SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Artificial Cervical Disc
Device Trade Name:	Synergy Disc
Device Product Code	MJO
Applicant's Name/Address:	Synergy Spine Solutions Inc. 357 S. McCaslin Blvd., Suite 120 Louisville, CO 80027
Date of Panel Recommendation:	None
Premarket Approval Application: (PMA Number)	P250028
Date of FDA Notice of Approval:	February 26, 2026

II. INDICATIONS FOR USE

The Synergy Disc is indicated in skeletally mature patients for reconstruction of the disc at one level from C3-C7 following single-level discectomy for intractable radiculopathy (arm pain and/or a neurological deficit) with or without neck pain, or myelopathy due to a single-level abnormality localized to the level of the disc space and at least one of the following conditions confirmed by radiographic imaging (CT, MRI, X-rays): herniated nucleus pulposus, spondylosis (defined by the presence of osteophytes), and/or visible loss of disc height compared to adjacent levels. The Synergy Disc is implanted using an anterior approach. Patients should have failed at least 6 weeks of conservative treatment or demonstrated progressive signs or symptoms despite nonoperative treatment prior to implantation of the Synergy Disc.

III. CONTRAINDICATIONS

Synergy Disc should not be implanted in patients with the following conditions:

- Tumor or trauma
- Intractable radiculopathy or myelopathy necessitating surgical treatment at more than one cervical level
- Allergy or sensitivity to the implant materials (e.g., titanium and polyethylene)
- Bridging osteophytes
- Radiographic instability on lateral, coronal or flexion / extension radiographs: translation greater than 3.5mm and/or greater than 11 degrees of angular difference from either adjacent segments
- Facet joint degeneration
- Active systemic or local infection
- Osteoporosis defined as Dual-Energy X-ray Absorptiometry (DEXA) bone mineral density T-score less than -2.5

- Advanced cervical spine conditions or diseases at the index level other than those included in the Indications for Use (e.g., rheumatoid arthritis, Diffuse Idiopathic Skeletal Hyperostosis (DISH), ankylosing spondylitis)

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Synergy Disc labeling.

V. DEVICE DESCRIPTION

The Synergy Disc is a three-piece cervical artificial disc manufactured from titanium alloy and Ultra-high-molecular-weight-polyethylene (UHMWPE). As shown in **Figure 1**, the three components of the Synergy Disc include a superior titanium alloy endplate, an UHMWPE core, and an inferior titanium alloy endplate. The titanium alloy endplates are coated with commercially pure titanium plasma spray.

Figure 1: Schematic of Synergy Disc (left), Exploded Schematic of the Synergy Disc (right)

The Synergy Disc is an intervertebral disc prosthesis designed to restore motion and balance to the intervertebral segment of the cervical spine when replacing a degenerated native disc. The Synergy Disc is designed to restore and maintain the natural behavior of a functional spinal unit by maintaining motion and balance, which are inherent to the properties of the native disc. The Synergy Disc is a cervical artificial disc manufactured from titanium alloy endplates and a UHMWPE core. As shown in **Figure 2**, flexion-extension, lateral bending, axial rotation, and translation are all semi-constrained.

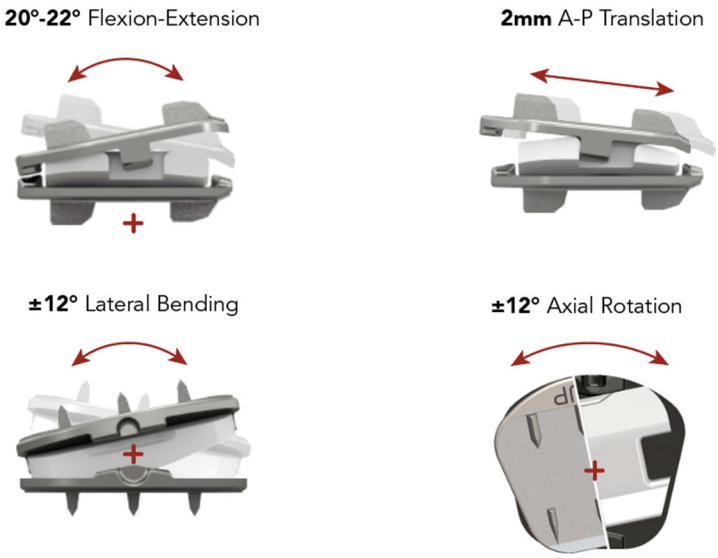

Figure 2: Synergy Disc Targeted Ranges of Motion

The Synergy Disc is available in the sizes shown below in **Table 1**.

Table 1: Synergy Disc Part Listing and Size Overview

Footprint Size	Disc Height	Lordotic Angle	Reference Number
Extra Small (12mm A/P x 15mm Lateral)	5mm	0°	1077-3050
	5mm	6°	1077-3056
	6mm	0°	1077-3060
	6mm	6°	1077-3066
	7mm	6°	1077-3076
Small (14mm A/P x 15mm Lateral)	5mm	0°	1077-3150
	5mm	6°	1077-3156
	6mm	0°	1077-3160
	6mm	6°	1077-3166
	7mm	6°	1077-3176
Small-Wide (14mm A/P x 17mm Lateral)	5mm	0°	1077-3450
	5mm	6°	1077-3456
	6mm	0°	1077-3460
	6mm	6°	1077-3466
	7mm	6°	1077-3476
Medium (16mm A/P x 17mm Lateral)	5mm	0°	1077-3250
	5mm	6°	1077-3256
	6mm	0°	1077-3260
	6mm	6°	1077-3266
	7mm	6°	1077-3276
Medium-Wide (16mm A/P x 19mm Lateral)	5mm	0°	1077-3550
	5mm	6°	1077-3556
	6mm	0°	1077-3560
	6mm	6°	1077-3566
	7mm	6°	1077-3576
Large (18mm A/P x 19mm Lateral)	5mm	0°	1077-3350
	5mm	6°	1077-3356
	6mm	0°	1077-3360
	6mm	6°	1077-3366
	7mm	6°	1077-3376

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the treatment of intractable radiculopathy (arm pain and/or a neurological deficit) with or without neck pain, or myelopathy due to a single-level abnormality localized to the level of the disc space. These alternative treatments are summarized below:

- Nonoperative alternative treatments, which include, but are not limited to, simple neck adjustments, physical therapy, traction, heat, medications, braces, chiropractic care, bed rest, spinal injections, or exercise programs.
- Surgical alternatives, which include, but are not limited to:
    - Surgical decompression alone
    - Surgical decompression via an anterior approach with fusion using various bone grafting and anterior plating techniques
    - Surgical decompression using intervertebral cages, with various bone grafting techniques, with or without supplemental anterior plating
    - Decompression with posterior spinal systems (e.g., rods, hooks, wires)
    - Another FDA-approved artificial cervical disc

Each option has advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The Synergy Disc received CE mark in 2013. It is currently distributed in the European Union, United Kingdom, Australia, Switzerland, Malaysia, South Africa, and Canada via Special Access. The Synergy Disc has not been withdrawn from any distribution/marketing in any country for safety or effectiveness reasons.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) identified from the Synergy Disc clinical study results, approved device labeling for other cervical total disc replacement (cTDR) devices, and published scientific literature including: (1) those associated with any general surgical procedure; (2) those associated with anterior cervical spine surgery; and (3) those associated with a cervical artificial disc device, including the Synergy Disc. In addition to the risks listed below, there is also the risk that surgery may not be effective in relieving symptoms or may cause worsening of symptoms. Additional surgery may be required to correct some of the adverse effects.

General Surgery Risks

General surgical risks include, but are not limited to:

- Abscess
- Superficial (shallow) infection
- Deep wound infection
- Pneumonia (lung infection)
- Atelectasis (collapsed lung)
- Septicemia (blood poisoning)
- Edema
- Hematoma
- Injury to blood vessels
- Soft tissue damage
- Nerve or muscular damage
- Phlebitis (inflammation of the blood vessel in your leg) or

thromboembolus (blood clot in the legs)
- Pulmonary embolism (blood clot in the lung)
- Hemorrhage (excessive bleeding)
- Respiratory distress or depression (slow, shallow, or difficulty breathing)
- Pulmonary edema (abnormal collection of fluid in the lungs)
- Thromboembolism (blood clot in the vessel)
- Reactions to the drugs or anesthesia used during and after surgery
- Reactions to blood transfusions
- Failure of the tissue to heal properly (e.g., hematoma [a pocket of blood caused by bleeding from a broken blood vessel]; wound dehiscence [failure of the incision to completely heal which may allow it to reopen]), cellulitis, or wound necrosis, which may require drainage, aspiration (removing a substance using suction), debridement (surgery to clean foreign material and dead tissue out of a wound), or other treatment
- Pain at the incision
- Complications of unknown pregnancy including miscarriage and fetal birth defects
- Inability to resume activities of daily living
- Myocardial infarction (heart attack)
- Stroke
- Seizure, convulsion, or change in mental status
- Death

Anterior Cervical Surgery Risks

Anterior cervical surgical risks include, but are not limited to:

- Damage to nerves that may result in changes in the sensation and/or muscle weakness in your neck, legs, arms, and/or shoulders
- Paralysis (loss of ability to move muscles with the loss of feeling also)
- Paresthesia (a sensation of pricking, tingling, or creeping on the skin)
- Dysphagia (trouble swallowing)
- Dysphonia (trouble with the voice or speaking)
- Hoarseness
- Dysarthria (difficulty articulating speech that is otherwise linguistically normal)
- Vocal cord paralysis
- Laryngeal palsy
- Sore throat
- Recurring aspirations (inhaling foreign substances into the lungs)
- Fistula (an abnormal passage)
- Tracheal, esophageal, and/or pharyngeal perforation (penetration of the windpipe, the tube that goes from the throat to the stomach, and/or the area between the mouth and esophagus that performs the swallowing action)
- Airway obstruction (blockage of the airway)
- Spinal stenosis (narrowing of the nerve passages that go from the spine to the rest of your body)
- Hardening or tearing of the tissue surrounding the implant
- Spondylosis
- Worsening of the degenerative disc disease condition at adjacent levels
- Discitis (inflammation of the disc), Arachnoiditis (inflammation of middle layer of the tissues that cover the spinal cord), or other types of inflammation

- External chylorrhea
- Damage to nerves, blood vessels, and nearby tissues including, for example, muscle and/or ligament injury
- Dural tear or leak
- Epidural bleeding (bleeding around the membrane covering the tissue surrounding your spinal cord that may require a blood transfusion or another operation)
- Epidural hematoma (a pocket of blood caused by a broken blood vessel or bone bleeding in the membrane covering the nerves or the tissues surrounding your spinal cord)
- Epidural fibrosis (scar tissue formation on the membrane covering the nerves)
- Instability of the operated or adjacent vertebrae
- Blindness by prolonged pressure on the eye during the operation
- Urinary or fecal incontinence
- Surgery at the wrong level of your spine
- Loss of bone around the implant (osteolysis related to debris from implant wear)
- Injury to the spinal cord or the nerves leaving or entering the spinal cord
- Disc herniation ("slipped disc")
- Loss of disc height
- Injury of the membrane (dura) surrounding the spinal nerves which may or may not result in leakage of spinal fluid
- Impaired muscle or nerve function (symptoms like clumsiness, numbness, foot drop, neurological weakness, etc.)
- Fracture of the vertebra, spinous process (the part of your spine that you can feel through the skin on your back), or other damage to bony structures during or after surgery
- Deterioration of the facet joints in the adjacent vertebrae (worsening of the condition)
- Postoperative muscle and tissue pain
- The chance that the surgery will not reduce the pain or symptoms felt before the surgery
- Failure of the fusion to heal
- Spontaneous fusion (unplanned, self-generated fusion of the vertebra)
- The spine may undergo unfavorable changes or deterioration at the operated level(s) and/or the levels above and below including loss of proper spinal curvature, correction, height, and/or reduction, or malalignment, which may require another surgery

Cervical Artificial Disc Risks

Risks specific to cervical artificial discs, including the Synergy Disc, include, but are not limited to:

- Airway obstruction
- Wear debris generation
- Foreign body (allergic) reaction to implant materials (titanium alloy, UHMWPE)
- Metallosis
- Staining
- Tumor formation
- Autoimmune disease
- Early or late loosening of the components; disassembly
- Bending or breakage of any or all of the components
- Implant subsidence (the implant may sink into the bone)
- Loss of fixation; sizing issues with components
- Anatomical or technical difficulties
- Bone fracture

- Scarring
- Bone resorption
- Bone formation (including heterotopic ossification (HO)) that may reduce spinal motion or result in a fusion, either at the treated level or at adjacent levels
- Development of new radiculopathy, myelopathy, or pain; tissue or nerve damage caused by improper positioning or placement of implants or instruments
- Bending or breakage of a surgical instrument
- Loss of neurological function
- Decreased strength of extremities
- Decreased reflexes
- Cord or nerve root injury
- Interference with radiographic imaging because of the presence of the implant
- Need for subsequent surgical intervention
- An unfavorable reaction where the bone and the implant meet
- Possible pain, infection, and permanent damage to the bone or surrounding tissues at the site where bone graft was taken
- Implant migration or malposition, (the implant could be improperly positioned) either peri-operatively or post-operatively
- Adverse reaction or foreign body reaction to implant materials (possible allergic reaction to the metal) or there may be some wearing of the implant material against bone or another part of the implant that creates very small particles; it is possible that these particles may eventually cause the local tissues such as bone, nerves and nearby soft tissue to respond badly
- Placement of the study device at the wrong level of the spine
- Implant may become loose, deform (permanently change shape), fail, break, wear out, or move which may require another surgery to correct the problem and/or remove the implant
- Instruments used to insert the implant may break or malfunction in use which may cause damage to the surgical site or surrounding tissues
- Pain, discomfort, and/or abnormal sensations caused by the presence of the implant
- Implanting the incorrect size may cause the device to be less effective or safe
- Surgery may be converted to Anterior Cervical Discectomy and Fusion (ACDF) if poor visualization at the index level due to anatomical limitations

These conditions do not include all potential adverse events (AEs) that may occur, but are important considerations in relation to the use of the Synergy Disc. For the specific AEs that occurred in the Synergy Disc clinical study, please see **Section 0**.

IX. SUMMARY OF NON-CLINICAL STUDIES

A variety of testing was conducted to characterize the performance of the Synergy Disc, including:

- Static Axial Compression
- Dynamic Axial Compression
- Static Compression Shear
- Dynamic Compression Shear
- Static Torsion
- Device Expulsion
- Device Subsidence
- Device Creep
- Pristine Wear Testing (Mode I Wear)
- Abrasive (Third Body) Wear Testing (Mode III Wear)
- Impingement Wear Testing (Mode IV Wear)
- Range of Motion (ROM)
- Coating Assessment
- Biocompatibility/Toxicity
- Neurotoxicity
- Device Sterilization/Packaging
- MR Compatibility

Table 2: Non-Clinical Study Summary

Test Name	Purpose	Test Method	Acceptance Criteria	Results
Static and Dynamic Strength				
Static Axial Compression	Verify static performance under simulated physiologic conditions is sufficient to withstand in vivo compressive loads	ASTM F2346	A minimum of 200 N in axial compression	Maximum compression: 0.80mm at 3449N.
Dynamic Axial Compression	Verify dynamic performance under simulated physiologic conditions is sufficient to withstand in vivo compressive loads	ASTM F2346	The implant must survive a fatigue test to 10 million cycles with a 100 N axial compression load	Dynamic strength ≥ 400N Change in disc height (max): 0.12mm At Runout 10 million cycles.
Static Compression Shear	Verify static performance under simulated	ASTM F2346	The implant should withstand at	Static shear yield load: 978N Compressive shear stiffness: 943 N/mm

Test Name	Purpose	Test Method	Acceptance Criteria	Results
	physiologic conditions is sufficient to withstand in vivo compressive shear loads		least 120 N in compression shear	
Dynamic Compression Shear	Verify dynamic performance under simulated physiologic conditions is sufficient to withstand in vivo compressive shear loads	ASTM F2346	The implant must survive a fatigue test to 10 million cycles with a 100 N compression shear load	Dynamic shear load: ≥1000N. Change in disc height (max): 0.28mm.
Static Torsion	Verify that the static torsion performance is sufficient to withstand anticipated in vivo torsional loads	ASTM F2346	N/A for characterization purposes	Static torsional yield torque: 0.40Nm. Torsional stiffness: 0.039Nm/degree.
Expulsion				
Expulsion	Verify ability of Synergy Disc to resist expulsion using simulated physiologic conditions	Synergy Discs implanted in foam blocks with 100N axial preload were subjected to anterior shear at a rate of 6 mm/min. Monotonic loading was applied to both endplates in the posterior to anterior direction.	Implant should resist at least 80 N in anterior expulsion and posterior migration	Synergy Disc was able to withstand an expulsion force of 104N. Results verify device will remain stable under in vivo shear loading conditions.
Subsidence				
Subsidence	Verify the ability of the Synergy Disc to resist subsidence using simulated physiologic conditions	ASTM F2267	Subsidence yield load required for 1mm plastic deformation should be greater than the 200 N axial compression	Kp value of the Synergy Disc (597N/mm).
Creep				
Implant Creep	Evaluate the creep properties of the Synergy Disc.	Three (3) Synergy Disc devices were		Mean core creep was significantly less than the

Test Name	Purpose	Test Method	Acceptance Criteria	Results
		tested in implant creep.	Implant Creep with 100 N axial compression load cannot exceed 0.5mm over 60 days	natural creep of the healthy native cervical disc.
Wear				

Test Name	Purpose	Test Method	Acceptance Criteria	Results
Pristine Wear Testing (Mode-I)	To determine the wear and durability characteristics of the Synergy Disc under complex physiologic conditions (Mode-I).	Two 10,000,000 cycles wear tests (based on ISO 18192-1 and ASTM F2423) were performed on six (6) 'Large' Synergy Disc test specimens. Specimens were subjected to combined ±7.5° flexion/extension, ±6°axial rotation, and ±6° lateral bending while submerged in bovine serum solution with a protein concentration of 30 g/L. One test was performed at 2.0 Hz with a 100 N axial load, and the second at 1.0 Hz with a 50-150 N axial load. Two (2) test specimens served as load soak controls. Wear particulate was collected at 1.0, 5.0, and 10.0 million cycle (MC) intervals, the 10Mc sample was analyzed via electron microscopy and low angle laser light scattering under ASTM F1877-05.	The implant must have an average total wear of less than 56mg during wear debris testing to 10 million cycles	8.1mg of total wear during 10MC. Average gravimetric wear rate at 2.0 Hz (100 N): 0.78 mg/MC. Average gravimetric wear rate at 1.0 Hz (150 N): 0.9 mg/MC. No devices demonstrated signs of fracture or functional failure. Wear particle analysis showed size distributions and morphology in ranges consistent with other well-tolerated spinal and orthopaedic devices. All acceptance criteria were met.

Test Name	Purpose	Test Method	Acceptance Criteria	Results
Abrasive Wear Testing (Mode-III)	To characterize in vitro wear properties under third-body abrasive wear conditions (Mode III)	Testing based on ISO 18192-1 and ASTM F2423. Specimens were subjected to combined ±7.5° flexion/extension, ±6°axial rotation, and ±6° lateral bending while submerged in third-body titanium particle slurry bovine serum lubricant. Testing was performed at 1.0 Hz with a 50-150 N applied load.	N/A, for characterization purposes	Mean mass wear rates – - Superior Endplate: 0.1 mg/MC at 1MC, 0.0 mg/MC at 5MC - Polyethylene Core: 3.5 mg/MC at 1MC, 2.0 mg/MC at 5MC - Inferior Endplate: 0.1 mg/MC at 1MC, 0.0 mg/MC at 5MC. Average scratch height of 4.7µm in the superior endplates and 2.7µm on the inferior endplates. Average penetration of 0.2 ± 0.0 mm for the wear stations and had a penetration measurement range of 0.0 mm to 0.1 mm for the load soak stations after 5.0 MC. No measurable penetration on the articulating surfaces of the superior and inferior endplates following 5.0 MC of testing. Particle analysis shows size distributions and morphology in ranges consistent with other spine/ ortho devices. No devices demonstrated signs of fracture or functional failure.

