

II. Executive Summary: Relevant Summary of Safety and Effectiveness Sections

The following is information relevant to this module and is presented as the Summary of Safety and Effectiveness for the clinical studies and the PMA in general.



SUMMARY OF SAFETY AND EFFECTIVENESS

A. General Information

DEVICE GENERIC NAME:	Artificial Cervical Disc
DEVICE TRADE NAME:	PRESTIGE® Cervical Disc
APPLICANT'S NAME:	Medtronic Sofamor Danek 1800 Pyramid Place Memphis, TN 38132
PREMARKET APPROVAL (PMA) APPLICATION NUMBER:	P060018
DATE OF PANEL RECOMMENDATION:	Pending
DATE OF NOTICE OF APPROVAL TO THE APPLICANT:	Pending

B. Indications for Use

The PRESTIGE® Cervical Disc is indicated in skeletally mature patients with cervical degenerative disc disease (DDD) at one level from C3-C7. DDD is defined as intractable radiculopathy and/or myelopathy with at least one of the following items producing symptomatic nerve root and/or spinal cord compression which is documented by patient history (e.g., pain [neck and/or arm pain], functional deficit, and/or neurological deficit), and radiographic studies (e.g., CT, MRI, x-rays, etc.): 1) herniated disc, and/or 2)

osteophyte formation. The PRESTIGE® device is to be implanted via an open anterior approach.

C. Contraindications

The PRESTIGE® Cervical Disc should not be implanted in patients with an active infection or with an allergy to stainless steel.

D. Warnings and Precautions

The PRESTIGE® Cervical Disc should only be used by surgeons who are experienced in the surgical procedure and have undergone adequate training with this device. A lack of adequate experience and/or training may lead to a higher incidence of adverse events, such as neurological complications.

E. Device Description

The PRESTIGE® Cervical Disc system is a two-piece articulating metal device that is inserted into the intervertebral disc space at a single cervical level using an anterior approach. The device is crafted of type 316 stainless steel (ASTM F-138) and consists of two metal plates which interact via a ball and trough mechanism. The superior component of the implant contains the ball portion of the mechanism, and the inferior component incorporates the trough portion. The flat portion of each component, which contacts the vertebral endplate, is aluminum oxide grit blasted for bone ongrowth.

Each component is affixed to the vertebral body by two bone screws through an anterior flange. The bone screws are held in place by a lock screw mechanism. In the implanted disc, the bone screws are divergent in the cephalic/caudal direction and convergent in the medial/lateral direction.

The device assembly design allows for a minimum of 10° motion off the neutral position in flexion/extension and lateral bending. The design also permits unconstrained axial rotation and 2 mm of anterior/posterior translation.

The available components are shown in the table below.

Table 1. PRESTIGE® Cervical Disc Device Configurations.

Catalog Number	Component Description
6961260	6 mm x 12 mm Disc Assembly
6961460	6 mm x 14 mm Disc Assembly
6961660	6 mm x 16 mm Disc Assembly
6961270	7 mm x 12 mm Disc Assembly
6961470	7 mm x 14 mm Disc Assembly
6961670	7 mm x 16 mm Disc Assembly
6961870	7 mm x 18 mm Disc Assembly
6961480	8 mm x 14 mm Disc Assembly
6961680	8 mm x 16 mm Disc Assembly
6961880	8 mm x 18 mm Disc Assembly
6961340	Self-Tap Bone Screw 4.0 mm x 13 mm
6961540	Self-Tap Bone Screw 4.0 mm x 15 mm
6961345	Self-Tap Bone Screw 4.5 mm x 13 mm
6961545	Self-Tap Bone Screw 4.5 mm x 15 mm
6961120	Lock Screw

No other warranties, express or implied, are made. Implied warranties of merchantability and fitness for a particular purpose or use are specifically excluded.

F. Alternate Practices and Procedures

Nonoperative alternative treatments include, but are not limited to, physical therapy, medications, braces, chiropractic care, bed rest, spinal injections, or exercise programs. In addition, there are alternative surgical techniques which include, but are not limited to, surgical decompression, or fusion using various bone grafting techniques (e.g., Cloward bone dowels, Smith Robinson tri-cortical wedges, and Keystone grafts) sometimes used in conjunction with

anterior/anterolateral spinal systems (e.g., plate and screw systems), posterior spinal systems (e.g., screw/rod, plate systems, posterior wiring systems), or cage devices.

G. Marketing History

In the United States, the PRESTIGE® Cervical Disc device has only been used under an IDE. Worldwide, most use of the PRESTIGE® device has also been confined to investigational use. However, since 2003, a limited number of devices have been sold in Australia, France, and Switzerland. The company has not received any complaints regarding the marketed product, and the device has not been withdrawn from marketing for any reason.

H. Potential Adverse Effects of the Device on Health

The adverse effects, as shown in the table below, were reported from the 276 PRESTIGE® device patients and 265 control patients enrolled in the multi-center clinical study of the PRESTIGE® Cervical Disc. The control treatment was a single level anterior interbody fusion procedure with allograft and plate stabilization. Adverse event rates presented are based on the number of patients having at least one occurrence for a particular adverse event divided by the total number of patients in that treatment group.

Table 2. Adverse Events in Pivotal Study.

