subjects had a treatment-associated SAE with one subject having both a surgical procedure-associated SAE (prolonged postoperative sequelae) and an implant/surgical procedure associated SAE (incision-related). In the control group, 2.1% (2/97) of subjects had a non-operative treatment-associated SAE. Additionally, neurological success, defined as maintenance of improvement in neurological status at 24 months, was comparable between the investigational cohort and non-operative care control cohort.

A total of 13 SSIs occurred in 12 (6.6%) subjects in the DIAM™ Spinal Stabilization System group through Month 24. Seven (7) SSIs occurred in 6 subjects within 6 months, 1 SSI occurred between 6 and 12 months, and 5 SSIs occurred in 5 subjects between 12 and 24 months. In the non-operative care group, 68 events in 65 (67%) subjects were classified as SSIs through Month 24. In the non-operative care group, 56 of the SSIs were crossovers to DIAM™ Spinal Stabilization System treatment, and the majority of the remaining 12 events were primary surgeries after failed non-operative care (control treatment). The events classified as SSIs between the investigational and control cohorts are not directly comparable. However, the rates of secondary surgeries observed for the DIAM™ Spinal Stabilization System appear acceptable as compared to the rates reported for other devices in this class that have received marketing approval in the U.S.

The LTFU study provides important information on the safety profile of the DIAM™ Spinal Stabilization System through more than a decade of follow-up. The LTFU study outcomes showed no increase in the rate of SSI during the LTFU, as a total of 16 SSIs occurred in 12 subjects (10.3%, 12/116) over the total duration of the LTFU study (mean follow-up of 11.5 years). Furthermore, the number of SSIs in the LTFU cohort involving a removal of the DIAM™ Spinal Stabilization System device was low. The survival rate of freedom from device removal was 95.7% (111/116) through final follow-up in the LTFU study. Additionally, no device-associated SAEs were reported in the LTFU study population. However, it is important to note that the LTFU study only included 116 of the 241 subjects (48%) treated with the DIAM™ Spinal Stabilization System (investigational cohort and crossover cohort) in the primary clinical trial, and the outcomes data in the LTFU may be inflated by survivorship bias.

Evaluation and characterization of spinous process fractures in subjects treated with the DIAM™ Spinal Stabilization System demonstrates no new or increased risks relative to previously approved interspinous devices. The spinous process fracture data comparison demonstrates that the risk of spinous process fracture associated with the DIAM™ Spinal Stabilization System through Month 24 is comparable to the risk of spinous process fracture for other approved interspinous devices. Furthermore, the risk of spinous process fracture at any time through 11.5 years of follow-up is not increased relative to the rate observed at Month 24.

In conclusion, the rate of SSIs observed for the DIAM™ Spinal Stabilization System subjects is comparable to the rate of SSIs noted for other similar spinal devices previously approved for use in the U.S. Additionally, there were no increased or unexpected risks relative to other interspinous devices as no unanticipated device AEs were seen in the IDE trial. No new or increased safety risks were observed during the LTFU study, following subjects through a mean final follow-up of 11.5 years.

C. Benefit-Risk Determination

The probable benefits and risks of the DIAM™ spinal stabilization system are based on

data collected in the IDE clinical study (G050025) and the subsequent LTFU study.

Table 43 summarizes notable treatment benefits and risks observed over the 24-month time period studied under the IDE study, and during the LTFU.

Table 43: Notable Treatment Benefits and Risks Observed for the DIAM™ Spinal Stabilization Device

Treatment Benefits	Functional Improvement	77.0% (97/126) of investigational subjects and 80.0% (36/45) of crossover subjects in the BPP cohort experienced a clinically meaningful improvement in pain and function from baseline (defined as a greater than or equal to 15-point decrease in ODI) at Month 24. 86.4% (76/88) of the LTFU* subjects experienced a clinically meaningful improvement at an average follow-up of 11.5 years.
	Back Pain Reduction	83.2% (104/125) of investigational subjects and 90.9% (40/44) of crossover subjects in the BPP cohort experienced clinically meaningful improvement from baseline (defined as a greater than or equal to 2-point decrease in NRS) at Month 24. 86.4% (76/88) of the LTFU subjects experienced a clinically meaningful improvement at an average follow-up of 11.5 years.
	Restored Quality of Life	75.6% (93/123) of investigational subjects and 86.4% (38/44) of crossover subjects experienced a clinically meaningful improvement in physical health-related quality of life (defined as an improvement of greater than or equal to 5 points in SF-36 PCS). 72.4% (63/87) of the LTFU subjects experienced a clinically meaningful improvement in this metric at an average follow-up of 11.5 years.
	Treatment Satisfaction	At Month 24, 81.2% (108/133) of investigational subjects and 87.2% (41/47) of crossover subjects were satisfied with their treatment, and 81.2% (108/133) of investigational subjects and 87.2% (41/47) of crossover subjects would have the treatment again. In the LTFU cohort, 85.9% (79/92) of subjects were satisfied with their treatment and 87.0% (80/92) would have the treatment again.
Risks	SSIs	Twelve investigational subjects (6.6%, 12/182) and three crossover subjects (5.1%, 3/59) had SSIs at index level through Month 24. Twelve LTFU subjects (10.3%, 12/116) had SSIs over the total