Test Name	Purpose	Test Method	Acceptance Criteria	Results
Impingement Wear Testing (Mode-IV)	To characterize the wear and durability of the Synergy Disc under simulated endplate-to-endplate impingement wear (Mode-IV).	Testing based on ASTM F3295-18, (ISO 18192-1, -3, and ASTM F2423-11 as guides) Three (3) 'Large' and three (3) 'Small' sized Synergy Disc were subjected to 1 x 10^6 cycles of combined 300 N axial load, 10°-26° extension, and ±6° axial rotation at 1 Hz per ASTM F3295-18 while submerged in bovine serum solution with a protein concentration of 30 g/L. Two (2) test specimens, one per size, served as load soak controls. Wear particulate was collected and analyzed via electron microscopy and low angle laser light scattering under ASTM F1877-05.	N/A (for characterization purposes)	Gravimetric wear rates: Size Small: 0.5 mg/Mc Size Large: 0.6 mg/Mc No devices demonstrated signs of fracture or functional failure.
Range of Motion				

Test Name	Purpose	Test Method	Acceptance Criteria	Results
Range of Motion (ROM)	Characterize ROM of Synergy Disc using finite element techniques.	N/A	Similar in character and magnitude to the natural model	The kinematic analysis shows that ROM kinematics of the single level total disc replacement (TDR) implanted at either the C4-C5 or C5-C6 levels is similar in character and magnitude to the natural model and experiments in flexion, lateral bending and axial rotation.
Coating				
Coating Assessment	Coating assessment provided.	ASTM F1580, ASTM F1147, ASTM F1044, ASTM F1160, ASTM F1854, ASTM F1978	N/A	Coating specifications and mechanical performance passed standardized criteria.
Biocompatibility/ Toxicity				
Cytotoxicity	Evaluate the cytotoxicity of the Synergy Disc	ISO 10993-5	Less than or equal to mild cellular reactivity (Grade ≤ 2)	Pass.
Sensitization	Evaluate the biological safety of the Synergy Disc	ISO 10993-1, ISO 14971	N/A	Pass. Utilizing the established biological safety of a device with identical materials and manufacturing, the subject device is determined to be biocompatible.
Irritation				
Acute Systemic Toxicity				
Material-Mediated Pyrogenicity				
Subacute/Subchronic Systemic Toxicity				
Genotoxicity				
Implantation				
Chronic Systemic Toxicity				
Carcinogenicity				
Neurotoxicity				
Neurotoxicity	Assess neurologic biocompatibility by evaluating the wear debris collected during Mode I wear testing (10 MC)	ASTM F2423 ISO 18192-1	The implant must have an average total wear of less than 56mg during wear debris, derived from Cunningham et al.	Pass.
Device Sterilization/Packaging				

Test Name	Purpose	Test Method	Acceptance Criteria	Results
Sterilization Validation	Validate sterility of Synergy Disc Ethylene Oxide (EO) sterilization method	ANSI/AAMI/ISO 11135:2014	Sterility assurance level (SAL) of 10^{-6}	EO sterilization validated to achieve a minimum sterility assurance level (SAL) of 10^{-6} of the Synergy Disc.
Ethylene Oxide Residuals	Validate EO residuals following sterilization are below standardized limits to minimize exposure to the patient.	ISO 10993-7	EO residuals must be at or below levels specified in ISO 10993-7: EO TCL < 10 µg/ cm^2	Pass.
Pyrogenicity (Bacterial Endotoxins)	Validate bacterial endotoxins are below a pre-established safety limit of 20 EU/device	ANSI/AMSI ST7; USP <85>	< 20.0 EU/device	Pass.
Packaging Validation	Validate the packaging strength and integrity to maintain a sterile barrier through transport and the stated shelf life	ISO 11607, ASTM D4169	-Devices should not be visibly damaged. -Sterile barrier must remain intact -Seal strength is ≥ 0.96PLI (pounds per a linear inch)	Passing results on real time and accelerated aged to support a 5-year shelf life.
MR Compatibility				
Induced Displacement Force	Evaluate magnetically induced displacement force under MRI at 3.0T	ASTM F2052	Angular displacement is ≤ 45° Calculated maximum allowable spatial gradient is ≥ 19 T/m	Induced force is substantially less than gravity.
Induced Torque	Evaluate magnetically induced torque under MRI at 3.0T	ASTM F2213	Minimal to no torque effects relative to gravity	MR-induced torque is substantially less than gravity.
Induced Heating	Evaluate radio frequency (RF) induced heating under MRI at 1.5 T and 3.0T	ASTM F2182	Less than 6°C over 15 minutes of scanning at a whole body console specific	MR-induced heating is ≤2.5°C at 1.5T and ≤4.0°C at 3.0T.

Test Name	Purpose	Test Method	Acceptance Criteria	Results
			absorption rate (SAR) of 2.0 W/kg or greater	
MRI Artifact	Evaluate MRI-induced artifact under MRI at 1.5 T and 3.0 T	ASTM F2119	N/A	The maximum MR-induced artifact is 1.7cm using slice thickness of 3T.

X. SUMMARY OF PRIMARY CLINICAL STUDIES

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of the Synergy Disc for reconstruction of the disc at one level from C3-C7 following single-level discectomy for intractable radiculopathy (arm pain and/or a neurological deficit) with or without neck pain, or myelopathy due to a single-level abnormality localized to the level of the disc space and at least one of the following conditions confirmed by radiographic imaging (CT, MRI, X-rays): herniated nucleus pulposus, spondylosis (defined by the presence of osteophytes), and/or visible loss of disc height compared to adjacent levels. The study was performed in the United States (US) under IDE G180090 with anterior cervical discectomy and fusion (ACDF) historical control data from a separate IDE study performed in the US (IDE G040081). A summary of the clinical study is presented below.

A. Study Design

Subjects in the Synergy Disc group of the pivotal clinical trial were treated between January 2021 and May 2023. The prospective, multi-center, non-randomized, historically controlled clinical study was conducted under IDE. The Synergy Disc database for this PMA reflects data collected through May 12, 2025, and includes 177 subjects enrolled across 20 sites. The Synergy Disc group results were compared to historical control data, non-concurrently enrolled, from the ACDF control group of the NuVasive Porous Coated Motion (PCM) Artificial Cervical Disc IDE study (G040081). An observational study design using propensity score (PS) subclassification was used to demonstrate covariate balance and enhance the quality of inferences regarding effectiveness and safety relative to ACDF control. The PS-selected control cohort included 192 subjects. The resultant PS-selected study cohort used for the pre-specified primary analysis population thus included all Synergy Disc subjects and historical control subjects (no PS-trimmed subjects were identified. Completers within the pre-specified primary analysis population are also analyzed.

1. Clinical Inclusion and Exclusion Criteria

To be eligible for the Synergy Disc IDE study, subjects had to be eligible for a fusion procedure and meet all of the inclusion criteria and none of the exclusion criteria in Table 3:

Table 3: Study Inclusion/Exclusion Criteria

Study Inclusion Criteria	Study Exclusion Criteria
1) Age 18-70 years; 2) Diagnosis of radiculopathy or myelopathy of the cervical spine, with either radiculopathy symptoms – pain, paresthesia, or paralysis in a specific nerve root distribution C4, C5, C6, or C7, including at least one of the following: a) Arm/shoulder pain (at least 30 mm on 100 mm VAS scale); b) Decreased muscle strength of at least one level on the 0-5 scale described below: i) Abnormal sensation, including hyperesthesia or hypoesthesia; And/or abnormal reflexes; Or myelopathy symptoms including positive Romberg evaluation, abnormal heel/toe walk, pathologic hyperreflexia or clonus in lower extremity, positive Babinski, or positive Hoffman's; 3) Symptomatic at only one level from C3-C4 to C6-C7; 4) Radiographically determined pathology at level to be treated correlating to primary symptoms, including at least one of the following: a) Decreased disc height compared to adjacent levels on radiographic film, CT, or MRI b) Degenerative spondylosis on CT or MRI c) Disc herniation on CT or MRI 5) Neck Disability Index (NDI) Score ≥ 30/100; 6) Unresponsive to non-operative treatment for six weeks, or has presence of progressive symptoms or signs of nerve root/spinal cord compression in the face of conservative treatment; 7) Appropriate for treatment using an anterior surgical approach, including having no more than one previous anterior surgical approach to the cervical spine; 8) Ability and willingness to comply with follow-up regimen; and 9) Written informed consent given by subject	1) Infection at the site of surgery; 2) History of, or anticipated treatment for, active systemic infections, including HIV infection or hepatitis C; 3) Prior attempted or completed cervical spine surgery, except (1) laminoforaminotomy (greater than 6 months prior to scheduled surgical treatment), which includes removal of disc material necessary to perform a nerve root decompression, with less than one-third facetectomy at any level, (2) a successful single-level anterior cervical fusion (greater than 6 months prior to scheduled surgical treatment); 4) More than one immobile vertebral level between C1-T1 from any cause, including but not limited to congenital abnormalities, osteoarthritic "spontaneous" fusions, and prior cervical spinal fusions; 5) Previous trauma to the C3-T1 levels resulting in significant bony or disco-ligamentous cervical spine injury; 6) Axial neck pain in the absence of other symptoms of radiculopathy or myelopathy justifying the need for surgical intervention; 7) Radiographic confirmation of severe facet joint disease or degeneration; 8) Osteoporosis: A screening questionnaire for osteoporosis, SCORE (Simple Calculated Osteoporosis Risk Estimation) for females or MORES (Male Osteoporosis Risk Estimation Score), will be used to screen patients to determine those patients who require a hip/spine DXA, a bone mineral density measurement. A SCORE or MORES ≥ 6 requires a DXA. If DXA is required, exclusion will be defined as a DXA bone density measured T score ≤ –2.5 (The World Health Organization definition of osteoporosis). DXA scans within the last 6 months prior to surgical treatment may be used; 9) Paget's disease, osteomalacia, or any other metabolic bone disease (excluding osteoporosis which is addressed above); 10) Severe diabetes mellitus requiring daily insulin management; 11) Active malignancy: a history of any invasive malignancy (except non-melanoma skin cancer), unless the patient has been treated with curative intent and there have been no clinical signs or symptoms of the malignancy for at least 5 years; 12) Tumor as a source of symptoms; 13) Symptomatic DDD or significant cervical spondylosis at two or more levels; 14) Marked cervical instability on resting lateral or flexion/extension radiographs demonstrated by: a) Translation > 3.5 mm and/or

Study Inclusion Criteria	Study Exclusion Criteria
	b) >11° angular difference to that of either adjacent level; 15) Known or suspected allergy to cobalt, chromium, molybdenum, titanium alloy or polyethylene 16) Severe myelopathy to the extent that the patient is wheelchair bound; 17) Congenital canal stenosis resulting in a canal diameter of < 10 mm, as measured by CT or MRI; 18) Kyphotic segmental angulation of greater than 11 degrees at treatment or adjacent levels; 19) Arachnoiditis; 20) Pregnant (verified in patients of childbearing potential by a negative urine pregnancy test when preadmission testing is obtained), or interested in becoming pregnant during the duration of the study; 21) Autoimmune disorders that impact the musculoskeletal system (e.g., lupus, rheumatoid arthritis; ankylosing spondylitis); 22) Congenital bony and/or spinal cord abnormalities that affect spinal stability; 23) Spinal axis disease (thoracic or lumbar) to the extent that surgical consideration is likely anticipated within 6 months after the cervical procedure; 24) Other degenerative joint disease (e.g. shoulder, hip, knee) to the extent that surgical consideration is likely anticipated within 6 months after the cervical procedure; 25) Diseases or conditions that would preclude accurate clinical evaluation (e.g. neuromuscular disorders such as diffuse idiopathic skeletal hyperostosis (DISH)); 26) Medications that could interfere with fusion or other bone/soft tissue healing (e.g. anticipated continued use of systemic steroid medication postoperatively); 27) Currently experiencing acute episode of major mental illness (psychosis, major affective disorder, or schizophrenia), or manifesting physical symptoms without a diagnosable medical condition to account for the symptoms, which may indicate symptoms of psychological rather than physical origin; 28) Current or recent history of substance (drug or alcohol) per site PI's determination; 29) Morbid obesity, defined as body max index ("BMI") > 40 or more than 100 lbs. over ideal body weight; 30) Currently using, or planning to use, bone growth stimulators in the cervical spine; 31) Use of any other investigational drug or medical device within the last 30 days prior to surgery; 32) Currently a prisoner; 33) Currently pursuing personal litigation (defined as litigation that will likely influence the patient's

Study Inclusion Criteria	Study Exclusion Criteria
	ability or willingness to accurately report their treatment outcomes) related to the neck or cervical spine injury; however, involvement in worker's compensation related litigation is not a required exclusion.

2. Control

As mentioned above, a historical control study design was used with control subjects obtained from the ACDF cohort of a previously completed multi-center, prospective, randomized non-inferiority clinical trial, for the NuVasive PCM Artificial Cervical Disc IDE study (G040081). A detailed comparison of the indications, inclusion/exclusion criteria, and study outcomes of the historical ACDF cohort and the Synergy Disc IDE study protocol concluded that this dataset is an appropriate comparator to support this PMA application.

A PS methodology was applied to address potential selection bias when combining historical control data with the prospectively enrolled investigational cohort. Historical control subjects were selected to achieve similarity in baseline covariates with Synergy Disc subjects within PS subclasses. Statistical and graphical balance assessments demonstrated that Synergy Disc subjects and PS-selected controls had comparable multivariate baseline covariate distributions within PS subclasses.

3. Follow-up Schedule

All subjects were evaluated pre-operatively, at treatment, and post-operatively at the immediate post-operative visit (up to 21 days post-treatment), and at Week 6 (± 14 days), Month 3 (± 2 weeks), Month 6 (± 2 months), Month 12 (± 2 months), Month 24 (± 2 months) and annually thereafter (± 2 months) until the last subject enrolled had completed Month 24 evaluation. The following parameters were measured throughout the study (Table 4):

Table 4: Synergy Disc IDE Study Assessment Schedule

VISIT	Enrollment/ Preoperative[10]	Surgery Day 0	Immediate Post-Op (7-21 days)	6-Wk (42 days) ± 14 days	3-Months (90 days) ± 14 days	6-Months (180 days) ± 60 days	12-Months (365 days) ± 60 days	24-Months (730 days) ± 60 days	Annually Thereafter ± 60 days	Unscheduled
Informed Consent Process	X	-	-	-	-	-	-	-	-	-
Inclusion/ Exclusion Criteria	X	X	-	-	-	-	-	-	-	-
Demographics	X	-	-	-	-	-	-	-	-	-
Medical History	X	-	-	-	-	-	-	-	-	-
Pregnancy test	-	X	-	-	-	-	-	-	-	-
MRI or CAT Scan	X	-	-	-	-	-	-	-	-	-
Hip DEXA Scan	X[2]	-	-	-	-	-	-	-	-	-
X-Ray	X[3,7]	X[6]	X[1]	X[1]	X[7]	X[7]	X[7]	X[7]	X[7]	X[7]
Assessments[9]	X[4,5]	-	-	X[4,5]	X[4,5]	X[4,5]	X[4,5]	X[4,5]	X[4,5]	X[4,5]
Record/Review Concomitant Medications	X	-	X	X	X	X	X	X	X	X
Record/Review Adverse Events	-	X	X	X	X	X	X	X	X	X
Record/Review Device Deficiencies	-	X	X	X	X	X	X	X	X	X
Review Rehabilitation[8]	-	-	X	X	X	-	-	-	-	X

[1] No flexion/extension x-ray immediate post-op or 6-wk.
[2] DEXA bone mineral density will be recorded when dictated by osteoporosis screening (SCORE or MORES).
[3] DDD pathology will be confirmed by MRI or CAT Scan.
[4] Patient will complete self-assessment tools: neck pain, arm/shoulder pain (VAS); Patient Satisfaction (not conducted at baseline) ; NDI Questionnaire, SF-36 Health Survey, and Dysphagia Assessment (Bazaz, Hoarseness Scale)
[5] The Investigator will complete the following assessments: physical examination, Nurick/Odom's Criteria, Subject Survey and Neurological Assessment. (*Odom's Criteria will only be assessed post-operatively.)
[6] Intraoperative AP and lateral radiographs should be taken prior to closure to verify proper implant positioning.
[7] Anteroposterior, upright neutral lateral and flexion-extension lateral films must be taken at this visit for all patients.
[8] Rehabilitation can be marked as completed at 3 month visit or continue if necessary per investigator discretion.
[9]The subject reported surveys should be administered prior to any other study visit assessments or procedures being performed to prevent information from the examination biasing the subject's responses.
[10]Enrollment/Preoperative clinical evaluation will occur within 60 days of Surgery. MRI and CAT Scans can be conducted within 6 months of Surgery. X-Rays can be conducted within 3 months of Surgery

4. Clinical Endpoints

The safety of the Synergy Disc was assessed by comparison to the historical ACDF control group with respect to the nature and frequency of AEs (overall and in terms of seriousness, severity, and relationship to the device or procedure), additional index level surgical procedures and maintenance or improvement in neurological status.

The effectiveness of the Synergy Disc was assessed by comparison to the historical ACDF control group with respect to a primary composite endpoint, as described below. Effectiveness was further evaluated by assessing improvement in the Neck Disability Index (NDI), neck and arm/shoulder pain based on a Visual Analog Scale (VAS), and quality of life using the short-form questionnaire

(SF-36), as well as patient satisfaction of the Synergy Disc group compared to the historical ACDF Control group. Similar criteria were used to measure success in both groups.

Primary Endpoint

The study hypothesis was that in subjects with DDD defined as intractable radiculopathy (arm pain and/or a neurological deficit) with or without neck pain or myelopathy due to a single-level abnormality localized to the level of the disc space at one level from C3 to C7 that is unresponsive to conservative management, the Month 24 composite clinical success (CCS) rate of the Synergy Disc would be non-inferior as compared to the historical ACDF control subjects at Month 24. If non-inferiority was determined, the hypothesis that the investigational device is superior to the ACDF control was also tested.

The primary endpoint for the Synergy Disc subjects required the subject to meet all of the following criteria at 24 months:

- At least a 15-point improvement in NDI Score (out of 100) at Month 24 compared to baseline;
- Maintenance or improvement in neurologic status (motor and sensory only) at Month 24 compared to baseline;
- No study failures due to secondary surgical interventions (revision, removal, reoperation, and/or supplemental fixation) at the index level;
- Absence of radiographic failure, defined as any implant or component breakage or migration at the index level; and,
- Absence of device-related serious adverse events (SAEs) as adjudicated by the Clinical Events Committee (CEC).

Similarly, the primary endpoint for the historical ACDF control group subjects was defined as:

- At least a 15-point improvement in NDI Score (out of 100) at Month 24 compared to baseline;
- Maintenance or improvement in neurologic status at Month 24 compared to baseline;
- No study failures due to secondary surgical interventions (revision, removal, reoperation, and/or supplemental fixation) at the index level;
- Fusion occurred; and,
- Absence of device-related SAEs through Month 24.

Device failure is defined as breakage, migration, or mechanical failure of the components. For purpose of determining individual subject success, a SAE is defined as any of the following which are definitely related to the device system or to a device component as determined by the CEC:

- Permanent neurologic damage or permanent nerve root injury related to a level at or below the level treated;
- Implant or component breakage or migration that does not require revision, reoperation or removal, but causes persistent or moderate to severe dysphagia; and/or,
- Subject death.

For the ACDF control group, the same components of the CCS were employed, with the exception that non-fusion was an indicator of overall clinical failure. For the purpose of evaluating whether a fusion has occurred, the following criteria were applied to the ACDF control cohort:

- Translational motion less than or equal to 3 mm;
- Angular motion less than or equal to 2 degrees; and,
- Bridging bone;
- Radiolucent lines around less than 50% of the assembly.

Per the FDA Guidance for the Preparation of IDEs for Spinal Systems (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-document-preparation-ides-spinal-systems-guidance-industry-andor-fda-staff), the following definitions apply:

- Reoperation - any surgical procedure at the index level that does not involve modification, addition or removal of any components of the device in the postoperative or follow-up period.
- Revision - any procedure in the postoperative or follow-up period that adjusts, modifies, or removes part of the original implant configuration with or without replacement of a component – may include adjusting the position of the original configuration in the postoperative or follow-up period.
- Removal - a procedure where the entire device is removed with or without replacement of the device in the postoperative or follow-up period.
- Supplemental fixation – a procedure in which additional instrumentation not under study is implanted (e.g., supplemental placement of a rod/ screw system).

Secondary Endpoints

The secondary endpoints included:

- Clinically significant improvement in one or more radicular symptoms or myelopathy at Month 24 compared to baseline for each group. The data collected reflect the number of subjects who improved (numbers were stratified to reflect clinical improvement), remain unchanged, and deteriorated at each study time point. These endpoints were graded and defined as follows:
    - Time to recovery (time to first 15-point NDI improvement)
    - A visual analog scale (VAS) was used to evaluate each of the following pain locations:
        - Neck pain;
        - Left arm/shoulder pain;
        - Right arm/shoulder pain;
        - Worse Arm/Shoulder pain;
        - Hoarseness
    - SF-36 at baseline and at each follow-up time-point;
    - Bazaz Dysphagia Score at Month 24 compared to baseline;
    - Results categorized according to Odom's Criteria;
    - Patient Satisfaction;
    - Myelopathy based on the Nurick scale;

In addition to the primary and secondary objectives listed above, various neurologic, operative, and radiographic (quantitative and qualitative) assessments were measured and evaluated.

5. Analysis Populations

The study defined the following populations for analysis:

- Intent-to-Treat (ITT) Analysis Set: The ITT analysis set will include all enrolled subjects, regardless of whether or not that treatment was actually received/completed. A subject must be selected into a PS subclass in order to be included in the ITT analysis set.
- As Treated (AT) Analysis Set: The AT analysis set includes those subjects in which treatment was actually completed with either the Investigational device or the Control device.
- Per-Protocol (PP) Analysis Set: The Per Protocol analysis set will consist of the subset of the AT analysis set with no major protocol violations as determined by the independent CEC, including important violations of inclusion or exclusion criteria and other post-surgical protocol violations expected to have substantial impact on the likelihood of interpreting Month 24 composite clinical success. The Per Protocol Set will be used for primary analysis, as is conservative for a test of non-inferiority. The Intention-to-Treat Set will be used to confirm these results.
- Safety Analysis Set: The safety analysis set included all subjects in the ITT analysis set.

6. Clinical Events Committees

An independent CEC, comprised of three spine surgeons who are not affiliated with the sponsor and did not participate in the study, reviewed all AEs including the appropriate AE term/code and category, relationship to the device and/or procedure, seriousness, and severity. In addition, the CEC adjudicated protocol deviations to determine which deviations were considered major or minor. The recommendation of the CEC overrode the investigator's classification and became part of the clinical trial data set.

The CEC also adjudicated neurologic status at Month 24 for all subjects to determine if neurologic status was maintained, improved or deteriorated relative to baseline.

B. Accountability of PMA Cohort

Table 5 below presents subject accounting and **Figure 3** presents the subject accounting tree for all subjects within the study. A total of 369 subjects (177 investigational subjects; 192 control subjects) comprised the Intent-to-Treat (ITT) Analysis Set.

- Two (2) subjects in the Synergy Disc group were enrolled but not treated with the Synergy Disc. Seven (7) subjects in the ACDF control group were enrolled but not treated, including one (1) subject removed from the study intra-operatively for additional treatment. The resulting 175 Synergy Disc subjects and 184 ACDF Control subjects comprised the As-Treated (AT) Analysis Set.
- Eleven (11) Synergy Disc and twenty-eight (28) ACDF control subjects had a major protocol deviation, resulting in 164 investigational subjects and 156 ACDF control subjects in the Per-Protocol (PP) Analysis Set.

Table 5: Subject Accounting

	Synergy Disc	Control
Enrolled (ITT Analysis Set)	177	192
Treated (AT Analysis Set)	175 (2 Synergy subjects were enrolled but not treated with the Synergy Disc)	184 (7 subjects not treated; 1 subject removed from study intraoperatively due to additional treatment required)
Per Protocol (PP) Analysis Set	164 (11 Synergy subjects had a Major Protocol Deviation)	156 (28 Control subjects had a Major Protocol Deviation)
# of Subjects (PP Analysis Set) yet to reach 24 Months (Day 730) as of Database Lock	5*	0
Theoretical Due (PP Analysis Set) (Day 730) as of Database Lock	159	156
Subjects with Complete Primary Outcome Data (PP Analysis Set)	155	136
Reasons for Missing Primary Outcome • **Not yet overdue (Have not reached Day 790)** • **Below day 730** • **Missing for other reasons (Withdrawal, loss to follow up etc.)**	9 subjects missing at least 1 component of CCS • 5 subjects missed the 24 Month Visit (> Day 790) • 1 subject was withdrawn from the study at 12 Months by site because subject did not return for visits • 3 subjects missing at least one component of primary endpoint	20 subjects missing at least 1 component of the CCS
***Subjects had yet to reach Day 730 at time of Database Lock but completed their Month-24 visit before the Database Lock. Subject data is included in the Per Protocol analysis set.**		

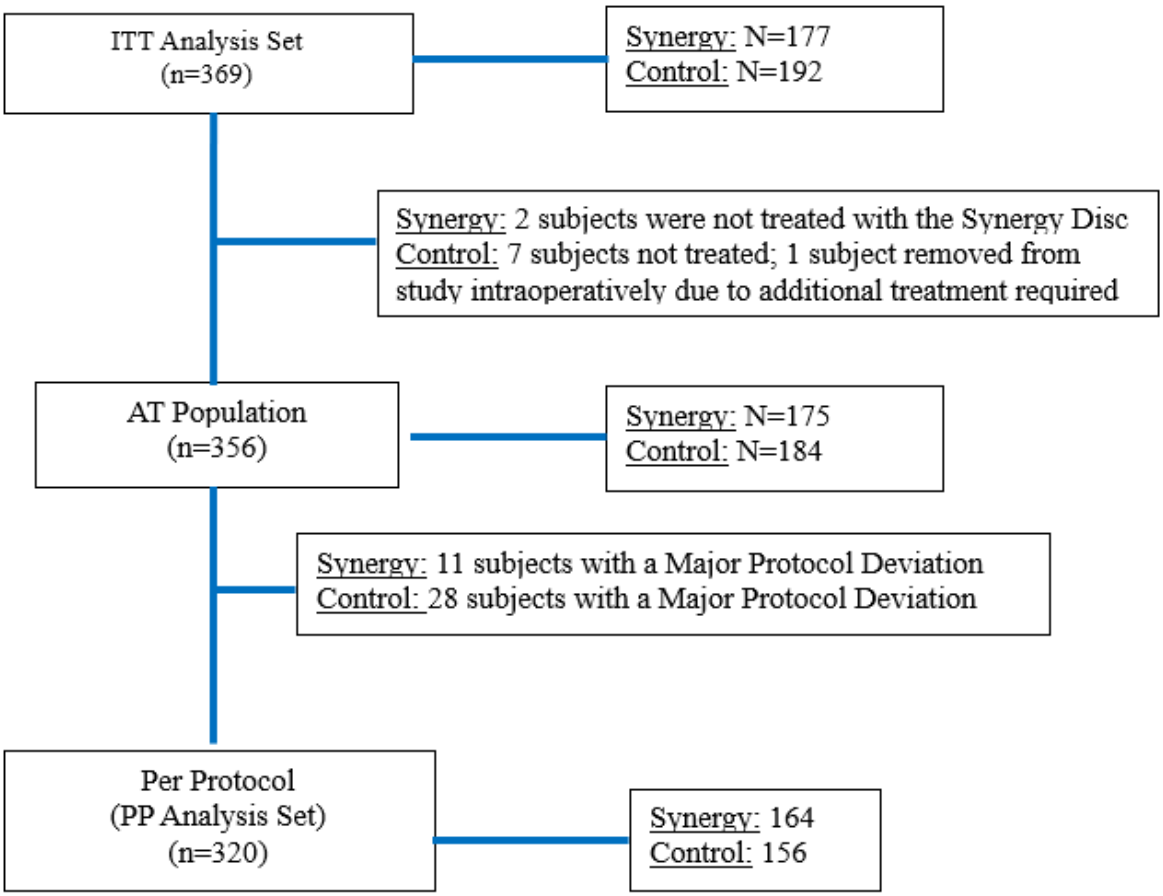

Figure 3: Subject Accounting Tree

C. Study Population Demographics and Baseline Parameters

Table 6 provides a summary of pre-operative and demographic variables for subjects in the ITT Analysis Set for both the investigational and control groups. The demographics of the study population are typical for a cTDR study performed in the US.

Table 6: Pre-Operative and Demographic Variables (ITT Analysis Set)

	Synergy Disc (N=177)					Control (N=192)				
Description	**n**	**Mean**	**S.D.**	**Median**	**Min, Max**	**n**	**Mean**	**S.D.**	**Median**	**Min, Max**
Age (years)	177	46.1	9.8	45	23.0, 70.0	192	43.6	8.6	44	19.0, 63.0
Height (in)	177	67.7	4.3	68	58.0, 77.0	191	67.4	3.8	67	58.0, 75.0
Weight (lbs)	177	189.4	39.6	185	110.2, 297.0	191	176.8	38.7	177	100.0, 295.0
BMI (kg/m^2)	177	29.0	4.9	28.6	18.9, 39.7	192	27.2	4.9	26	19.0, 41.0

Table 7 identifies categorial demographic information for investigational and control subjects in the ITT Analysis Set. The proportions enrolled are consistent with the sex, age, racial and ethnicity of other cTDR studies conducted to support a PMA with one-level indications in the US. The table also presents information on the number of subjects with prior cervical fusion.

Table 7: Categorical Demographic Information (ITT Analysis Population)

	Synergy Disc (N=177)		Control (N=192)	
Description	**n**	**%**	**n**	**%**
Sex				
Male	94	53.1	100	52.1
Female	83	46.9	92	47.9
Race*				
Black or African American	7	4	7	3.6
Native Hawaiian or Other Pacific Islander	1	0.6	0	0
Asian	4	2.3	5	2.6
White	165	93.2	176	91.7
American Indian or Alaska Native	0	0	0	0
Other	3	1.7	4	2.1
Ethnicity				
Hispanic or Latino	11	6.2	0	0
Not Hispanic or Latino	166	93.8	0	0
Missing	0	0	192	100
Educational Status				
Some high school	5	2.8	8	4.2
High school graduate	19	10.7	44	22.9
Some college	62	35	76	39.6
Complete bachelor's degree	56	31.6	31	16.1
Some graduate work	3	1.7	3	1.6
Completed graduate degree (MBA, MD, PhD)	32	18.1	30	15.6
Prior cervical Fusion	18	10.2	22	11.5
N = Total number of subjects n = Number of subjects in each category *More than one can be selected				

D. Intra-Operative Data

Table 8 provides a summary of intra-operative variables for investigational and control subjects in the ITT Analysis Set. In the investigational group, the mean surgery time was 66.5 minutes as compared to a mean surgery time of 85.7 minutes in the control group. The mean estimated blood loss in the investigational group was 21.4 cc as compared to a mean estimated blood loss of 57.9 cc in the control group. Please note, if a subject was discharged on the same day as surgery, that would count as 1 day for length of stay. If discharge is the following day, the length of stay would be 2. The exact times of discharge are not available. Therefore, the 1.3 mean length of stay is not indicative of a length of stay of 31 hours.

Table 8: Intra-Operative Variables (ITT Analysis Set)

	Synergy Disc (N=177)					Control (N=192)				
Description	**n**	**Mean**	**S.D.**	**Median**	**Min, Max**	**n**	**Mean**	**S.D.**	**Median**	**Min, Max**
Surgery time (min)	177	66.5	25.1	62	28.0, 153.0	184	85.7	40.5	72	23.0, 258.0
Estimated blood loss (cc)	175	21.4	17.5	20	0.0, 150.0	184	57.9	46.2	50	0.0, 325.0
Length of hospital stay (days)	175	1.3	0.5	1	1.0, 4.0	184	2.4	0.7	2	1.0, 7.0

E. Safety and Effectiveness Results

1. Safety Results

Adverse Events Summary

The CEC reviewed all safety events through Month 24 for both the Synergy Disc and ACDF Control group including AEs and subsequent surgical interventions (SSIs). This allowed for uniform resolution of study-related events and evaluations and eliminated any site-by-site

variations in reporting. The same AE code list and relationship definitions were applied to both the investigational and control groups by the CEC. All safety tables presented below include the following data:

- N = total number of subjects
- n = total number of subjects in category
- m = number of mentions (events) in each category
- % = total number of subjects in each category divided by total number of subjects (n/N)

Table 9 identifies a summary of AE categories and rates between the investigational and control subjects in the ITT Analysis Set. Overall, the investigational group reported a numerically greater rate of any AEs (79.7% - 141/177) as compared to the rate of any AEs recorded in the control subjects (71.4% - 137/192). However, the investigational group reported a numerically lower rate of SAEs (18.1% - 32/177) as compared to the rate of SAEs calculated for the control group (22.9% - 44/192).

Table 9: Comparisons of Summary Adverse Event Percentages between Synergy Disc and ACDF Groups (ITT Analysis Set)

	Synergy Disc (N=177)			Control (N=192)		
Description	**n**	**%**	**m**	**n**	**%**	**m**
Any Treatment-emergent Adverse Event	141	79.7	408	137	71.4	271
Mild	115	65	241	76	39.6	105
Moderate	84	47.5	138	85	44.3	118
Severe	28	15.8	28	43	22.4	48
Unknown	1	0.6	1	0	0	0
Any Device Related Treatment-emergent Adverse Event[1]	32	18.1	36	66	34.4	83
Any Definitely Device Related Treatment-emergent Adverse Event	3	1.7	3	1	0.5	1
Any Procedure Related Treatment-emergent Adverse Event[1]	72	40.7	90	75	39.1	104
Any Definitely Procedure Related Treatment-emergent Adverse Event	39	22	44	28	14.6	34
Any Serious Treatment-emergent Adverse Event	32	18.1	35	44	22.9	52
Mild	2	1.1	2	0	0	0
Moderate	8	4.5	8	7	3.6	8
Severe	24	13.6	24	39	20.3	44
Unknown	1	0.6	1	0	0	0
Any Device Related Serious Treatment-emergent Adverse Event[1]	5	2.8	6	21	10.9	21
Any Definitely Device Related Serious Treatment-emergent Adverse Event	2	1.1	2	0	0	0
Any Procedure Related Serious Treatment-emergent Adverse Event[1]	6	3.4	7	23	12	24
Any Definitely Procedure Related Serious Treatment emergent Adverse Event	5	2.8	6	8	4.2	8

N = Total number of subjects.
n = Number of subjects in each category.
The percentage calculation is based on the total number of subjects in the sections denoted by indent.
m = Number of mentions in each category.
1 Includes 'Possibly Related', 'Probably Related' and 'Definitely Related'.

All Adverse Events

Table 10 lists all AEs reported as of the database lock by AE code, with the number of subjects experiencing the events. Percentages are calculated as the number of subjects experiencing an event divided by the number of subjects treated in the ITT Analysis Set. As mentioned above, the

investigational group presented with 408 events occurring in 79.7% (141/177) of subjects, compared to 271 events occurring in 71.4% (137/192) of the control subjects.

The most commonly reported AEs included: Radiculopathy (investigational - 19.8%, 35/177; control - 15.6%, 30/192); Cervical Pain (investigational – 16.4%, 75/177; control - 15.1%, 29/192); and Trauma (investigational - 10.7%, 19/177; control – 6.8% 13/192).

Table 10: All Adverse Events (ITT Analysis Set)

System Organ Class Preferred Term	Synergy Disc (N=177)			Control (N=192)		
	n	%	m	n	%	m
Any Adverse Event	141	79.7	408	137	71.4	271
Musculoskeletal and Connective Tissue Disorders	75	42.4	114	98	51	133
Cervical Pain	29	16.4	32	29	15.1	33
Adjacent Segment Degeneration	3	1.7	3	29	15.1	29
Lumbar Pain	18	10.2	20	13	6.8	14
Musculoskeletal Inflammation	17	9.6	19	12	6.3	16
Joint Pain	12	6.8	13	3	1.6	3
Other Musculoskeletal Pain	11	6.2	11	3	1.6	3
Soft Tissue Injury	2	1.1	3	11	5.7	11
Pseudarthrosis	0	0	0	7	3.6	7
Osteoarthritis	3	1.7	3	3	1.6	3
Fracture, Any Bone	2	1.1	2	3	1.6	3
Other Musculoskeletal and Connective Tissue Disorder	2	1.1	2	3	1.6	3
Herniated Disc	1	0.6	1	2	1	2
Spasms	1	0.6	1	1	0.5	1
Spondyloslistesis	1	0.6	1	1	0.5	1
Sprain	0	0	0	2	1	2
Cervical Degenerative Disc Disease	0	0	0	1	0.5	1
Joint Instability	0	0	0	1	0.5	1
Joint Stiffness	1	0.6	1	0	0	0
Muscle Weakness	1	0.6	1	0	0	0
Spinal Stenosis	1	0.6	1	0	0	0
Nervous System Disorders	60	33.9	88	47	24.5	58
Radiculopathy	35	19.8	44	30	15.6	36
Compressive Neuropathy	11	6.2	13	10	5.2	11
Numbness/Tingling	12	6.8	13	3	1.6	3
Headache	9	5.1	9	2	1	2
Other Nervous System Disorder	3	1.7	3	0	0	0
Cerebrospinal fluid leak	1	0.6	1	1	0.5	1
Dizziness	2	1.1	2	0	0	0
Horner's Syndrome	0	0	0	2	1	2
Ataxia	1	0.6	1	0	0	0
Cognitive Disturbance	1	0.6	1	0	0	0
Dysesthesia	0	0	0	1	0.5	1
Myelopathy	0	0	0	1	0.5	1
Neurological Deterioration (Motor, Sensory or Reflex)	0	0	0	1	0.5	1
Tremors	1	0.6	1	0	0	0
Other Complications/Events	35	19.8	41	18	9.4	25
Trauma	19	10.7	24	13	6.8	17
Cancer	7	4	7	1	0.5	1
Other Event, Describe	2	1.1	2	4	2.1	6
Adverse Reaction to Medication	4	2.3	4	1	0.5	1
Surgery at a location other than the spine	4	2.3	4	0	0	0
Gastrointestinal Disorders	30	16.9	37	18	9.4	19
Dysphagia	11	6.2	11	15	7.8	15
Constipation	7	4	8	1	0.5	1
Other Gastrointestinal Disorder	6	3.4	6	1	0.5	1
Gastrointestinal Pain	3	1.7	3	0	0	0
Nausea	2	1.1	2	1	0.5	1
Colitis	2	1.1	2	0	0	0
Diarrhea	1	0.6	1	1	0.5	1
Gastroesophageal Reflux Disease	2	1.1	2	0	0	0
Pancreatitis	1	0.6	1	0	0	0
Vomiting	1	0.6	1	0	0	0

System Organ Class Preferred Term	Synergy Disc (N=177)			Control (N=192)		
	n	%	m	n	%	m
Infections and Infestations	29	16.4	35	10	5.2	11
Infection, Not at Surgical Site	15	8.5	18	7	3.6	8
Infection, Surgical Site	7	4	7	1	0.5	1
Rash	4	2.3	4	2	1	2
Sinusitis	5	2.8	5	0	0	0
Sepsis	1	0.6	1	0	0	0
COVID-19 Infection	15	8.5	16	0	0	0
COVID-19	15	8.5	16	0	0	0
Respiratory, Thoracic and Mediastinal Disorders	12	6.8	13	2	1	2
Hoarseness	4	2.3	4	1	0.5	1
Nasal Congestion	3	1.7	3	0	0	0
Pneumonia	2	1.1	2	1	0.5	1
Pulmonary Edema	2	1.1	2	0	0	0
Airway Obstruction	1	0.6	1	0	0	0
Sleep Apnea	1	0.6	1	0	0	0
Cardiac Disorders	10	5.6	12	3	1.6	3
Congestive Heart Failure	3	1.7	4	1	0.5	1
Other Cardiac Disorders	3	1.7	3	0	0	0
Atrial Fibrillation	2	1.1	2	0	0	0
Syncope/Fainting	1	0.6	1	1	0.5	1
Hyperlipidemia	1	0.6	1	0	0	0
Mitral Valve Disease	1	0.6	1	0	0	0
Ventricular Arrhythmia	0	0	0	1	0.5	1
Immune System Disorders	8	4.5	8	3	1.6	3
Allergic Reaction	3	1.7	3	1	0.5	1
Inflammation	2	1.1	2	2	1	2
Autoimmune Disorder	3	1.7	3	0	0	0
Vascular Disorders	7	4	8	3	1.6	3
Hypertension	3	1.7	3	0	0	0
Other Vascular Disorder	2	1.1	3	0	0	0
Thromboembolic Event	2	1.1	2	0	0	0
Hypotension	0	0	0	1	0.5	1
Lymphedema	0	0	0	1	0.5	1
Phlebitis	0	0	0	1	0.5	1
Psychiatric Disorders	5	2.8	5	3	1.6	4
Depression	4	2.3	4	2	1	2
Anxiety Disorders	1	0.6	1	0	0	0
Delirium	0	0	0	1	0.5	1
Insomnia	0	0	0	1	0.5	1
Skin and Subcutaneous Tissue Disorders	5	2.8	5	2	1	3
Other Skin and Subcutaneous Tissue Disorder	1	0.6	1	1	0.5	2
Urticaria	2	1.1	2	0	0	0
Itching/Pruritus	1	0.6	1	0	0	0
Wound complications (e.g., dehiscence, bruising) and soft tissue damage	1	0.6	1	0	0	0
Wound secretions / drainage	0	0	0	1	0.5	1
Eye Disorders	6	3.4	6	1	0.5	1
Blurred Vision	2	1.1	2	0	0	0
Conjunctivitis	2	1.1	2	0	0	0
Other Eye Disorders	1	0.6	1	1	0.5	1
Glaucoma	1	0.6	1	0	0	0

System Organ Class Preferred Term	Synergy Disc (N=177)			Control (N=192)		
	n	%	m	n	%	m
Ear and Labyrinth Disorders	4	2.3	4	2	1	2
Vertigo	1	0.6	1	2	1	2
Other Ear and Labyrinth Disorders	2	1.1	2	0	0	0
Impaired Hearing	1	0.6	1	0	0	0
Endocrine Disorders	5	2.8	5	1	0.5	1
Other Endocrine Disorder	2	1.1	2	1	0.5	1
Hypothyroidism	2	1.1	2	0	0	0
Diabetes Mellitus	1	0.6	1	0	0	0
General Disorders and Administrative Site Conditions	4	2.3	4	2	1	2
Fatigue	2	1.1	2	1	0.5	1
Flu-like symptoms	2	1.1	2	0	0	0
Fever	0	0	0	1	0.5	1
Renal and Urinary Disorders	5	2.8	5	1	0.5	1
Urinary Retention	2	1.1	2	1	0.5	1
Renal Calculi	2	1.1	2	0	0	0
Other Renal and Urinary Disorder	1	0.6	1	0	0	0
Blood and Lymphatic System Disorders	1	0.6	1	0	0	0
Anemia	1	0.6	1	0	0	0
Hepatobiliary Disorders	1	0.6	1	0	0	0
Cholecystitis	1	0.6	1	0	0	0

N = Total number of subjects.
n = Number of subjects in each category.
The percentage calculation is based on the total number of subjects in the sections denoted by indent.
m = Number of mentions in each category.