		duration of the LTFU.
	Implant- and Surgical Procedure-Associated Serious Adverse Events	Fourteen investigational (7.7%, 14/182) and six crossover (10.2%, 6/59) subjects experienced an implant- and/ or surgical procedure-associated SAE through Month 24.
	Device Migration	No investigational or crossover subjects experienced a migration of any component of the subject device through Month 24, and no LTFU subjects experienced a migration through the mean follow-up of 11.5 years.
	Device Failure	There was no evidence of any device breakage/failure in the investigational or crossover subjects through Month 24, or the LTFU subjects through the mean 11.5-year follow-up.
	Spinous Process Fracture	Fourteen investigational (7.7%, 14/182) and 6 crossover subjects (10.2%, 6/59) experienced a spinous process fracture at any time through 24 months. Of the 116 subjects who enrolled in the LTFU study, 12 subjects (10.3%, 12/116) experienced a spinous process fracture at any time through the mean 11.5 years LTFU.

*LTFU Study success rates may be inflated by survivorship bias.

As shown in the table above, a substantial proportion of investigational and crossover subjects experienced clinically meaningful improvement in ODI, back pain (NRS), and SF-36 PCS scores, and showed satisfaction with their treatment, at Month 24 and at LTFU. Additionally, investigational and crossover subjects experienced low rates of SSIs and implant- and surgical procedure-associated SAEs. There were no instances of device migration or device failure, and a low rate of spinous process fracture events in the investigational and crossover subjects through 24 months and through the LTFU (in a subset of subjects).

Additional factors that were considered in determining the probable benefits and risks for the DIAM™ Spinal Stabilization System included limitations in the clinical study design, such as use of a non-operative care regimen as the control comparator and allowing control subjects to crossover and receive the investigational treatment after Month 6. Additional analyses were performed comparing the investigational subjects to control subjects with the crossover subjects removed (as shown in the "Effectiveness Conclusions" section above). The success rates remained numerically in favor of the investigational cohort in these additional analyses. Based on the target population for the DIAM™ Spinal Stabilization System, an ideal clinical study control group is challenging to design. However, the safety and effectiveness profiles of the investigational and crossover

subjects through Month 24 and during LTFU support that the probable benefits outweigh the risks.

Patient perspectives considered during this review include ODI, NRS, SF-36 PCS, and a treatment satisfaction questionnaire. Please see the table above for a summary of results for these patient-reported outcome measures.

In conclusion, given the available information above, the data supports that for moderate to severe primary low back pain (greater than leg pain) due to degenerative disc disease (DDD) at a single lumbar level (L2-L5) as outlined above in the Indications for Use, the probable benefits of using the DIAM™ Spinal Stabilization System device as a treatment option outweigh the probable risks to health.

D. Overall Conclusions

The non-clinical and clinical data presented in this PMA application support the reasonable assurance of safety and effectiveness of the DIAM™ Spinal Stabilization System when used in accordance with the indications for use. Based on the clinical study results, it is reasonable to conclude that the clinical benefits of the use of the DIAM™ Spinal Stabilization System in terms of functional improvement, reduction in back pain and maintenance or improvement in neurological status outweigh the risks associated with the device and surgical procedure when used in the indicated population and in accordance with the directions for use. In conclusion, the DIAM™ Spinal Stabilization System is a reasonable alternative to other treatment options for subjects suffering from moderate to severe primary low back pain (greater than leg pain) secondary to lumbar degenerative disc disease (DDD) at a single level (L2-L5).

XV. CDRH DECISION

CDRH issued an approval order on December 10, 2025.

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

XVI. APPROVAL SPECIFICATIONS

Directions for Use: See device labeling.

Hazards to Health from Use of the Devices: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the labeling.