All Adverse Events Time Course

Table 11 presents all AEs through Month 24 for both treatment groups. Counts in this table represent the number of mentions, i.e., events. The time course interval where the highest number of AEs took place was between Month 12 and Month 24 for both the investigational and control groups.

Table 11: Counts of Specific Adverse Events by Time of Occurrence – (ITT Analysis Population) (I = Synergy Disc, C = ACDF)

System Organ Class Preferred Term	<1		1-3		4-31		32-91		92-181		182-366		367-729		730-790	
	I	C	I	C	I	C	I	C	I	C	I	C	I	C	I	C
Any Adverse Event	0	1	28	18	58	25	67	37	67	43	91	55	94	76	3	17
Musculoskeletal and Connective Tissue Disorders	0	1	4	1	10	10	24	18	18	23	28	29	28	41	2	11
Cervical Pain	0	0	1	1	3	6	6	4	2	7	10	6	9	8	1	1
Musculoskeletal Inflammation	0	0	0	0	2	1	6	5	4	1	3	4	4	3	0	2
Lumbar Pain	0	0	1	0	1	1	5	0	4	2	6	4	3	5	0	2
Adjacent Segment Degeneration	0	0	0	0	0	0	1	1	0	2	2	8	0	14	0	4
Joint Pain	0	0	1	0	1	0	2	0	2	1	2	1	5	1	0	0
Other Musculoskeletal Pain	0	0	0	0	0	0	4	0	4	2	1	0	2	1	0	0
Soft Tissue Injury	0	0	0	0	1	2	0	3	0	2	2	1	0	2	0	1
Pseudarthrosis	0	0	0	0	0	0	0	1	0	0	0	4	0	2	0	0
Osteoarthritis	0	0	0	0	0	0	0	1	0	1	1	0	1	1	1	0
Fracture, Any Bone	0	0	0	0	0	0	0	0	0	1	0	1	2	1	0	0
Other Musculoskeletal and Connective Tissue Disorder	0	0	0	0	0	0	0	1	2	1	0	0	0	1	0	0
Herniated Disc	0	0	0	0	0	0	0	1	0	0	0	0	1	0	0	1
Spasms	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0
Spondylolisthesis	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	0
Sprain	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0
Cervical Degenerative Disc Disease	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
Joint Instability	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
Joint Stiffness	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
Lumbar Degenerative Disc Disease	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Muscle Weakness	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Spinal Stenosis	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
Nervous System Disorders	0	0	6	4	17	4	15	9	18	12	17	12	15	14	0	3
Radiculopathy	0	0	2	1	7	3	9	6	10	8	8	9	8	7	0	2
Compressive Neuropathy	0	0	1	0	2	0	2	2	2	3	3	3	3	3	0	0
Numbness/Tingling	0	0	1	0	3	1	3	0	2	1	4	0	0	1	0	0
Headache	0	0	1	0	2	0	1	1	2	0	1	0	2	1	0	0
Other Nervous System Disorder	0	0	0	0	2	0	0	0	0	0	1	0	0	0	0	0
Cerebrospinal fluid leak	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1
Dizziness	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
Horner's Syndrome	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0
Ataxia	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Cognitive Disturbance	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
Dysesthesia	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
Myelopathy	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
Neurological Deterioration (Motor, Sensory or Reflex)	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
Tremors	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
Other Complications/Events	0	0	0	1	3	2	4	3	8	4	15	7	11	8	0	0
Trauma	0	0	0	0	2	2	3	2	5	4	8	4	6	5	0	0
Cancer	0	0	0	0	0	0	0	0	1	0	4	0	2	1	0	0
Other Event, Describe	0	0	0	0	0	0	0	1	1	0	1	3	0	2	0	0
Adverse Reaction to Medication	0	0	0	1	1	0	1	0	1	0	0	0	1	0	0	0
Surgery at a location other than the spine	0	0	0	0	0	0	0	0	0	0	2	0	2	0	0	0
Gastrointestinal Disorders	0	0	7	5	10	1	4	4	4	1	5	1	7	5	0	2

System Organ Class Preferred Term	<1		1-3		4-31		32-91		92-181		182-366		367-729		730-790	
	I	C	I	C	I	C	I	C	I	C	I	C	I	C	I	C
Dysphagia	0	0	4	4	3	0	2	4	0	0	1	1	1	4	0	2
Constipation	0	0	3	0	3	1	0	0	1	0	0	0	1	0	0	0
Other Gastrointestinal Disorder	0	0	0	0	0	0	0	0	2	1	1	0	3	0	0	0
Gastrointestinal Pain	0	0	0	0	0	0	1	0	0	0	1	0	1	0	0	0
Nausea	0	0	0	0	2	0	0	0	0	0	0	0	0	1	0	0
Colitis	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0
Diarrhea	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0
Gastroesophageal Reflux Disease	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0
Pancreatitis	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
Vomiting	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
Infections and Infestations	0	0	2	2	7	5	9	0	5	0	3	1	9	2	0	1
Infection, Not at Surgical Site	0	0	0	1	1	3	4	0	5	0	1	1	7	2	0	1
Infection, Surgical Site	0	0	0	0	5	1	2	0	0	0	0	0	0	0	0	0
Rash	0	0	2	1	1	1	0	0	0	0	1	0	0	0	0	0
Sinusitis	0	0	0	0	0	0	3	0	0	0	1	0	1	0	0	0
Sepsis	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
COVID-19 Infection	0	0	0	0	1	0	3	0	4	0	4	0	4	0	0	0
COVID-19	0	0	0	0	1	0	3	0	4	0	4	0	4	0	0	0
Respiratory, Thoracic and Mediastinal Disorders	0	0	3	1	2	0	1	0	3	0	2	0	1	1	1	0
Hoarseness	0	0	1	0	2	0	0	0	1	0	0	0	0	1	0	0
Nasal Congestion	0	0	0	0	0	0	1	0	1	0	0	0	1	0	0	0
Pneumonia	0	0	1	1	0	0	0	0	0	0	0	0	0	0	1	0
Pulmonary Edema	0	0	1	0	0	0	0	0	0	0	1	0	0	0	0	0
Airway Obstruction	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
Sleep Apnea	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
Cardiac Disorders	0	0	1	0	0	1	1	0	1	0	4	1	5	1	0	0
Congestive Heart Failure	0	0	0	0	0	0	0	0	0	0	1	1	3	0	0	0
Other Cardiac Disorders	0	0	0	0	0	0	1	0	0	0	2	0	0	0	0	0
Atrial Fibrillation	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
Syncope/Fainting	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0
Hyperlipidemia	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
Mitral Valve Disease	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
Ventricular Arrhythmia	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
Immune System Disorders	0	0	3	1	1	0	0	0	0	1	2	1	2	0	0	0
Allergic Reaction	0	0	2	1	0	0	0	0	0	0	1	0	0	0	0	0
Inflammation	0	0	1	0	0	0	0	0	0	1	1	1	0	0	0	0
Autoimmune Disorder	0	0	0	0	1	0	0	0	0	0	0	0	2	0	0	0
Vascular Disorders	0	0	0	1	1	0	2	0	2	1	3	0	0	1	0	0
Hypertension	0	0	0	0	0	0	1	0	0	0	2	0	0	0	0	0
Other Vascular Disorder	0	0	0	0	0	0	1	0	2	0	0	0	0	0	0	0
Thromboembolic Event	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0
Hypotension	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
Lymphedema	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
Phlebitis	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
Psychiatric Disorders	0	0	0	1	1	0	0	0	1	0	1	2	2	1	0	0
Depression	0	0	0	0	0	0	0	0	1	0	1	2	2	0	0	0
Anxiety Disorders	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
Delirium	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
Insomnia	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
Skin and Subcutaneous Tissue Disorders	0	0	0	0	3	0	0	3	1	0	0	0	1	0	0	0

System Organ Class Preferred Term	<1		1-3		4-31		32-91		92-181		182-366		367-729		730-790	
	I	C	I	C	I	C	I	C	I	C	I	C	I	C	I	C
Other Skin and Subcutaneous Tissue Disorder	0	0	0	0	0	0	0	2	0	0	0	0	1	0	0	0
Urticaria	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
Itching/Pruritus	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
Wound complications (e.g., dehiscence, bruising) and soft ti ssue damage	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
Wound secretions / drainage	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0
Eye Disorders	0	0	0	0	1	0	1	0	0	0	2	0	2	1	0	0
Blurred Vision	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0	0
Conjunctivitis	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0
Other Eye Disorders	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0
Glaucoma	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
Ear and Labyrinth Disorders	0	0	0	0	0	1	0	0	0	1	2	0	2	0	0	0
Vertigo	0	0	0	0	0	1	0	0	0	1	1	0	0	0	0	0
Other Ear and Labyrinth Disorders	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0
Impaired Hearing	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
Endocrine Disorders	0	0	0	0	0	0	1	0	1	0	1	1	2	0	0	0
Other Endocrine Disorder	0	0	0	0	0	0	0	0	1	0	0	1	1	0	0	0
Hypothyroidism	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0
Diabetes Mellitus	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
General Disorders and Administrative Site Conditions	0	0	0	0	1	1	1	0	0	0	1	0	1	1	0	0
Fatigue	0	0	0	0	1	0	1	0	0	0	0	0	0	1	0	0
Flu-like symptoms	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0	0
Fever	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
Renal and Urinary Disorders	0	0	2	1	0	0	0	0	1	0	1	0	1	0	0	0
Urinary Retention	0	0	2	1	0	0	0	0	0	0	0	0	0	0	0	0
Renal Calculi	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0	0
Other Renal and Urinary Disorder	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
Blood and Lymphatic System Disorders	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
Anemia	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
Hepatobiliary Disorders	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
Cholecystitis	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0

All Adverse Events Severity – Investigational Group

Table 12 presents the AEs observed in the investigational group stratified by severity. These AEs were classified as Mild, Moderate, or Severe events. Overall, there were 241 mild AEs, 138 moderate AEs, and 28 Severe AEs reported in the investigational group for the ITT Analysis Set.

Table 12: Treatment Emergent Adverse Events (Severity) by Code (ITT Analysis Set) (Synergy Disc Group, N=177)

	Synergy Disc (N=177)											
	Mild			Moderate			Severe			Unknown		
System Organ Class Preferred Term	n	%	m	n	%	m	n	%	m	n	%	m
Any Adverse Event	115	65	241	84	47.5	138	28	15.8	28	1	0.6	1
Musculoskeletal and Connective Tissue Disorders	49	27.7	66	34	19.2	41	7	4	7	0	0	0
Cervical Pain	21	11.9	24	8	4.5	8	0	0	0	0	0	0
Lumbar Pain	11	6.2	11	7	4	7	2	1.1	2	0	0	0
Adjacent Segment Degeneration	0	0	0	1	0.6	1	2	1.1	2	0	0	0
Musculoskeletal Inflammation	13	7.3	15	4	2.3	4	0	0	0	0	0	0
Joint Pain	5	2.8	5	8	4.5	8	0	0	0	0	0	0
Other Musculoskeletal Pain	6	3.4	6	3	1.7	3	2	1.1	2	0	0	0
Soft Tissue Injury	0	0	0	2	1.1	3	0	0	0	0	0	0
Pseudarthrosis	0	0	0	0	0	0	0	0	0	0	0	0
Osteoarthritis	0	0	0	2	1.1	2	1	0.6	1	0	0	0
Fracture, Any Bone	0	0	0	2	1.1	2	0	0	0	0	0	0
Other Musculoskeletal and Connective Tissue Disorder	2	1.1	2	0	0	0	0	0	0	0	0	0
Herniated Disc	0	0	0	1	0.6	1	0	0	0	0	0	0
Spasms	0	0	0	1	0.6	1	0	0	0	0	0	0
Spondyloslistesis	0	0	0	1	0.6	1	0	0	0	0	0	0
Sprain	0	0	0	0	0	0	0	0	0	0	0	0
Cervical Degenerative Disc Disease	0	0	0	0	0	0	0	0	0	0	0	0
Joint Instability	0	0	0	0	0	0	0	0	0	0	0	0
Joint Stiffness	1	0.6	1	0	0	0	0	0	0	0	0	0
Muscle Weakness	1	0.6	1	0	0	0	0	0	0	0	0	0
Spinal Stenosis	1	0.6	1	0	0	0	0	0	0	0	0	0
Nervous System Disorders	38	21.5	49	26	14.7	33	6	3.4	6	0	0	0
Radiculopathy	16	9	19	16	9	19	6	3.4	6	0	0	0
Compressive Neuropathy	5	2.8	6	7	4	7	0	0	0	0	0	0
Numbness/Tingling	10	5.6	11	2	1.1	2	0	0	0	0	0	0
Headache	8	4.5	8	1	0.6	1	0	0	0	0	0	0
Other Nervous System Disorder	1	0.6	1	2	1.1	2	0	0	0	0	0	0
Cerebrospinal fluid leak	0	0	0	1	0.6	1	0	0	0	0	0	0
Dizziness	1	0.6	1	1	0.6	1	0	0	0	0	0	0
Horner's Syndrome	0	0	0	0	0	0	0	0	0	0	0	0
Ataxia	1	0.6	1	0	0	0	0	0	0	0	0	0
Cognitive Disturbance	1	0.6	1	0	0	0	0	0	0	0	0	0
Dysesthesia	0	0	0	0	0	0	0	0	0	0	0	0
Myelopathy	0	0	0	0	0	0	0	0	0	0	0	0
Neurological Deterioration (Motor, Sensory or Reflex)	0	0	0	0	0	0	0	0	0	0	0	0
Tremors	1	0.6	1	0	0	0	0	0	0	0	0	0
Other Complications/Events	15	8.5	16	17	9.6	20	5	2.8	5	0	0	0
Trauma	10	5.6	11	9	5.1	12	1	0.6	1	0	0	0
Cancer	0	0	0	5	2.8	5	2	1.1	2	0	0	0
Other Event, Describe	2	1.1	2	0	0	0	0	0	0	0	0	0
Adverse Reaction to Medication	3	1.7	3	1	0.6	1	0	0	0	0	0	0
Surgery at a location other than the spine	0	0	0	2	1.1	2	2	1.1	2	0	0	0
Gastrointestinal Disorders	24	13.6	28	6	3.4	7	2	1.1	2	0	0	0
Dysphagia	11	6.2	11	0	0	0	0	0	0	0	0	0
Constipation	6	3.4	7	1	0.6	1	0	0	0	0	0	0
Other Gastrointestinal Disorder	2	1.1	2	3	1.7	3	1	0.6	1	0	0	0
Gastrointestinal Pain	1	0.6	1	2	1.1	2	0	0	0	0	0	0
Nausea	2	1.1	2	0	0	0	0	0	0	0	0	0
Colitis	2	1.1	2	0	0	0	0	0	0	0	0	0
Diarrhea	0	0	0	1	0.6	1	0	0	0	0	0	0
Gastroesophageal Reflux Disease	2	1.1	2	0	0	0	0	0	0	0	0	0
Pancreatitis	0	0	0	0	0	0	1	0.6	1	0	0	0
Vomiting	1	0.6	1	0	0	0	0	0	0	0	0	0

	Synergy Disc (N=177)											
	Mild			Moderate			Severe			Unknown		
System Organ Class Preferred Term	**n**	**%**	**m**	**n**	**%**	**m**	**n**	**%**	**m**	**n**	**%**	**m**
Infections and Infestations	17	9.6	22	9	5.1	9	4	2.3	4	0	0	0
Infection, Not at Surgical Site	9	5.1	12	4	2.3	4	2	1.1	2	0	0	0
Infection, Surgical Site	2	1.1	2	4	2.3	4	1	0.6	1	0	0	0
Rash	4	2.3	4	0	0	0	0	0	0	0	0	0
Sinusitis	4	2.3	4	1	0.6	1	0	0	0	0	0	0
Sepsis	0	0	0	0	0	0	1	0.6	1	0	0	0
COVID-19 Infection	11	6.2	11	5	2.8	5	0	0	0	0	0	0
COVID-19	11	6.2	11	5	2.8	5	0	0	0	0	0	0
Cardiac Disorders	6	3.4	6	5	2.8	5	0	0	0	1	0.6	1
Congestive Heart Failure	0	0	0	3	1.7	3	0	0	0	1	0.6	1
Other Cardiac Disorders	2	1.1	2	1	0.6	1	0	0	0	0	0	0
Atrial Fibrillation	1	0.6	1	1	0.6	1	0	0	0	0	0	0
Syncope/Fainting	1	0.6	1	0	0	0	0	0	0	0	0	0
Hyperlipidemia	1	0.6	1	0	0	0	0	0	0	0	0	0
Mitral Valve Disease	1	0.6	1	0	0	0	0	0	0	0	0	0
Ventricular Arrhythmia	0	0	0	0	0	0	0	0	0	0	0	0
Respiratory, Thoracic and Mediastinal Disorders	8	4.5	8	4	2.3	4	1	0.6	1	0	0	0
Hoarseness	3	1.7	3	1	0.6	1	0	0	0	0	0	0
Nasal Congestion	3	1.7	3	0	0	0	0	0	0	0	0	0
Pneumonia	2	1.1	2	0	0	0	0	0	0	0	0	0
Pulmonary Edema	0	0	0	1	0.6	1	1	0.6	1	0	0	0
Airway Obstruction	0	0	0	1	0.6	1	0	0	0	0	0	0
Sleep Apnea	0	0	0	1	0.6	1	0	0	0	0	0	0
Immune System Disorders	6	3.4	6	2	1.1	2	0	0	0	0	0	0
Allergic Reaction	2	1.1	2	1	0.6	1	0	0	0	0	0	0
Inflammation	2	1.1	2	0	0	0	0	0	0	0	0	0
Autoimmune Disorder	2	1.1	2	1	0.6	1	0	0	0	0	0	0
Vascular Disorders	4	2.3	4	3	1.7	3	1	0.6	1	0	0	0
Hypertension	3	1.7	3	0	0	0	0	0	0	0	0	0
Other Vascular Disorder	1	0.6	1	1	0.6	1	1	0.6	1	0	0	0
Thromboembolic Event	0	0	0	2	1.1	2	0	0	0	0	0	0
Hypotension	0	0	0	0	0	0	0	0	0	0	0	0
Lymphedema	0	0	0	0	0	0	0	0	0	0	0	0
Phlebitis	0	0	0	0	0	0	0	0	0	0	0	0
Psychiatric Disorders	2	1.1	2	3	1.7	3	0	0	0	0	0	0
Depression	2	1.1	2	2	1.1	2	0	0	0	0	0	0
Anxiety Disorders	0	0	0	1	0.6	1	0	0	0	0	0	0
Delirium	0	0	0	0	0	0	0	0	0	0	0	0
Insomnia	0	0	0	0	0	0	0	0	0	0	0	0
Skin and Subcutaneous Tissue Disorders	3	1.7	3	2	1.1	2	0	0	0	0	0	0
Other Skin and Subcutaneous Tissue Disorder	1	0.6	1	0	0	0	0	0	0	0	0	0
Urticaria	0	0	0	2	1.1	2	0	0	0	0	0	0
Itching/Pruritus	1	0.6	1	0	0	0	0	0	0	0	0	0
Wound complications (e.g., dehiscence, bruising) and soft tissue damage	1	0.6	1	0	0	0	0	0	0	0	0	0
Wound secretions / drainage	0	0	0	0	0	0	0	0	0	0	0	0
Eye Disorders	3	1.7	3	1	0.6	1	2	1.1	2	0	0	0
Blurred Vision	2	1.1	2	0	0	0	0	0	0	0	0	0
Conjunctivitis	1	0.6	1	0	0	0	1	0.6	1	0	0	0
Other Eye Disorders	0	0	0	0	0	0	1	0.6	1	0	0	0
Glaucoma	0	0	0	1	0.6	1	0	0	0	0	0	0
Ear and Labyrinth Disorders	3	1.7	3	1	0.6	1	0	0	0	0	0	0
Vertigo	1	0.6	1	0	0	0	0	0	0	0	0	0
Other Ear and Labyrinth Disorders	2	1.1	2	0	0	0	0	0	0	0	0	0
Impaired Hearing	0	0	0	1	0.6	1	0	0	0	0	0	0
Endocrine Disorders	5	2.8	5	0	0	0	0	0	0	0	0	0
Other Endocrine Disorder	2	1.1	2	0	0	0	0	0	0	0	0	0
Hypothyroidism	2	1.1	2	0	0	0	0	0	0	0	0	0
Diabetes Mellitus	1	0.6	1	0	0	0	0	0	0	0	0	0

	Synergy Disc (N=177)											
	Mild			Moderate			Severe			Unknown		
System Organ Class Preferred Term	**n**	**%**	**m**	**n**	**%**	**m**	**n**	**%**	**m**	**n**	**%**	**m**
General Disorders and Administrative Site Conditions	4	2.3	4	0	0	0	0	0	0	0	0	0
Fatigue	2	1.1	2	0	0	0	0	0	0	0	0	0
Flu-like symptoms	2	1.1	2	0	0	0	0	0	0	0	0	0
Fever	0	0	0	0	0	0	0	0	0	0	0	0
Renal and Urinary Disorders	4	2.3	4	1	0.6	1	0	0	0	0	0	0
Urinary Retention	2	1.1	2	0	0	0	0	0	0	0	0	0
Renal Calculi	1	0.6	1	1	0.6	1	0	0	0	0	0	0
Other Renal and Urinary Disorder	1	0.6	1	0	0	0	0	0	0	0	0	0
Blood and Lymphatic System Disorders	1	0.6	1	0	0	0	0	0	0	0	0	0
Anemia	1	0.6	1	0	0	0	0	0	0	0	0	0
Hepatobiliary Disorders	0	0	0	1	0.6	1	0	0	0	0	0	0
Cholecystitis	0	0	0	1	0.6	1	0	0	0	0	0	0

N = Total number of subjects.
n = Number of subjects in each category.
The percentage calculation is based on the total number of subjects in the sections denoted by indent.
m = Number of mentions in each category.

All Adverse Events Severity – Control Group

Table 13 identifies the AEs observed in the control group stratified by severity. These AEs were classified as Mild, Moderate, or Severe events. Overall, there were 105 mild AEs, 118 moderate AEs, and 48 Severe AEs reported in the control group for the ITT Analysis Set.

Table 13: Treatment Emergent Adverse Events (Severity) by Code (ITT Analysis Set) (Control Group, N=192)

	Control (N=192)											
	Mild			Moderate			Severe			Unknown		
System Organ Class Preferred Term	n	%	m	n	%	m	n	%	m	n	%	m
Any Adverse Event	76	39.6	105	85	44.3	118	43	22.4	48	0	0	0
Musculoskeletal and Connective Tissue Disorders	35	18.2	41	58	30.2	67	24	12.5	25	0	0	0
Cervical Pain	11	5.7	11	20	10.4	21	1	0.5	1	0	0	0
Lumbar Pain	4	2.1	4	8	4.2	8	1	0.5	2	0	0	0
Adjacent Segment Degeneration	3	1.6	3	12	6.3	12	14	7.3	14	0	0	0
Musculoskeletal Inflammation	8	4.2	9	5	2.6	7	0	0	0	0	0	0
Joint Pain	2	1	2	1	0.5	1	0	0	0	0	0	0
Other Musculoskeletal Pain	1	0.5	1	1	0.5	1	1	0.5	1	0	0	0
Soft Tissue Injury	3	1.6	3	7	3.6	7	1	0.5	1	0	0	0
Pseudarthrosis	1	0.5	1	4	2.1	4	2	1	2	0	0	0
Osteoarthritis	3	1.6	3	0	0	0	0	0	0	0	0	0
Fracture, Any Bone	0	0	0	2	1	2	1	0.5	1	0	0	0
Other Musculoskeletal and Connective Tissue Disorder	2	1	2	1	0.5	1	0	0	0	0	0	0
Herniated Disc	0	0	0	1	0.5	1	1	0.5	1	0	0	0
Spasms	1	0.5	1	0	0	0	0	0	0	0	0	0
Spondyloslistesis	0	0	0	0	0	0	1	0.5	1	0	0	0
Sprain	1	0.5	1	1	0.5	1	0	0	0	0	0	0
Cervical Degenerative Disc Disease	0	0	0	0	0	0	1	0.5	1	0	0	0
Joint Instability	0	0	0	1	0.5	1	0	0	0	0	0	0
Joint Stiffness	0	0	0	0	0	0	0	0	0	0	0	0
Muscle Weakness	0	0	0	0	0	0	0	0	0	0	0	0
Spinal Stenosis	0	0	0	0	0	0	0	0	0	0	0	0
Nervous System Disorders	26	13.5	28	21	10.9	22	7	3.6	8	0	0	0
Radiculopathy	12	6.3	13	17	8.9	17	6	3.1	6	0	0	0
Compressive Neuropathy	9	4.7	9	2	1	2	0	0	0	0	0	0
Numbness/Tingling	3	1.6	3	0	0	0	0	0	0	0	0	0
Headache	1	0.5	1	1	0.5	1	0	0	0	0	0	0
Other Nervous System Disorder	0	0	0	0	0	0	0	0	0	0	0	0
Cerebrospinal fluid leak	0	0	0	0	0	0	1	0.5	1	0	0	0
Dizziness	0	0	0	0	0	0	0	0	0	0	0	0
Horner's Syndrome	1	0.5	1	0	0	0	1	0.5	1	0	0	0
Ataxia	0	0	0	0	0	0	0	0	0	0	0	0
Cognitive Disturbance	0	0	0	0	0	0	0	0	0	0	0	0
Dysesthesia	0	0	0	1	0.5	1	0	0	0	0	0	0
Myelopathy	0	0	0	1	0.5	1	0	0	0	0	0	0
Neurological Deterioration (Motor, Sensory or Reflex)	1	0.5	1	0	0	0	0	0	0	0	0	0
Tremors	0	0	0	0	0	0	0	0	0	0	0	0
Other Complications/Events	6	3.1	7	10	5.2	13	5	2.6	5	0	0	0
Trauma	5	2.6	6	8	4.2	9	2	1	2	0	0	0
Cancer	0	0	0	0	0	0	1	0.5	1	0	0	0
Other Event, Describe	0	0	0	2	1	4	2	1	2	0	0	0
Adverse Reaction to Medication	1	0.5	1	0	0	0	0	0	0	0	0	0
Surgery at a location other than the spine	0	0	0	0	0	0	0	0	0	0	0	0
Gastrointestinal Disorders	12	6.3	12	5	2.6	5	2	1	2	0	0	0
Dysphagia	12	6.3	12	2	1	2	1	0.5	1	0	0	0
Constipation	0	0	0	1	0.5	1	0	0	0	0	0	0
Other Gastrointestinal Disorder	0	0	0	0	0	0	1	0.5	1	0	0	0
Gastrointestinal Pain	0	0	0	0	0	0	0	0	0	0	0	0
Nausea	0	0	0	1	0.5	1	0	0	0	0	0	0
Colitis	0	0	0	0	0	0	0	0	0	0	0	0
Diarrhea	0	0	0	1	0.5	1	0	0	0	0	0	0
Gastroesophageal Reflux Disease	0	0	0	0	0	0	0	0	0	0	0	0
Pancreatitis	0	0	0	0	0	0	0	0	0	0	0	0
Vomiting	0	0	0	0	0	0	0	0	0	0	0	0

	Control (N=192)											
	Mild			Moderate			Severe			Unknown		
System Organ Class Preferred Term	**n**	**%**	**m**	**n**	**%**	**m**	**n**	**%**	**m**	**n**	**%**	**m**
Infections and Infestations	7	3.6	8	0	0	0	3	1.6	3	0	0	0
Infection, Not at Surgical Site	4	2.1	5	0	0	0	3	1.6	3	0	0	0
Infection, Surgical Site	1	0.5	1	0	0	0	0	0	0	0	0	0
Rash	2	1	2	0	0	0	0	0	0	0	0	0
Sinusitis	0	0	0	0	0	0	0	0	0	0	0	0
Sepsis	0	0	0	0	0	0	0	0	0	0	0	0
COVID-19 Infection	0	0	0	0	0	0	0	0	0	0	0	0
COVID-19	0	0	0	0	0	0	0	0	0	0	0	0
Cardiac Disorders	0	0	0	2	1	2	1	0.5	1	0	0	0
Congestive Heart Failure	0	0	0	0	0	0	1	0.5	1	0	0	0
Other Cardiac Disorders	0	0	0	0	0	0	0	0	0	0	0	0
Atrial Fibrillation	0	0	0	0	0	0	0	0	0	0	0	0
Syncope/Fainting	0	0	0	1	0.5	1	0	0	0	0	0	0
Hyperlipidemia	0	0	0	0	0	0	0	0	0	0	0	0
Mitral Valve Disease	0	0	0	0	0	0	0	0	0	0	0	0
Ventricular Arrhythmia	0	0	0	1	0.5	1	0	0	0	0	0	0
Respiratory, Thoracic and Mediastinal Disorders	1	0.5	1	1	0.5	1	0	0	0	0	0	0
Hoarseness	1	0.5	1	0	0	0	0	0	0	0	0	0
Nasal Congestion	0	0	0	0	0	0	0	0	0	0	0	0
Pneumonia	0	0	0	1	0.5	1	0	0	0	0	0	0
Pulmonary Edema	0	0	0	0	0	0	0	0	0	0	0	0
Airway Obstruction	0	0	0	0	0	0	0	0	0	0	0	0
Sleep Apnea	0	0	0	0	0	0	0	0	0	0	0	0
Immune System Disorders	1	0.5	1	2	1	2	0	0	0	0	0	0
Allergic Reaction	1	0.5	1	0	0	0	0	0	0	0	0	0
Inflammation	0	0	0	2	1	2	0	0	0	0	0	0
Autoimmune Disorder	0	0	0	0	0	0	0	0	0	0	0	0
Vascular Disorders	3	1.6	3	0	0	0	0	0	0	0	0	0
Hypertension	0	0	0	0	0	0	0	0	0	0	0	0
Other Vascular Disorder	0	0	0	0	0	0	0	0	0	0	0	0
Thromboembolic Event	0	0	0	0	0	0	0	0	0	0	0	0
Hypotension	1	0.5	1	0	0	0	0	0	0	0	0	0
Lymphedema	1	0.5	1	0	0	0	0	0	0	0	0	0
Phlebitis	1	0.5	1	0	0	0	0	0	0	0	0	0
Psychiatric Disorders	1	0.5	1	0	0	0	3	1.6	3	0	0	0
Depression	0	0	0	0	0	0	2	1	2	0	0	0
Anxiety Disorders	0	0	0	0	0	0	0	0	0	0	0	0
Delirium	0	0	0	0	0	0	1	0.5	1	0	0	0
Insomnia	1	0.5	1	0	0	0	0	0	0	0	0	0
Skin and Subcutaneous Tissue Disorders	1	0.5	1	1	0.5	2	0	0	0	0	0	0
Other Skin and Subcutaneous Tissue Disorder	0	0	0	1	0.5	2	0	0	0	0	0	0
Urticaria	0	0	0	0	0	0	0	0	0	0	0	0
Itching/Pruritus	0	0	0	0	0	0	0	0	0	0	0	0
Wound complications (e.g., dehiscence, bruising) and soft tissue damage	0	0	0	0	0	0	0	0	0	0	0	0
Wound secretions / drainage	1	0.5	1	0	0	0	0	0	0	0	0	0
Eye Disorders	0	0	0	0	0	0	1	0.5	1	0	0	0
Blurred Vision	0	0	0	0	0	0	0	0	0	0	0	0
Conjunctivitis	0	0	0	0	0	0	0	0	0	0	0	0
Other Eye Disorders	0	0	0	0	0	0	1	0.5	1	0	0	0
Glaucoma	0	0	0	0	0	0	0	0	0	0	0	0
Ear and Labyrinth Disorders	0	0	0	2	1	2	0	0	0	0	0	0
Vertigo	0	0	0	2	1	2	0	0	0	0	0	0
Other Ear and Labyrinth Disorders	0	0	0	0	0	0	0	0	0	0	0	0
Impaired Hearing	0	0	0	0	0	0	0	0	0	0	0	0
Endocrine Disorders	1	0.5	1	0	0	0	0	0	0	0	0	0
Other Endocrine Disorder	1	0.5	1	0	0	0	0	0	0	0	0	0
Hypothyroidism	0	0	0	0	0	0	0	0	0	0	0	0
Diabetes Mellitus	0	0	0	0	0	0	0	0	0	0	0	0

	Control (N=192)											
	Mild			Moderate			Severe			Unknown		
System Organ Class Preferred Term	**n**	**%**	**m**	**n**	**%**	**m**	**n**	**%**	**m**	**n**	**%**	**m**
Infections and Infestations	7	3.6	8	0	0	0	3	1.6	3	0	0	0
Infection, Not at Surgical Site	4	2.1	5	0	0	0	3	1.6	3	0	0	0
Infection, Surgical Site	1	0.5	1	0	0	0	0	0	0	0	0	0
Rash	2	1	2	0	0	0	0	0	0	0	0	0
General Disorders and Administrative Site Conditions	1	0.5	1	1	0.5	1	0	0	0	0	0	0
Fatigue	1	0.5	1	0	0	0	0	0	0	0	0	0
Flu-like symptoms	0	0	0	0	0	0	0	0	0	0	0	0
Fever	0	0	0	1	0.5	1	0	0	0	0	0	0
Renal and Urinary Disorders	0	0	0	1	0.5	1	0	0	0	0	0	0
Urinary Retention	0	0	0	1	0.5	1	0	0	0	0	0	0
Renal Calculi	0	0	0	0	0	0	0	0	0	0	0	0
Other Renal and Urinary Disorder	0	0	0	0	0	0	0	0	0	0	0	0
Blood and Lymphatic System Disorders	0	0	0	0	0	0	0	0	0	0	0	0
Anemia	0	0	0	0	0	0	0	0	0	0	0	0
Hepatobiliary Disorders	0	0	0	0	0	0	0	0	0	0	0	0
Cholecystitis	0	0	0	0	0	0	0	0	0	0	0	0

N = Total number of subjects.
n = Number of subjects in each category.
The percentage calculation is based on the total number of subjects in the sections denoted by indent.
m = Number of mentions in each category.

Device-Related Adverse Events

As presented in **Table 14,** there were 36 device-related AEs events in 32 investigational subjects as compared to 83 device-related AEs in 66 control subjects that were determined to be definitely device-related. This resulted in a device-related SAE rate of 18.1% (32/177) for the investigational group, which was numerically lower as compared to the device-related AE rate of 34.4% (66/192) for the control group. The majority of these device-related AEs occurred in the category of musculoskeletal and connective tissue disorders, specifically adjacent segment disease.

Table 14: Counts and Percentages of Subjects with Specific Device-Related Adverse Event– (ITT Analysis Set)

	Synergy Disc (N=177)			Control (N=192)		
System Organ Class Preferred Term	**n**	**%**	**m**	**n**	**%**	**m**
Any Device Related Adverse Event	32	18.1	36	66	34.4	83
Musculoskeletal and Connective Tissue Disorders	13	7.3	13	48	25	50
Adjacent Segment Degeneration	2	1.1	2	28	14.6	28
Cervical Pain	11	6.2	11	12	6.3	13
Pseudarthrosis	0	0	0	7	3.6	7
Cervical Degenerative Disc Disease	0	0	0	1	0.5	1
Soft Tissue Injury	0	0	0	1	0.5	1
Nervous System Disorders	15	8.5	16	19	9.9	22
Radiculopathy	12	6.8	13	17	8.9	20
Headache	2	1.1	2	0	0	0
Dysesthesia	0	0	0	1	0.5	1
Myelopathy	0	0	0	1	0.5	1
Numbness/Tingling	1	0.6	1	0	0	0
Gastrointestinal Disorders	4	2.3	4	10	5.2	10
Dysphagia	4	2.3	4	10	5.2	10
Infections and Infestations	2	1.1	2	0	0	0
Infection, Not at Surgical Site	1	0.6	1	0	0	0
Infection, Surgical Site	1	0.6	1	0	0	0
Respiratory, Thoracic and Mediastinal Disorders	1	0.6	1	1	0.5	1
Hoarseness	1	0.6	1	1	0.5	1

N = Total number of subjects.
n = Number of subjects in each category.
The percentage calculation is based on the total number of subjects in the sections
m = Number of mentions in each category.
Includes 'Possibly Related', 'Probably Related' and 'Definitely Related'.

In the investigational group, the most device-related AEs (n=9) were reported between Month 6 and Month 12 window (and n=9 device-related AEs between the Month 12 and Month 24 window), while in the control group, the most device-related AEs (n=28) were reported between Month 12 and Month 18.

Procedure-Related Adverse Events

As described in **Table 15,** there were 90 procedure-related AEs in 72 investigational subjects, and 104 procedure-related AEs in 75 control subjects. This resulted in a procedure-related AE rate of 40.7% (72/177) for the investigational group, with the majority of these events described as nervous system disorders. The procedure-related AE rate was similar for the control group at 39.1% (75/192), with the majority of these AEs categorized as musculoskeletal and connective tissue disorders.

In the investigational group, the most procedure-related AEs (n=54) occurred within Month 1, while in the control group, the most procedure-related AEs (n=26) were reported between Month 12 and Month 24.

Table 15: Counts and Percentages of Subjects with Specific Procedure Related Adverse Event– (ITT Analysis Set)

	Synergy Disc (N=177)			Control (N=192)		
System Organ Class Preferred Term	**n**	**%**	**m**	**n**	**%**	**m**
Any Procedure Related Adverse Event	72	40.7	90	75	39.1	104
Musculoskeletal and Connective Tissue Disorders	19	10.7	21	49	25.5	51
Adjacent Segment Degeneration	2	1.1	2	28	14.6	28
Cervical Pain	15	8.5	15	13	6.8	14
Pseudarthrosis	0	0	0	7	3.6	7
Cervical Degenerative Disc Disease	0	0	0	1	0.5	1
Joint Pain	1	0.6	1	0	0	0
Muscle Weakness	1	0.6	1	0	0	0
Musculoskeletal Inflammation	1	0.6	1	0	0	0
Soft Tissue Injury	0	0	0	1	0.5	1
Spasms	1	0.6	1	0	0	0
Nervous System Disorders	24	13.6	27	24	12.5	27
Radiculopathy	16	9	17	19	9.9	22
Headache	4	2.3	4	1	0.5	1
Numbness/Tingling	4	2.3	4	1	0.5	1
Horner's Syndrome	0	0	0	2	1	2
Ataxia	1	0.6	1	0	0	0
Cerebrospinal fluid leak	1	0.6	1	0	0	0
Myelopathy	0	0	0	1	0.5	1
Gastrointestinal Disorders	15	8.5	15	10	5.2	11
Dysphagia	9	5.1	9	9	4.7	9
Constipation	6	3.4	6	1	0.5	1
Diarrhea	0	0	0	1	0.5	1
Infections and Infestations	11	6.2	11	5	2.6	6
Infection, Surgical Site	7	4	7	1	0.5	1
Infection, Not at Surgical Site	1	0.6	1	3	1.6	4
Rash	3	1.7	3	1	0.5	1
Respiratory, Thoracic and Mediastinal Disorders	5	2.8	5	2	1	2
Hoarseness	4	2.3	4	1	0.5	1
Pneumonia	0	0	0	1	0.5	1
Pulmonary Edema	1	0.6	1	0	0	0
Skin and Subcutaneous Tissue Disorders	3	1.7	3	1	0.5	1
Itching/Pruritus	1	0.6	1	0	0	0
Urticaria	1	0.6	1	0	0	0
Wound complications (e.g., dehiscence, bruising) and soft tissue damage	1	0.6	1	0	0	0
Wound secretions / drainage	0	0	0	1	0.5	1
Renal and Urinary Disorders	2	1.1	2	1	0.5	1
Urinary Retention	2	1.1	2	1	0.5	1
Cardiac Disorders	1	0.6	1	1	0.5	1
Syncope/Fainting	1	0.6	1	1	0.5	1
Immune System Disorders	2	1.1	2	0	0	0
Allergic Reaction	1	0.6	1	0	0	0
Inflammation	1	0.6	1	0	0	0
Other Complications/Events	1	0.6	1	1	0.5	1
Adverse Reaction to Medication	1	0.6	1	1	0.5	1
Vascular Disorders	1	0.6	1	1	0.5	1
Phlebitis	0	0	0	1	0.5	1
Thromboembolic Event	1	0.6	1	0	0	0
General Disorders and Administrative Site Conditions	0	0	0	1	0.5	1
Fever	0	0	0	1	0.5	1
Hepatobiliary Disorders	1	0.6	1	0	0	0
Cholecystitis	1	0.6	1	0	0	0
Psychiatric Disorders	0	0	0	1	0.5	1
Delirium	0	0	0	1	0.5	1

N = Total number of subjects.
n = Number of subjects in each category.
The percentage calculation is based on the total number of subjects in the sections denoted by
m = Number of mentions in each category.
Includes 'Possibly Related', 'Probably Related' and 'Definitely Related'.

Serious Adverse Events

Table 16 identifies SAEs by AE term, with number of subjects experiencing events (n) and number of reported events (m), for the ITT Analysis Set. A total of 35 SAEs were reported in 32 investigational subjects as compared to 52 SAEs that were reported in 44 control subjects. This resulted in a SAE rate of 18.1% (32/177) for the investigational group which was numerically lower than the calculated SAE rate of 22.9% (44/192) for the control group. The most commonly reported SAE in the investigational group was radiculopathy (n=7), while the most commonly reported SAEs in the control group was adjacent segment degeneration (n=13).

In the investigational group, the most SAEs (n=13) were reported between Month 6 and Month 12, while in the control group, the most SAEs (n=19) were reported between Month 12 and Month 24.

Table 16: Counts and Percentages of Subjects with Specific Serious Adverse Event– (ITT Analysis Set)

	Synergy Disc (N=177)			Control (N=192)		
System Organ Class Preferred Term	**n**	**%**	**m**	**n**	**%**	**m**
Any Serious Adverse Event	32	18.1	35	44	22.9	52
Musculoskeletal and Connective Tissue Disorders	7	4	7	25	13	26
Adjacent Segment Degeneration	2	1.1	2	13	6.8	13
Lumbar Pain	3	1.7	3	1	0.5	2
Cervical Pain	0	0	0	3	1.6	3
Pseudarthrosis	0	0	0	3	1.6	3
Other Musculoskeletal Pain	1	0.6	1	1	0.5	1
Cervical Degenerative Disc Disease	0	0	0	1	0.5	1
Fracture, Any Bone	0	0	0	1	0.5	1
Herniated Disc	0	0	0	1	0.5	1
Osteoarthritis	1	0.6	1	0	0	0
Spondyloslistesis	0	0	0	1	0.5	1
Nervous System Disorders	8	4.5	8	5	2.6	6
Radiculopathy	7	4	7	5	2.6	5
Cerebrospinal fluid leak	0	0	0	1	0.5	1
Other Nervous System Disorder	1	0.6	1	0	0	0
Other Complications/Events	6	3.4	6	5	2.6	6
Trauma	2	1.1	2	3	1.6	3
Cancer	1	0.6	1	1	0.5	1
Other Event, Describe	0	0	0	2	1	2
Surgery at a location other than the spine	2	1.1	2	0	0	0
Adverse Reaction to Medication	1	0.6	1	0	0	0
Infections and Infestations	3	1.7	3	3	1.6	3
Infection, Not at Surgical Site	1	0.6	1	3	1.6	3
Infection, Surgical Site	1	0.6	1	0	0	0
Sepsis	1	0.6	1	0	0	0
Cardiac Disorders	2	1.1	2	3	1.6	3
Congestive Heart Failure	1	0.6	1	1	0.5	1
Other Cardiac Disorders	1	0.6	1	0	0	0
Syncope/Fainting	0	0	0	1	0.5	1
Ventricular Arrhythmia	0	0	0	1	0.5	1
Gastrointestinal Disorders	2	1.1	2	3	1.6	3
Dysphagia	0	0	0	2	1	2
Other Gastrointestinal Disorder	1	0.6	1	1	0.5	1
Pancreatitis	1	0.6	1	0	0	0
Psychiatric Disorders	0	0	0	3	1.6	3
Depression	0	0	0	2	1	2
Delirium	0	0	0	1	0.5	1
Respiratory, Thoracic and Mediastinal Disorders	3	1.7	3	0	0	0
Pulmonary Edema	2	1.1	2	0	0	0
Pneumonia	1	0.6	1	0	0	0
Eye Disorders	1	0.6	1	1	0.5	1
Other Eye Disorders	1	0.6	1	1	0.5	1
COVID-19 Infection	1	0.6	1	0	0	0
COVID-19	1	0.6	1	0	0	0
Ear and Labyrinth Disorders	0	0	0	1	0.5	1
Vertigo	0	0	0	1	0.5	1
Renal and Urinary Disorders	1	0.6	1	0	0	0
Renal Calculi	1	0.6	1	0	0	0
Vascular Disorders	1	0.6	1	0	0	0
Other Vascular Disorder	1	0.6	1	0	0	0

N = Total number of subjects.
n = Number of subjects in each category.
The percentage calculation is based on the total number of subjects in the sections denoted by
m = Number of mentions in each category.

Device-Related Serious Adverse Events

Table 17 lists SAEs that were determined by the CEC to be device-related for the ITT Analysis Set. There were 5 device-related SAEs in 2.8% (5/177) of the investigational subjects, which was less than the 21 device-related SAEs reported in 10.9% (21/192) of the control subjects. The most commonly reported device-related SAE in the investigational group was radiculopathy (n=3), while the most commonly reported device-related SAEs in the control group was adjacent segment degeneration (n=13).

Table 17: Device-Related Serious Adverse Events by Code (ITT Analysis Set)

	Synergy Disc (N=177)			Control (N=192)		
System Organ Class Preferred Term	**n**	**%**	**m**	**n**	**%**	**m**
Any Device Related Serious Adverse Event	5	2.8	6	21	10.9	21
Musculoskeletal and Connective Tissue Disorders	1	0.6	1	18	9.4	18
Adjacent Segment Degeneration	1	0.6	1	13	6.8	13
Pseudarthrosis	0	0	0	3	1.6	3
Cervical Degenerative Disc Disease	0	0	0	1	0.5	1
Cervical Pain	0	0	0	1	0.5	1
Nervous System Disorders	3	1.7	3	2	1	2
Radiculopathy	3	1.7	3	2	1	2
Infections and Infestations	2	1.1	2	0	0	0
Infection, Not at Surgical Site	1	0.6	1	0	0	0
Infection, Surgical Site	1	0.6	1	0	0	0
Gastrointestinal Disorders	0	0	0	1	0.5	1
Dysphagia	0	0	0	1	0.5	1

N = Total number of subjects.
n = Number of subjects in each category.
The percentage calculation is based on the total number of subjects in the sections
m = Number of mentions in each category.
Includes 'Possibly Related', 'Probably Related' and 'Definitely Related'.

Procedure-Related Serious Adverse Events

Table 18 reports all SAEs that were determined by the CEC to be procedure-related for the ITT Analysis Set. There were 6 procedure-related SAEs in 3.4% (6/177) of the investigational subjects, which was less than the 23 procedure-related SAEs reported in 12.0% (23/192) of the control subjects. Similar to the device-related SAEs, the most commonly reported procedure-related SAE in the investigational group was radiculopathy (n=3), while the most commonly reported procedure-related SAEs in the control group was adjacent segment degeneration (n=13).

Table 18: Procedure-Related Serious Adverse Events by AE Code (ITT Analysis Set)

	Synergy Disc (N=177)			Control (N=192)		
System Organ Class Preferred Term	**n**	**%**	**m**	**n**	**%**	**m**
Any Procedure Related Serious Adverse Event	6	3.4	7	23	12	24
Musculoskeletal and Connective Tissue Disorders	1	0.6	1	19	9.9	19
Adjacent Segment Degeneration	1	0.6	1	13	6.8	13
Pseudarthrosis	0	0	0	3	1.6	3
Cervical Pain	0	0	0	2	1	2
Cervical Degenerative Disc Disease	0	0	0	1	0.5	1
Nervous System Disorders	3	1.7	3	2	1	2
Radiculopathy	3	1.7	3	2	1	2
Infections and Infestations	2	1.1	2	0	0	0
Infection, Not at Surgical Site	1	0.6	1	0	0	0
Infection, Surgical Site	1	0.6	1	0	0	0
Cardiac Disorders	0	0	0	1	0.5	1
Syncope/Fainting	0	0	0	1	0.5	1
Gastrointestinal Disorders	0	0	0	1	0.5	1
Dysphagia	0	0	0	1	0.5	1
Psychiatric Disorders	0	0	0	1	0.5	1
Delirium	0	0	0	1	0.5	1
Respiratory, Thoracic and Mediastinal Disorders	1	0.6	1	0	0	0
Pulmonary Edema	1	0.6	1	0	0	0

N = Total number of subjects.
n = Number of subjects in each category.
The percentage calculation is based on the total number of subjects in the sections denoted by indent.
m = Number of mentions in each category.
Includes 'Possibly Related', 'Probably Related' and 'Definitely Related'.

Subsequent Surgical Intervention

Table 19 reports SSIs that were prospectively classified as revisions, removals, reoperations or supplemental fixations, reviewed by the CEC, and qualified as study failures, in the ITT Analysis Set. A total of 5 SSIs were reported in 4 investigational subjects, while a total of 8 SSIs occurred in 8 control subjects.

Table 19: Surgical Intervention Time Course by Treatment Type – (ITT Analysis Set)

SSI Type	Event Time Course (months)						Total	
	<6 Months		6-12 Months		12-24 Months			
	I	C	I	C	I	C	I	C
Reoperation	1				1		2	0
Revision		1		1		3	0	5
Removal			2	1		2	2	3
Supplemental Fixation					1		1	0
Total	**1**	**1**	**2**	**2**	**2**	**5**	**5**	**8**

2. Effectiveness Results

The clinical trial was designed to test the non-inferiority of the investigational device as compared to the historical ACDF control when used at a single-level in the spine through the use of a primary composite endpoint.

Overall Success

Overall success was determined based upon the PP Analysis Set at Month 24. **Table 20** identifies overall success for Completers in the primary analysis population.

Table 20: Overall Effectiveness (Completers of the Primary Analysis Population (PP Analysis Set))

Row		Synergy Disc			Control		
		N	n	%	N	n	%
1	>= 15-point decrease in NDI calculated score	155	141	91.0%	136	98	72.1%
2	Maintenance or improvement in neurological status	155	150	96.8%	136	129	94.8%
3	No study failure due to secondary surgical interventions	155	151	97.4%	136	129	94.8%
4	Absence of device-related Serious Adverse Event	155	150	96.8%	136	118	86.8%
5	Fusion occurred (Control) / Absence of radiographic failure (Synergy Disc)	155	153	98.7%	136	120	88.2%
6	Composite Clinical Success (Completers)	155	135	87.1%	136	77	56.6%
--	Non-Inferiority[a]	95% CI (One-Sided)			p-value		
--		0.1847			<0.0001		
--	Superiority[a]	Estimate		95% CI (Two-Sided)		p-value	
--		0.2679		0.1687 – 0.3671		<0.0001	

N = Total number of subjects with available data (Completers) for the primary endpoint (CCS) assessment

[a]Statistical test data in this table reflect observed data on completers (no imputations) with PS adjustments

The success rates above show the number of subjects meeting success criteria in each category divided by the total number of composite completer subjects. The Statistical Analysis Plan (SAP) indicated that a one-sided 95% confidence interval would be presented for non-inferiority, and a two-sided 95% confidence interval would be presented for superiority. At Month 24, the overall success rate was 87.1% (135/155) for the investigational group as compared to 56.6% (77/136) for the control group.

The primary endpoint (non-inferiority), and subsequently superiority, was also met based on the pre-specified primary analysis method (with multiple imputation and PS adjustment) for the PP Analysis Set (see also Error! Reference source not found. in the section below**)**.

The CCS in the control arm was driven by the NDI success rate of 72.1% (since the minimum of each component of the composite determines the maximum of the CCS in a subject-level composite); therefore, the statistic tests of non-inferiority and superiority depend upon this NDI success rate. The generalizability of the results depends on how representative this NDI success rate is of clinical norms for ACDF surgery.

Primary Endpoint Assessment for Various Populations, Imputations, and Adjustments

Additional primary analyses and sensitivity analyses demonstrated consistent results in the outcomes for Completers of the primary analysis population, as assessed across various populations, imputations, and adjustments.

Error! Reference source not found. depicts the outcomes for each population pre-specified in the statistical analysis plan with and without multiple imputation with propensity score adjustments. As can be seen by the results, the claim of non-inferiority and superiority for the investigational group as compared to the control group at Month 24 is further supported through these additional analyses.

Table 21: Primary Endpoint Results for Various Populations and Imputations

Description	Population	Non-inferiority 90% CI	One-sided p-value	Estimated Difference	Superiority 95% CI	Two-sided p-value
MI, PS Adjusted	ITT	(20%, 36%)	<0.0001	28.0 %	(18%, 38%)	<0.0001
	As Treated	(20%, 36%)	<0.0001	28.3 %	(19%, 38%)	<0.0001
	PP*	**(19%, 36%)**	**<0.0001**	**27.2 %**	**(17%, 37%)**	**<0.0001**
No MI, PS Adjusted	ITT	(18%, 34%)	<0.0001	26.2 %	(17%, 36%)	<0.0001
	As Treated	(18%, 34%)	<0.0001	26.2 %	(17%, 36%)	<0.0001
	PP	(18%, 35%)	<0.0001	26.8 %	(17%, 37%)	<0.0001

***Pre-specified primary endpoint for the study**

Primary Endpoint Subcomponents

Synergy Disc subjects had higher observed success rates than control subjects in each individual component of the CCS.

NDI is scored on a 50-point scale (10 questions with a score of 0-5 for each) that is then normalized to a scale of 100. A higher NDI score is representative of greater symptomatology. At Month 24, 91.0% (141/155) of investigational subjects reported an improvement in NDI score of greater than or equal to 15 points, as compared to 72.1% (98/136) of control subjects that reported an improvement in NDI score of greater than or equal to 15 points (completer analysis, missing values were considered failures).

Neurologic status at all time points is assigned by the investigator or delegated clinician. Neurologic status at Month 24 postoperative compared to pre-operative was reviewed and adjudicated by the CEC. Neurologic status data are censored following intra-operative deviation or SSI. A total of 96.8% (150/155) of the investigational subjects and 94.8% (129/136) of the control subjects were assessed to have maintained or improved neurologic status (completer analysis, missing values considered failures).

A total of 151 (97.4%) of the investigational subjects were a success compared to 129 (94.8%) of the control subjects for freedom from SSI through Month 24.

A total of 150 (96.8%) investigational subjects were a success compared to 118 (86.8%) of control subjects in regards to any failure by AE as adjudicated by the CEC.

For the radiographic failure component, a total of 153 (98.7%) investigational subjects were considered to be successful through Month 24, as compared to 120 (88.2%) of control subjects through Month 24 (completer analysis, missing values considered failures).

Secondary Endpoint Analyses

In addition to the CCS subcomponents, a number of secondary endpoints were evaluated in the ITT Analysis Set, including: NDI, VAS, SF-36, Bazaz Dysphagia Score, Odom's Criteria, Patient Satisfaction, and Nurick Scale for Myelopathy.

The confidence intervals were calculated without multiplicity adjustment. As such, these confidence intervals should not be used to draw any statistical conclusion.

Neck Disability Index

Table 22 shows the mean NDI score for the ITT Analysis Set over time through Month 24. In the investigational group, the mean NDI score decreased from 57.9 at screening to 13.3 at Month 24. In the control group, the mean NDI score decreased from 55.4 at screening to 25.0 at Month 24.

Table 22: NDI score values over time (ITT Analysis Set, Excluding subjects with SSIs at Index Level)*

	Synergy Disc (N=177)						Control (N=192)							
Visit	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	delta	95% CL
Screening	176	57.9	16.09	57.0	30	96	191	55.4	13.88	54	28	92	2.5	(-0.61, 5.59)
6 Week	162	19.6	15.57	17	0	68	166	33.8	18.53	32	0	80	-14.2	(-17.93,-10.50)
3 Month	158	15.2	15.19	10	0	62	172	27.9	20.68	24	0	80	-12.6	(-16.55, -8.74)
6 Month	164	14.4	15.75	10	0	82	162	25.3	20.61	22	0	92	-10.9	(-14.91, -6.90)
12 Month	167	13.4	15.01	8	0	72	157	27	21.13	24	0	80	-13.6	(-17.65, -9.59)
24 Month	156	13.3	16.2	6	0	66	150	25	21.08	18	0	76	-11.7	(-15.92, -7.44)

* The confidence intervals were calculated without multiplicity adjustment. As such, these confidence intervals should not be used to draw any statistical conclusion.

Table 23 presents the number and percentage of subjects showing an improvement in NDI score greater than 15 points as compared to all subjects in the study at each follow up time point for both the investigational and control groups. At Month 24, 91.67% (143/156) of investigational subjects achieved greater than a 15-point improvement in NDI score as compared to baseline, while 75.17% (112/149) of control subjects achieved greater than a 15-point improvement in NDI score as compared to baseline.

Table 23: NDI 15-Point Responder (ITT Analysis Set, Excluding subjects with SSIs at Index Level)

	Synergy Disc (N = 177)			Control (N = 192)		
Visit	N	N	%	N	N	%
6 Week	162	139	85.80%	165	102	61.82%
3 Month	158	139	87.97%	171	129	75.44%
6 Month	164	150	91.46%	161	131	81.37%
12 Month	167	153	91.62%	156	119	76.28%
24 Month	156	143	91.67%	149	112	75.17%

VAS – Neck Pain

Table 24 reports the mean VAS – Neck Pain score for the ITT Analysis Set over time through Month 24. In the investigational group, the mean VAS – Neck Pain score decreased from 68.7 at screening to 15.6 at Month 24. In the control group, the mean VAS – Neck Pain score decreased from 74.7 at screening to 30.2 at Month 24.

Table 24: VAS Pain (Neck) values over time (ITT Analysis Set, Excluding subjects with SSIs at Index Level)*

	Synergy Disc (N=177)						Control (N=192)							
Visit	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	delta	95% CL
Screening	176	68.7	21.51	72	0	100	192	74.7	17.93	78	2	100	-6.0	(-10.05, -1.89)
6 Week	165	20.9	21.52	13	0	86	175	32.5	24.07	28	0	100	-11.6	(-16.48, -6.72)
3 Month	158	17.8	21.58	9	0	78	175	28.2	23.82	21	0	94	-10.4	(-15.33, -5.50)
6 Month	164	16.5	21.34	6.5	0	94	165	28.6	24.09	22.0	0	84	-12.1	(-17.04, -7.17)
12 Month	167	15.6	21.72	5	0	100	160	33.5	27.16	27	0	99	-17.9	(-23.29,-12.56)
24 Month	155	15.6	20.86	5	0	100	150	30.2	28.02	19.5	0	93	-14.5	(-20.12, -8.95)

***** The confidence intervals were calculated without multiplicity adjustment. As such, these confidence intervals should not be used to draw any statistical conclusion.

Table 25 presents the number and percentage of subjects showing an improvement in VAS – Neck Pain score greater than 20 points as compared to all subjects in the study at each follow up time point for both the investigational and control groups. At Month 24, 83.87% (130/155) of investigational subjects achieved greater than a 20-point improvement in VAS – Neck Pain score as compared to baseline, while 75.33% (113/150) of control subjects achieved greater than a 20-point improvement in VAS – Neck pain score as compared to baseline.

Table 25: VAS Pain (Neck) Responder (ITT Analysis Set, Excluding subjects with SSIs at Index Level)

	Synergy Disc (N = 177)			Control (N = 192)		
Visit	N	N	%	N	n	%
6 Week	165	136	82.42%	175	143	81.71%
3 Month	158	131	82.91%	175	147	84.00%
6 Month	164	140	85.37%	165	135	81.82%
12 Month	167	144	86.23%	160	119	74.38%
24 Month	155	130	83.87%	150	113	75.33%

VAS – Left Shoulder/Arm Pain

Table 26 describes the mean VAS – Left Shoulder/Arm Pain score for the ITT Analysis Set over time through Month 24. In the investigational group, the mean VAS – Left Shoulder/Arm Pain score decreased from 46.4 at screening to 10.8 at Month 24. In the control group, the mean VAS – Left Shoulder/Arm Pain score decreased from 52.0 at screening to 22.7 at Month 24.

Table 26: VAS (Left Arm/Shoulder) values over time (ITT Analysis Set, Excluding subjects with SSIs at Index Level)*

	Synergy Disc (N=177)						Control (N=192)							
Visit	N	Mean	SD	Med	Min	Max	n	Mean	SD	Med	Min	Max	delta	95% CL
Screening	176	46.4	35.48	50.5	0	100	192	52	33.18	55.5	0	100	-5.7	(-12.69, 1.38)
6 Week	165	12.7	18.25	4	0	88	174	19.8	24.62	9	0	99	-7.2	(-11.80, -2.57)
3 Month	158	12.1	20.44	2	0	94	174	20.6	26.15	8	0	100	-8.6	(-13.64, -3.55)
6 Month	164	10.7	17.72	2	0	100	165	19.3	23.93	9	0	86	-8.6	(-13.16, -4.02)
12 Month	167	12.3	20.3	2	0	100	160	22.7	26.01	12	0	97	-10.5	(-15.56, -5.37)
24 Month	155	10.8	17.9	2	0	83	150	22.7	24.93	14.5	0	89	-11.9	(-16.78, -6.97)

* The confidence intervals were calculated without multiplicity adjustment. As such, these confidence intervals should not be used to draw any statistical conclusion.

Table 27 identifies the number and percentage of subjects showing an improvement in VAS – Left Shoulder/Arm Pain score greater than 20 points as compared to all subjects in the study at each follow up time point for both the investigational and control groups. At Month 24, 55.48% (86/155) of investigational subjects achieved greater than a 20-point improvement in VAS – Left Shoulder/Arm Pain score as compared to baseline, while 52.67% (79/150) of control subjects achieved greater than a 20-point improvement in VAS – Left Shoulder/Arm Pain score as compared to baseline.

Table 27: VAS Left Arm/Shoulder 20-Point Responder (ITT Analysis Set, Excluding subjects with SSIs at Index Level)

	Synergy Disc (N = 177)			Control (N = 192)		
Visit	**N**	**N**	**%**	**N**	**n**	**%**
6 Week	165	91	55.15%	174	106	60.92%
3 Month	158	88	55.70%	174	96	55.17%
6 Month	164	89	54.27%	165	99	60.00%
12 Month	167	92	55.09%	160	83	51.88%
24 Month	155	86	55.48%	150	79	52.67%

VAS – Right Shoulder/Arm Pain

Table 28 reports the mean VAS – Right Shoulder/Arm Pain score for the ITT Analysis Set over time through Month 24. In the investigational group, the mean VAS – Right Shoulder/Arm Pain score decreased from 46.4 at screening to 10.5 at Month 24. In the control group, the mean VAS – Right Shoulder/Arm Pain score decreased from 49.4 at screening to 24.1 at Month 24.

Table 28: VAS (Right Arm/Shoulder) values over time (ITT Analysis Set, Excluding subjects with SSIs at Index Level)*

	Synergy Disc (N=177)						Control (N=192)							
Visit	**n**	**Mean**	**SD**	**Med**	**Min**	**Max**	**n**	**Mean**	**SD**	**Med**	**Min**	**Max**	**Delta**	**95% CL**
Screening	176	46.8	34.34	51.5	0	100	192	49.4	33.21	59	0	100	-2.6	(-9.55, 4.31)
6 Week	165	13.8	19.17	4	0	90	175	20.7	24.86	11	0	91	-6.9	(-11.61, -2.17)
3 Month	158	12.6	19.54	3	0	82	175	21.3	23.98	13	0	94	-8.7	(-13.39, -4.00)
6 Month	164	10.7	16.34	3	0	79	165	22.2	25.58	14	0	95	-11.5	(-16.16, -6.85)
12 Month	167	11.3	19.06	2	0	100	160	23.5	27.38	12	0	98	-12.2	(-17.34, -7.03)
24 Month	155	10.5	18.42	2	0	88	150	24.1	27.86	12.5	0	92	-13.6	(-18.94, -8.25)

* The confidence intervals were calculated without multiplicity adjustment. As such, these confidence intervals should not be used to draw any statistical conclusion.

Table 29 presents the number and percentage of subjects showing an improvement in VAS – Right Shoulder/Arm Pain score greater than 20 points as compared to all subjects in the study at each follow up time point for both the investigational and control groups. At Month 24, 59.35% (92/155) of investigational subjects achieved greater than a 20-point improvement in VAS – Right Shoulder/Arm Pain score as compared to baseline, while 52.00% (78/150) of control subjects achieved greater than a 20-point improvement in VAS – Right Shoulder/Arm Pain score as compared to baseline.

Table 29: VAS Right Arm/Shoulder 20-Point Responder (ITT Analysis Set, Excluding subjects with SSIs at Index Level)

	Synergy Disc (N = 177)			Control (N = 192)		
Visit	**N**	**N**	**%**	**N**	**n**	**%**
6 Week	165	100	60.61%	175	96	54.86%
3 Month	158	94	59.49%	175	97	55.43%
6 Month	164	103	62.80%	165	92	55.76%
12 Month	167	99	59.28%	160	87	54.38%
24 Month	155	92	59.35%	150	78	52.00%

A greater percentage of Synergy Disc subjects achieved 20-point improvement at VAS Right Arm pain compared to the ACDF Control group.

VAS – Worst Shoulder/Arm Pain

Table 30 reports the mean VAS – Worst Shoulder/Arm Pain score for the ITT Analysis Set over time through Month 24. In the investigational group, the mean VAS – Worst Shoulder/Arm Pain score decreased from 69.9 at screening to 15.0 at Month 24. In the control group, the mean VAS – Worst Shoulder/Arm Pain score decreased from 75.2 at screening to 32.2 at Month 24.

Table 30: VAS (Worst Arm/Shoulder) values over time (ITT Analysis Set, Excluding subjects with SSIs at Index Level)*

	Synergy Disc (N=177)						Control (N=192)							
Visit	**n**	**Mean**	**SD**	**Med**	**Min**	**Max**	**n**	**Mean**	**SD**	**Med**	**Min**	**Max**	**delta**	**95% CL**
Screening	176	69.9	23.50	73.5	2	100	192	75.2	17.83	78.5	5	100	-5.3	(-9.60, -0.98)
6 Week	165	19.1	20.85	11	0	90	175	27.7	28.02	17	0	99	-8.6	(-13.85, -3.35)
3 Month	158	17.8	22.91	7	0	94	175	29.1	27.6	21	0	100	-11.2	(-16.66, -5.76)
6 Month	164	15.9	20.35	7	0	100	165	28.9	27.80	20	0	95	-13.0	(-18.30, -7.73)
12 Month	167	16.7	22.33	4	0	100	160	32.4	29.52	22	0	98	-15.7	(-21.42, -9.99)
24 Month	155	15	21.11	4	0	88	150	32.2	29.07	23.5	0	92	-17.2	(-22.92,-11.43)

* The confidence intervals were calculated without multiplicity adjustment. As such, these confidence intervals should not be used to draw any statistical conclusion.

Table 31 lists the number and percentage of subjects showing an improvement in VAS – Worst Shoulder/Arm Pain score greater than 20 points as compared to all subjects in the study at each follow up time point for both the investigational and control groups. At Month 24, 82.58% (128/155) of investigational subjects achieved greater than a 20-point improvement in VAS – Worst Shoulder/Arm Pain score as compared to baseline, while 70.67% (106/150) of control subjects achieved greater than a 20-point improvement in VAS – Worst Shoulder/Arm Pain score as compared to baseline.

Table 31: VAS Worst Arm/Shoulder 20-Point Responder (ITT Analysis Set, Excluding subjects with SSIs at Index Level)

	Synergy Disc (N = 177)			Control (N = 192)		
Visit	**N**	**N**	**%**	**N**	**n**	**%**
6 Week	165	139	84.24%	175	143	81.71%
3 Month	158	129	81.65%	175	135	77.14%
6 Month	164	140	85.37%	165	127	76.97%
12 Month	167	138	82.63%	160	112	70.00%
24 Month	155	128	82.58%	150	106	70.67%

VAS – Hoarseness

Table 32 reports the mean VAS – Hoarseness score (0=hoarseness has no impact; 100=hoarseness has maximal impact, negative or adverse effect) for question, "How did hoarseness affect your post-operative recovery?", in the ITT Analysis Set over time through Month 24. In the investigational group, the mean VAS – Hoarseness score decreased from 11.8 at screening to 5.5 at Month 24. In the control group, the mean VAS – Hoarseness score decreased from 13.8 at Week 6 (no screening value) to 9.4 at Month 24.

Table 32: VAS (Hoarseness) values over time (ITT Analysis Set, Excluding subjects with SSIs at Index Level)*

	Synergy Disc (N=177)						Control (N=192)							
Visit	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	Delta	95% CL
Screening (Baseline)	176	11.8	19.78	3	0	95	0	-	-	-	-	-	-	-
6 Week	160	15.1	20.15	5	0	79	175	13.8	18.55	6	0	94	1.3	(-2.83, 5.49)
3 Month	158	8.8	14.44	2	0	69	169	10.1	15.82	2	0	75	-1.3	(-4.57, 2.03)
6 Month	166	8.7	16.88	1	0	89	161	8.9	15.7	2	0	85	-0.2	(-3.75, 3.35)
12 Month	166	7.9	15.56	1	0	89	158	10.5	18.45	3	0	99	-2.6	(-6.37, 1.11)
24 Month	155	5.5	11.55	1	0	77	147	9.4	17.92	2	0	100	-3.9	(-7.36, -0.48)

* The confidence intervals were calculated without multiplicity adjustment. As such, these confidence intervals should not be used to draw any statistical conclusion.

VAS - Dysphagia

Table 33 reports the mean VAS – Dysphagia score (0=dysphagia has no impact; 100=dysphagia has maximal impact, negative or adverse effect) for question, "How does swallowing difficulty affect your post-operative recovery?", in the ITT Analysis Set over time through Month 24. In the investigational group, the mean VAS – Dysphagia score decreased from 10.4 at screening to 8.0 at Month 24. In the control group, the mean VAS – Dysphagia score decreased from 28.3 at Week 6 (no screening value) to 11.5 at Month 24.

Table 33: How did swallowing difficulty affect your post-operative recovery? (ITT Analysis Set, Excluding subjects with SSIs at Index Level)*

	Synergy Disc (N=177)						Control (N=192)							
Visit	n	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	delta	95% CL
Screening (Baseline)	176	10.4	18.29	2	0	95	0	-	-	-	-	-	-	-
6 Week	160	22.4	23.58	14.5	0	79	175	28.3	26.66	18	0	98	-5.9	(-11.33, -0.47)
3 Month	158	14.6	20.81	3.5	0	69	169	15.3	19.83	6	0	100	-0.7	(-5.14, 3.70)
6 Month	166	11	19.14	2	0	89	161	14	19.84	4	0	83	-3	(-7.21, 1.27)
12 Month	166	10.6	18.12	1.5	0	89	158	13.7	21.04	4	0	100	-3.1	(-7.34, 1.23)
24 Month	155	8	14.05	1	0	77	147	11.5	19.49	3	0	100	-3.5	(-7.39, 0.35)

* The confidence intervals were calculated without multiplicity adjustment. As such, these confidence intervals should not be used to draw any statistical conclusion.

SF-36 – Physical Component Score

Table 34 present the results of the SF-36 Physical Component Score (PCS) for subjects in the ITT Analysis Set, except SSI. In the investigational group, the mean PCS at screening was 33.03, improving to a mean PCS of 49.54 at Month 24. In the control group, the mean PCS at screening was 34.60, increasing to 45.23 at Month 24.

Table 34: SF-36 (Physical Component Score – PCS) values over time ITT Analysis Set, Excluding subjects with SSIs at Index Level)*

	Synergy Disc (N=177)						Control (N=192)							
Visit	n	Mean	SD	Med	Min	Max	n	Mean	SD	Med	Min	Max	delta	95% CL
Screening	176	33.03	7.738	33.50	15.6	54.4	191	34.60	6.457	34.20	20.2	51.5	-1.564	(-3.034,-0.094)
6 Week	160	45.92	8.704	46.2	18.9	60.3	174	39.92	8.65	39.05	19	61.2	6.001	(4.132, 7.871)
3 Month	157	49.01	8.483	50.1	16.7	60.5	175	43.81	9.797	42.63	17.8	63.9	5.2	(3.211, 7.189)
6 Month	166	49.14	8.973	50.92	12.3	64.2	165	45.11	10.144	44.94	25.2	66.3	4.029	(1.958, 6.099)

12 Month	167	49.84	9.407	52.56	7	63.3	160	44.08	10.457	42.65	17.1	60	5.763	(3.601, 7.925)
24 Month	156	49.54	9.776	52.46	19.8	63.2	150	45.23	10.56	47.54	20.1	64.2	4.31	(2.022, 6.598)

* The confidence intervals were calculated without multiplicity adjustment. As such, these confidence intervals should not be used to draw any statistical conclusion.

SF-36 – Mental Component Score

Table 35 presents the results of the SF-36 Mental Component Score *(*MCS) scores for subjects in the ITT Analysis Set, except SSI. In the investigational group, the mean MCS at screening was 43.44, improving to a mean MCS of 52.08 at Month 24. In the control group, the mean MCS at screening was 42.00, increasing to 49.80 at Month 24.

Table 35: SF-36 (Mental Component Score – MCS) values over time (ITT Analysis Set, Excluding subjects with SSIs at Index Level)*

	Synergy Disc (N=177)						Control (N=192)							
Visit	n	Mean	SD	Med	Min	Max	n	Mean	SD	Med	Min	Max	delta	95% CL
Screening	176	43.44	13.007	44.32	11.9	67.3	191	42.00	12.031	42.01	13.8	65.0	1.442	(-1.128, 4.012)
6 Week	160	51.28	10.652	54.01	11.2	71.5	174	48.34	12.068	51.86	19.7	66.3	2.944	(0.485, 5.403)
3 Month	157	51.74	11.426	55.93	14.3	67.8	175	48.35	12.357	52.94	15.5	67.3	3.391	(0.812, 5.970)
6 Month	166	51.39	11.225	55.44	9.3	71.5	165	50.41	11.008	55.13	17.3	67.6	0.98	(-1.424, 3.384)
12 Month	167	51.72	11.103	55.09	6.4	68.8	160	49.98	10.97	53.4	18.5	66.9	1.747	(-0.655, 4.149)
24 Month	156	52.08	10.175	55.72	-0.3	64.9	150	49.8	11.108	54.24	16.3	63.9	2.288	(-0.107, 4.683)

* The confidence intervals were calculated without multiplicity adjustment. As such, these confidence intervals should not be used to draw any statistical conclusion.

Bazaz Dysphagia Score

Table 36 reports the results of the Bazaz Dysphagia Score for subjects in the ITT Analysis Set, except SSI. The Bazaz Dysphagia Score is graded as follows:

- **None** (Liquid - None, Solid - None)
- **Mild** (Liquid - None, Solid - Rare)
- **Moderate** (Liquid - None or Rare, Solid - Occasionally (only with specific solids))
- **Severe** (Liquid - None or Rare, Solid - Frequent (Majority of solids))

By Month 24, the majority of subjects (76.3% (135/177) – investigational; 60.4% (116/192) – Control) reported no dysphagia using the Bazaz Dysphagia Score.

Table 36: Bazaz Dysphagia Score Change Over Time (ITT Analysis Set, Excluding subjects with SSIs at Index Level)

	Screening				Week 6				Month 3			
	Synergy Disc		Control		Synergy Disc		Control		Synergy Disc		Control	
Description	n	%	n	%	N	%	n	%	n	%	N	%
None	137	77.4	152	79.2	99	55.9	84	43.8	129	72.9	121	63
Mild	22	12.4	23	12	43	24.3	44	22.9	17	9.6	39	20.3
Moderate	17	9.6	14	7.3	17	9.6	38	19.8	10	5.6	13	6.8
Severe	0	0	3	1.6	2	1.1	5	2.6	2	1.1	1	0.5
	Month 6				Month 12				Month 24			
	Synergy Disc		Control		Synergy Disc		Control		Synergy Disc		Control	
Description	n	%	n	%	N	%	n	%	n	%	n	%
None	144	81.4	126	65.6	144	81.4	121	63	135	76.3	116	60.4
Mild	15	8.5	18	9.4	14	7.9	23	12	14	7.9	18	9.4
Moderate	6	3.4	17	8.9	7	4	16	8.3	6	3.4	13	6.8
Severe	1	0.6	1	0.5	1	0.6	1	0.5	0	0	1	0.5

Odom's Criteria
Odom's criteria were assessed for each subject by the physician as described below:

- **Excellent:** No complaints referable to cervical disease and able to carry out daily activities without impairment.
- **Good:** Intermittent discomfort related to cervical disease but no significant interfering with daily activities.
- **Satisfactory:** Subjective improvement but physical activities significantly limited.
- **Poor:** No improvement or worse as compared with condition before operation.

At Month 24, 81.8% (135/165) were categorized as "Excellent" in the investigational group, compared to 54.6% (83/152) in the control group.

Treatment Satisfaction
A Treatment Satisfaction questionnaire was administered to all subjects, except SSI.

In response to the question, "How satisfied are you with your treatment?," 84.5% (131/155) in the investigational group responded "Very Satisfied," compared to 61.6% (93/151) in the control group, at Month 24.

In response to the question, "Would you recommend the same treatment to a friend with the same health problem?," 84.5% (131/155) responded "Definitely Yes" in the investigational group as compared to 67.5% (102/151) in the Control group, at Month 24.

In response to the question, "How effective is this treatment in eliminating your symptoms?" 64.5% (100/155) responded "Very effective, relieved all of my symptoms" in the investigational group as compared to 33.8% (51/151) in the control group, at Month 24.

Myelopathy – Nurick Scale

Myelopathy was evaluated in all subjects (except SSI) using the Nurick scale which is measured using the following criteria:

- **Grade 0**: Signs and symptoms of root involvement without spinal cord disease
- **Grade 1**: Signs of spinal cord disease without difficulty in walking
- **Grade 2**: Slight difficulty in walking that does not prevent full time employment
- **Grade 3**: Difficulty in walking that prevents full-time employment or daily tasks but does not require assistance with walking
- **Grade 4**: Able to walk only with someone else's help or with the aid of a frame
- **Grade 5**: Chair bound or bedridden

At Month 24, 98% (148/158) in the investigational group, and 94% (142/151) in the control group, were assessed as Grade 0.

Radiographic Assessments - Quantitative

Angular Motion

Angular motion (rotation) at the index level was assessed using the definition of the change in angle between the adjacent endplates of the motion segment in the sagittal plane from flexion to extension. **Table 37** presents the angular motion at the index level in the ITT Analysis Set, except SSI. In the investigational group, mean angular motion decreased from 8.22 degrees at screening to 6.47 degrees at Month 24. In the control group, mean angular motion decreased from 7.1 degrees at screening to 0.8 degrees at Month 24, which is to be expected for a fusion procedure.

Table 37: Angular Motion (Index Level) [degrees] (ITT Analysis Set, Excluding subjects with SSIs at Index Level)

	Synergy Disc (N=177)						Control (N=192)					
Visit	N	Mean	SD	Med	Min	Max	n	Mean	SD	Med	Min	Max
Screening (Baseline)	165	8.22	4.325	7.9	0.6	21	175	7.8	4.332	7.1	-0.5	19.6
3 Month	148	6.58	3.459	6	0.4	18.3	167	1.7	1.501	1.4	-0.3	9.1
6 Month	156	7.01	3.658	7.05	0.7	15.5	162	1.38	1.341	0.95	0	7.6
12 Month	160	6.47	3.896	6.1	0.1	20.1	154	1.04	1.064	0.8	-0.2	6.6
24 Month	150	6.47	3.949	6.3	0.2	19.5	150	0.8	0.834	0.6	-0.1	6.3

Translational Motion

Translational motion at the index level was assessed using the definition of displacement of the posterior-inferior corner of the superior vertebra in a direction defined parallel to the superior endplate of the inferior vertebra from flexion to extension.

Table 38 presents the amount of translational motion at the index level in the ITT Analysis Set, except SSI. In the investigational group, mean translational motion decreased from 0.91 mm at screening to 0.78 mm at Month 24. In the control group, mean translational motion decreased from 0.88 mm at screening to 0.09 mm at Month 24, which is to be expected for a fusion procedure.

Table 38: Translational Motion (Index Level) [mm] (ITT Analysis Set, Excluding subjects with SSIs at Index Level)

	Synergy Disc (N=177)						Control (N=192)					
Visit	N	Mean	SD	Med	Min	Max	n	Mean	SD	Med	Min	Max
Screening (Baseline)	162	0.91	0.622	0.8	0	3.1	167	0.88	0.661	0.7	-0.2	3
3 Month	145	0.84	0.574	0.7	0	3.2	161	0.18	0.227	0.1	-0.5	1.1
6 Month	153	0.88	0.575	0.7	0	2.8	156	0.13	0.163	0.1	-0.1	0.7
12 Month	158	0.78	0.563	0.65	0	3.2	148	0.11	0.132	0.1	-0.2	0.6
24 Month	147	0.78	0.592	0.7	0	3.3	144	0.09	0.114	0.1	-0.1	0.7

Average Disc Height

Average disc height is calculated as the simple mean of the anterior and posterior disc heights.

Table 39 describes the average disc height at the index level in the ITT Analysis Set, excluding SSI. In the investigational group, the mean average disc height increased from 3.27 mm at screening to 4.79 mm at Month 24. In the control group, the mean average disc height increased from 3.41 at screening to 4.70 mm at Month 24.

Table 39: Average Disc Height (Index Level) [mm] (ITT Analysis Set, Excluding subjects with SSIs at Index Level)

	Synergy Disc (N=177)						Control (N=192)					
Visit	N	Mean	SD	Med	Min	Max	n	Mean	SD	Med	Min	Max
Screening (Baseline)	171	3.27	0.729	3.2	1.4	5	168	3.41	0.858	3.4	1.1	5.7
Immediate post-operative	166	5.33	0.804	5.3	3	7.3	163	5.32	1.192	5.3	2.2	8.1
3 Month	154	5.11	0.797	5.1	2.9	6.9	165	4.88	1.292	4.9	1.6	7.9
6 Month	160	5.01	0.867	5	2.3	6.9	157	4.72	1.316	4.6	1.6	8
12 Month	161	4.92	0.986	5	0.3	6.8	151	4.73	1.351	4.7	1.7	8
24 Month	152	4.79	1.050	4.8	-0.1	6.8	142	4.70	1.290	4.6	1.6	7.9

Shell Angle

Shell angle is defined as the angle between the inferior surface of the superior device component (or "shell") and the superior surface of the inferior device component when the subject is in a neutral neck position. **Table 40** identifies the shell of investigational subjects in the ITT Analysis Set, excluding SSI. In investigational subjects, the mean shell angle increased from 3.82 degrees immediately post-operative to 4.49 degrees at Month 24.

Table 40: Shell Angle [degrees] Over Time, Synergy Disc (ITT Analysis Set, Excluding subjects with SSIs at Index Level)

	Synergy Disc (N=177)					
Visit	n	Mean	SD	Med	Min	Max
Immediate post-operative	172	3.82	2.889	4.0	-5.8	12.4
3 Month	161	4.40	2.914	4.3	-5.8	13.1
6 Month	164	4.40	3.070	4.3	-5.8	13.0
12 Month	167	4.52	3.189	4.2	-5.7	15.8
24 Month	156	4.49	3.195	4.4	-5.7	14.9

Disc Angle

Disc angle is defined as the angle formed between the endplates of adjacent vertebrae with the subject in a neutral neck position. A disc angle greater than 0 degrees corresponds to local lordosis and a disc angle less than 0 degrees corresponds to local kyphosis. **Table 41** presents the disc angle at the index level in the ITT Analysis Set, excluding SSI. In the investigational group, mean disc angle increased from 2.64 degrees at screening to 6.48 degrees at Month 24. In the control group, mean disc angle increased from 2.85 degrees at screening to 8.1 degrees at Month 24.

Table 41: Disc Angle (Index Level) [degrees] (ITT Analysis Set, Excluding subjects with SSIs at Index Level)

	Synergy Disc (N=177)						Control (N=192)					
Visit	n	Mean	SD	Med	Min	Max	n	Mean	SD	Med	Min	Max
Screening (Baseline)	174	2.64	4.792	2.2	-7.3	15.6	176	2.85	4.556	2.4	-9.0	20.1
Immediate post-operative	169	7.58	4.555	7.5	-4.0	19.3	171	9.20	4.617	9.3	-3.8	24.5
3 Month	157	7.26	4.763	7.2	-4.0	20.6	170	9.26	5.288	9.5	-4.9	24.6
6 Month	163	6.80	4.763	6.7	-5.6	21.9	162	8.88	5.353	9.2	-5.4	23.8
12 Month	164	6.69	4.877	6.7	-4.5	22.1	157	8.40	5.273	8.5	-5.4	24.0
24 Month	155	6.48	4.938	6.6	-3.7	22.8	148	8.14	5.264	8.1	-5.5	24.2

Segmental Lordosis

Segmental lordosis is defined as the angle formed between the endplates of adjacent vertebrae when the patient subject is in a neutral neck position. **Table 42** presents the segmental lordosis of

investigational subjects in the ITT Analysis Set, excluding SSI. In investigational subjects, the mean segmental lordosis decreased from 1.03 degrees at screening to 4.83 degrees at Month 24.

Table 42: Segmental Lordosis (Index Level) [degrees] (ITT Analysis Set, Excluding subjects with SSIs at Index Level)

	Synergy Disc (N=177)					
Visit	**n**	**Mean**	**SD**	**Med**	**Min**	**Max**
Screening (Baseline)	174	1.03	5.275	0.4	-9.0	17.6
Immediate post-operative	169	5.96	4.944	6.2	-10.2	22.2
3 Month	157	5.62	5.101	5.0	-8.3	23.5
6 Month	163	5.18	5.142	4.6	-7.7	24.8
12 Month	164	5.07	5.279	4.7	-9.5	24.9
24 Month	155	4.83	5.221	4.5	-7.8	25.7

Radiographic Assessments – Qualitative

Device Condition
Device Condition was assessed for both the investigational and control group in the ITT Analysis Set, excluding SSIs. At Month 24, 99.4% (156/157) of investigational devices were classified as intact (i.e., no evidence of device disassembly, fracture or loosening). In the control group, there 11 graft failures, and 3 screw failures, through Month 24. At Month 24, 98% (148/151) of control ACDF hardware was classified as intact (i.e., no failed graft, loose screws or fractured hardware).

Device Migration
There were no confirmed cases of device migration (i.e., evidence of anterior-posterior or lateral change in implant position greater than 3 mm) in the ITT Analysis Set, excluding SSIs, through Month 24.

Device Protrusion
At Month 24, 96.8% (152/157) of investigational devices were classified as having no confirmed evidence of protrusion.

Device Subsidence
Device subsidence (i.e., cranial or caudal subsidence of the implant greater than 3mm) was assessed in the ITT Analysis Set, excluding SSIs, through Month 24. At Month 24, 97.5% (153/157) of investigational devices and 100% (151/151) of ACDF control hardware did not have evidence of subsidence.

Heterotopic Ossification

Table 43 reports on evidence of HO in the investigational group of the ITT Analysis Set, excluding SSIs, through Month 24, using the following HO definitions:

- **None**: No evidence of osteophyte formation or heterotopic ossification.
- **Class I**: HO is present in islands of bone within soft tissue but is not influencing the range of motion of the vertebral motion segment. Bone is not between the planes formed by the two vertebral endplates.
- **Class II**: HO or post-operative osteophytes are present between the two planes formed by the vertebral endplates but are not significantly blocking or articulating between adjacent vertebral endplates or osteophytes.
- **Class III**: The range of motion of the vertebral endplates is blocked by the formation of HO and/or postoperative osteophytes on flexion-extension or lateral bending radiographs.
- **Class IV**: An apparent continuous connection of bone exists across the adjacent vertebral endplate caused by bridging osteophytes or heterotopic ossification.

There is increasing progression of HO over time, with Class II being the predominant type at later timepoints. At Month 24, 54.1% (85/157) of investigational subjects were assessed to have Class II HO.

Table 43: Heterotopic Ossification (Index Level) (ITT Analysis Set, Excluding subjects with SSIs at Index Level)

Synergy Disc (N = 177)										
	6 Week		3 Month		6 Month		12 Month		24 Month	
Description	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
None	0	0	107	66	80	48.5	35	20.8	11	7
Class I	0	0	45	27.8	48	29.1	55	32.7	40	25.5
Class II	0	0	7	4.3	33	20	68	40.5	85	54.1
Class III	0	0	2	1.2	2	1.2	6	3.6	15	9.6
Class IV	0	0	0	0	2	1.2	3	1.8	6	3.8
Indeterminate	0	0	0	0	0	0	1	0.6	0	0
Unable to Assess	0	0	1	0.6	0	0	0	0	0	0
Not Required	0	0	0	0	0	0	0	0	0	0

Adjacent Level Disc Disease (Kellgren-Lawrence)

Table 44 and

Table 45 identify evidence of Adjacent Level Disc Degeneration – Kellgren-Lawrence (ALDD) in the investigational group of the ITT Analysis Set, excluding SSIs, through Month 24, using the following definitions:

- **Grade 0:** No degenerative changes.
- **Grade 1:** Minimal osteophytosis only.
- **Grade 2:** Definite anterior osteophytosis with possible narrowing of disc space and some sclerosis of vertebral plates.
- **Grade 3:** Moderate narrowing of disc space with definite sclerosis of vertebral plates and osteophytosis.
- **Grade 4:** Severe narrowing of disk space with sclerosis of vertebral plates and multiple large osteophytes.
- **NA:** Pre-existing fusion or the subject was surgically fused at the adjacent level.

The assessment of adjacent level disc disease (Kellgren-Lawrence) is graded by the reviewers based on an assessment from x-rays of three component factors: disc space narrowing (assessed relative to a nearby normal disc), osteophyte formation and endplate sclerosis.

At the spinal level above the index procedure, there is increasing progression of ALDD over time, with Grade 0 or 1 being the predominant type at later timepoints. At Month 24, 38.2% (60/157) of investigational subjects were assessed to have Grade 0 ALDD, and 39.5% (62/157) of investigational subjects were assessed to have Grade 1 ALDD.

At the spinal level below the index procedure, there is also increasing progression of ALDD over time, with Grade 0 or 1 being the predominant type at later timepoints. At Month 24, 33.1% (52/157) of investigational subjects were assessed to have Grade 0 ALDD, and 36.9% (58/157) of investigational subjects were assessed to have Grade 1 ALDD.

Table 44: Kellgren-Lawrence Adjacent Level Disc Disease, Synergy Disc (Above Index Level) (ITT Analysis Set, Excluding subjects with SSIs at Index Level)

	Immediate Post Operative		6 Week		3 Month		6 Month		12 Month		24 Month	
Description	**N**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Grade 0	111	64.2	112	65.5	102	63	102	61.8	83	49.4	60	38.2
Grade 1	39	22.5	33	19.3	35	21.6	39	23.6	54	32.1	62	39.5
Grade 2	18	10.4	21	12.3	20	12.3	20	12.1	24	14.3	27	17.2
Grade 3	0	0	0	0	1	0.6	1	0.6	2	1.2	3	1.9
Grade 4	0	0	0	0	0	0	0	0	0	0	0	0
Indeterminate	0	0	0	0	0	0	0	0	0	0	0	0
Unable to Assess	0	0	0	0	1	0.6	0	0	0	0	0	0
Not Applicable	5	2.9	5	2.9	3	1.9	3	1.8	5	3	5	3.2

Table 45: Kellgren-Lawrence Adjacent Level Disc Disease, Synergy Disc (Below Index Level) (ITT Analysis Set, Excluding subjects with SSIs at Index Level)

	Immediate Post Operative		6 Week		3 Month		6 Month		12 Month		24 Month	
Description	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Grade 0	112	64.7	108	63.2	98	60.5	95	57.6	76	45.2	52	33.1
Grade 1	15	8.7	18	10.5	18	11.1	22	13.3	39	23.2	58	36.9
Grade 2	8	4.6	8	4.7	5	3.1	5	3	7	4.2	8	5.1
Grade 3	5	2.9	5	2.9	6	3.7	8	4.8	8	4.8	9	5.7
Grade 4	0	0	0	0	0	0	0	0	0	0	0	0
Indeterminate	22	12.7	21	12.3	23	14.2	24	14.5	28	16.7	20	12.7
Unable to Assess	0	0	0	0	1	0.6	0	0	0	0	0	0
Not Applicable	11	6.4	11	6.4	11	6.8	11	6.7	10	6	10	6.4

3. Exploratory Analysis

Prior Fusion

There was enrollment of subjects with prior cervical fusion under this IDE clinical trial. Although the sample size was limited (n=14), 85.7% (12/14) of these subjects demonstrated overall success at Month 24 as shown in **Table 46** below.

Table 46: Month 24 Overall Efficacy - Synergy Disc Group Stratified by Prior Fusion (PP Analysis Set)

Description	Prior Fusion			No Prior Fusion		
	(N=15)			(N=149)		
	N	N	%	N	n	%
Fusion occurred/Absence of radiographic failure	13	13	100.0%	142	142	100.0%
>= 15-point decrease in NDI calculated score	14	13	92.9%	141	129	91.5%
Maintenance or improvement in neurological status	14	13	92.9%	143	140	97.9%
No study failure due to secondary surgical interventions	15	14	93.3%	149	146	98.0%
Absence of device-related Serious Adverse Event	15	14	93.3%	149	145	97.3%
Composite Clinical Success	14	12	85.7%	141	123	87.2%

4. Subgroup Analyses

The study was not specifically powered for any subgroup analyses.

5. Pediatric Extrapolation

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

F. 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 22 principal investigators. None of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

XI. PANEL RECOMMENDATIONS

In accordance with the provisions of section 515(c)(2) of the Act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Orthopaedic and Rehabilitation Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XII. CONCLUSIONS DRAWN FROM THE PRECLINICAL AND CLINICAL STUDIES

The valid scientific evidence presented in the preceding sections provides reasonable assurance that the Synergy Disc is a safe and effective disc replacement in skeletally mature patients for reconstruction of the disc at one level from C3-C7 following single-level discectomy for intractable radiculopathy (arm pain and/or a neurological deficit) with or without neck pain, or myelopathy due to a single-level abnormality localized to the level of the disc space and at least one of the following conditions confirmed by radiographic imaging (CT, MRI, X-rays): herniated

nucleus pulposus, spondylosis (defined by the presence of osteophytes), and/or visible loss of disc height compared to adjacent levels.

A. Effectiveness Conclusions

A total of 177 subjects were enrolled under the Synergy Disc IDE study and were intended to be treated with the Synergy Disc. Two (2) subjects dropped out of the study prior to the procedure, and 175 subjects were treated with the investigational device. The historical ACDF control population included 192 subjects. The combined total of 369 available subjects (177 – investigational; 192 – control) were assessed via the PS sub-classification process. After applying an established heuristic for 3 iterations (6 models), a total of 177 investigational subjects and 192 control subjects were retained in the final PS-selected sample. The ITT Analysis Set was used to evaluate safety, while the PP Set was used to test the primary endpoint for non-inferiority and subsequent superiority.

Overall success was defined based on a primary composite endpoint which included the following components: greater than or equal to 15-point improvement in NDI Score (out of 100) in subjects at Month 24 compared to baseline; maintenance or improvement in neurological status (motor and sensory only) at Month 24 compared to baseline as adjudicated by the CEC; no study failure due to secondary surgical interventions (revision, removal, re-operation, supplemental fixation) at the index level; absence of radiographic failure, defined as any implant or component breakage or migration at the index level; and, absence of device-related Serious Adverse Event as adjudicated by the CEC.

The overall success rate for the investigational group based on Completers in the Primary Analysis Population was 87.1% (135/155) as compared to the success rate of 56.6% (77/136) for the control group. The study's pre-specified success criteria were met, and non-inferiority and superiority were demonstrated. Sensitivity analyses further demonstrated that non-inferiority and superiority were met in the ITT Analysis Set and Completers population.

In conclusion, the clinical data provided demonstrate that at Month 24, the Synergy Disc is superior to the ACDF control, for the patient population and indications studied in this investigation, in terms of overall success according to the primary composite endpoint, and provides a reasonable assurance of effectiveness.

B. Safety Conclusions

In the ITT Analysis Set, the investigational group reported a numerically greater rate of any AEs (79.7% - 141/177) as compared to the rate of any AEs recorded in the control subjects (71.4% - 137/192). However, the investigational group reported a numerically lower rate of SAEs (18.1% - 32/177) as compared to the rate of SAEs calculated for the control group (22.9% - 44/192). A total of 5 SSIs occurred in 4 investigational subjects as compared to 8 SSIs which were reported for the control subjects.

In conclusion, the clinical data provided demonstrate that the Synergy Disc is at least as safe as the ACDF Control for the patient population and indications studied and provides a reasonable assurance of safety.

C. Benefit-Risk Determination

The probable benefits of the Synergy Disc are based on data collected in the clinical study conducted to support PMA approval. The clinical study demonstrated several benefits of the Synergy Disc through Month 24.

- The overall success rate for the investigational group based on Completers in the Primary Analysis Population was 87.1% (135/155) as compared to the success rate of 56.6% (77/136) for the control group.

- The benefit of the investigational device was evaluated in terms of clinically meaningful improvement in function (as measured by an improvement in NDI of at least 15 points) at Month 24. At Month 24, 91.67% (143/156) of the investigational device subjects experienced a clinically meaningful level of improvement as compared to 75.17% (112/149) of the control subjects.

- In terms of improvement in neck pain (as measured by a 20mm improvement in pain on a 100mm VAS as compared to baseline) at Month 24, 83.87% (130/155) of investigational subjects achieved a greater than 20mm improvement in VAS-Neck Pain, compared to 75.33% (113/150) in the control group.

- In terms of improvement in left arm pain (as measured by a 20mm improvement in pain on a 100mm VAS as compared to baseline) at Month 24, investigational subjects demonstrated a comparable level of change (55.48%, 86/155) as compared to control subjects (52.67%, 79/150).

- In terms of improvement in right arm pain (as measured by a 20mm improvement in pain on a 100mm VAS as compared to baseline) at Month 24, 59.35% (92/155) of investigational subjects achieved a 20mm improvement, compared to 52.00% (78/150) in the control group.

- The subject's perception of their benefit and risk was indirectly measured by administering the question, "How satisfied are you with your treatment?" At Month 24, 84.5% (131/155) of investigational subjects and 61.6% (93/151) of control subjects responded that they were "very satisfied", indicating a positive response from the patient perspective regarding the operative procedure.

- The investigational group had a lower percentage of device-related adverse events than the control group (18.1% (32/177) investigational, 34.4% (66/192) control) and a lower percentage of device-related SAEs (2.8% (5/177) investigational, 10.9% (21/192) control).

The probable risks of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. At the Month 24 time-point, similar rates of any AE, any SAE, and any definitely device-related AE occurred in the two groups. The Synergy Disc group experienced a higher AE rate than the ACDF Control (79.7% versus 71.4%), though this difference was not significant. The ACDF Control group experienced a higher rate of SAEs (18.1%

versus 22.9%). In terms of SSI, the ACDF Control had a greater number of SSI than the Synergy Disc group through Day 790 (8 events versus 5 events through day 790).

Additional factors that were considered in determining the probable benefits and risks for the Synergy Disc included limitations of the clinical study designs, including the inability to mask subjects to their treatment assignment, reliance on subjective endpoints, and subjectivity in AE classification. Prospective Synergy Disc and historical ACDF studies were harmonized using subject level data for the historical control and adjudication by the CEC.

Patient perspectives considered during this review include: NDI, VAS – Neck Pain; VAS – Left Shoulder/Arm Pain; VAS – Right Shoulder/Arm Pain; VAS – Worst Shoulder/Arm Pain; VAS – Hoarseness; VAS – Dysphagia; PCS; MCS; and Bazaz Dysphagia Score.

In conclusion, given the available information above, the data support that, for reconstruction of the disc at one level from C3-C7 following single-level discectomy for intractable radiculopathy (arm pain and/or a neurological deficit) with or without neck pain, or myelopathy due to a single-level abnormality localized to the level of the disc space and at least one of the following conditions confirmed by radiographic imaging (CT, MRI, X-rays): herniated nucleus pulposus, spondylosis (defined by the presence of osteophytes), and/or visible loss of disc height compared to adjacent levels as outlined above in the Indications for Use, the probable benefits of the Synergy Disc outweigh the probable risks through Month 24.

D. Overall Conclusions

The non-clinical and clinical data in this application support the reasonable assurance of safety and effectiveness of the Synergy Disc when used in accordance with the indications for use. Based on the clinical study results, it is reasonable to conclude that the clinical benefits associated with the use of the Synergy Disc in terms of improvement in pain and disability, outweigh the risks, both in terms of the risks associated with the Synergy Disc and surgical procedure when used in the indicated population in accordance with the instructions for use, and as compared to the ACDF control treatment in the same indicated population.

XIII. CDRH DECISION

CDRH issued an approval order on February 26, 2026. The final clinical conditions of approval are described below.

> *Synergy Disc Continued Follow-Up Study*:
> Based on the protocol outline received on February 17, 2026, this PAS is intended to evaluate the longer-term safety and effectiveness of the Synergy Disc in n=160 Synergy Disc subjects available from the As Treated Analysis Set who were enrolled in the pivotal study. Subjects will be followed 60 months from the time of each subject's index surgery (Month 60).
>
> The primary safety endpoints are serious adverse events (SAEs), and device- or procedure-related adverse events (AEs). Additional safety analyses will include the rate of AEs, including by relatedness to device or procedure and severity (mild,

moderate, or severe), time-to-event, including mean and ranges if applicable, and Subsequent Surgical Intervention (SSI) by rate and type.

The primary effectiveness endpoint is a composite clinical success (CCS) responder endpoint based on clinical status at Month 60. An individual subject will be regarded as achieving Month 60 CCS only if they meet all of the following criteria at Month 60 compared to baseline:

1. At least a 15-point improvement in NDI Score (out of 100) at Month 60 compared to baseline;

2. Maintenance or improvement in neurologic status (motor and sensory only) at Month 60 compared to baseline;

3. No study failures due to secondary surgical interventions (revision, removal, reoperation, and/or supplemental fixation) at the index level;

4. Absence of radiographic failure, defined as any implant or component breakage or migration at the index level; and,

5. Absence of device-related SAEs as adjudicated by the CEC.

The data presentation and statistical analyses will be conducted using observed data on a minimum of 85% follow-up of the pivotal study cohort at 36-months, 48-months, and 60-months post-implantation. Explant analysis will be conducted per the outline agreed to on February 25, 2026.

The applicant's manufacturing facility was inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820), which was in effect at the time of the inspection. As of February 2, 2026, the revised part 820, referred to as the Quality Management System Regulation (QMSR), is effective.

XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

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

Post-approval Requirements and Restrictions: See approval order.