ADVERSE EVENTS*																
Complication	Surgery		Postoperative 1 day - <4 Weeks		6 Weeks ≥4 Wks - <9 Weeks		3 Months (≥9 Wks - <5 Months)		6 Months (≥5 Mos- <9 Months)		12 Months (≥9 Mos- <19 Months)		24 Months (≥19 Mos- <30 Months)		# of Patients Reporting & Total adverse events	
	Inves.	Control	Inves.	Control	Inves.	Control	Inves.	Control	Inves.	Control	Inves.	Control	Inves.	Control	Investig. # Patients (% of 276) Total # Events	Control # Patients (% of 265) Total # Events
Anatomical/Technical Difficulty	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1 (0.4) 1	0 (0.0) 0
Cancer	0	0	0	1	0	0	0	0	0	0	2	0	3	1	5 (1.8) 5	2 (0.8) 2
Cardiovascular	0	0	2	1	0	1	2	2	1	0	7	2	3	3	14 (5.1) 15	8 (3.0) 9
Carpal Tunnel Syndrome	0	0	1	1	1	1	3	1	0	0	8	2	1	2	12 (4.3) 14	7 (2.6) 7
Death	0	0	0	0	0	0	0	1	0	0	0	1	0	1	0 (0.0) 0	3 (1.1) 3
Dysphagia/Dysphonia	2	3	16	12	3	3	0	3	1	0	1	1	0	0	23 (8.3) 23	22 (8.3) 22
Gastrointestinal	0	2	4	3	1	1	3	2	4	2	11	11	3	5	25 (9.1) 26	24 (9.1) 26
Implant Displacement/ Loosening	0	0	0	0	0	2	1	0	0	0	0	1	1	1	2 (0.7) 2	4 (1.5) 4
Infection	2	0	6	3	2	4	6	2	3	2	8	4	3	7	27 (9.8) 30	20 (7.5) 22
Neck and/or Arm Pain	1	0	25	17	32	17	27	34	48	38	34	42	23	25	138 (50.0) 190	127 (47.9) 173
Neurological	4	1	8	9	12	5	14	10	14	8	19	18	7	14	66 (23.9) 78	55 (20.8) 65
Non-Union	0	0	0	0	0	1	0	2	0	2	0	1	0	0	0 (0.0) 0	6 (2.3) 6
Other	2	2	18	18	14	12	9	9	19	6	32	18	15	17	70 (25.4) 109	66 (24.9) 82
Other Pain	2	2	4	4	10	5	13	13	14	15	28	18	17	11	69 (25.0) 88	56 (21.1) 68
Pending Non-Union	0	0	0	0	0	0	0	1	0	5	0	7	0	3	0 (0.0) 0	16 (6.0) 16
Respiratory	1	0	1	2	0	1	1	0	1	1	2	3	2	2	8 (2.9) 8	8 (3.0) 9
Spinal Event	0	0	2	2	1	3	6	9	3	9	6	5	0	4	17 (6.2) 18	30 (11.3) 32
Subsidence	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1 (0.4) 1	0 (0.0) 0
Trauma	0	0	4	2	7	8	13	11	17	10	20	6	8	10	59 (21.4) 69	40 (15.1) 47
Urogenital	0	0	0	0	0	0	3	4	2	1	8	1	3	0	15 (5.4) 16	5 (1.9) 6
Vascular Intra-Op	2	1	2	1	1	0	0	0	0	0	0	0	0	0	5 (1.8) 5	2 (0.8) 2
Any Adverse Event															226 (81.9)	212 (80.0)

* Based on 24-month cohort.

The reported rates of several adverse events were greater than 10% in both the investigational and control groups. These events included neck and/or arm pain, neurological, other, other pain, and trauma. Spinal events occurred in 11.3% of the control patients but 6.2% of the investigational patients.

Some of the reported adverse events required surgical interventions subsequent to the initial surgery. The number of subjects requiring a second surgical intervention classified as a revision, removal, reoperation, or supplemental fixation was 3.3% (9/276) in the investigational group and 9.1% (24/265) in the control group. The investigational group had a statistically lower rate of revisions and supplemental fixations than the control group.

The incidence of most adverse events that were considered to be implant- or implant/surgical procedure-associated, including implant displacement/loosening and neck and/or arm pain, were greater in the control group compared to the investigational group. However, the rates of all these events were low in both groups. Six serious (WHO Grade 3 or 4), implant- or implant/surgical procedure-associated adverse events were reported; all of these occurred in control patients. No deaths were reported among investigational patients. Three control group deaths were reported, all of which were due to myocardial infarction or cardiac arrest.

The investigational group had a statistically lower rate of secondary surgical procedures related to implant revisions and supplemental fixations. Investigational patients also experienced a lower rate of implant removals, but it was not statistically different. These findings resulted in a lower second surgery failure rate for investigational patients.

Potential Adverse Events:

Risks associated with the use of the PRESTIGE® Cervical Disc include: 1) those commonly associated with any surgery; 2) those specifically associated with cervical spinal surgery using an anterior approach; and 3) those associated with a spinal implant, as well as those pertaining to the PRESTIGE® Cervical Disc. There is also the risk that this surgical procedure will not be effective, and may not relieve or may cause worsening of preoperative symptoms. Some of these effects may have been previously reported in the adverse events table.

1. Risks associated with any surgical procedure are those such as adverse reactions to anesthesia; pulmonary complications such as pneumonia or atelectasis; infection of the wound; systemic infection; abscess; cellulitis; wound dehiscence; swelling; wound hematoma; thrombosis; ischemia pulmonary embolism; thromboembolism; hemorrhage; thrombophlebitis; organ, nerve or muscular damage and death.
2. Risks associated with anterior interbody replacements of the cervical spine include dysphagia; dysphasia; dysphonia; otitis media; recurring aspirations; fistula; nerve deficits or damage; malunion of the mandible; tracheal, esophageal, and pharyngeal perforation; airway obstruction; external chylorrhea; hoarseness; vocal cord paralysis; warmth or tingling in the extremities; neural damage; damage to the spinal cord or nerve root; or graft in the neural canal; dural tears or leaking; loss of disc height; loss of proper curvature, correction, height or reduction of the spine; vertebral slipping; nerve root trauma; scarring, herniation or degeneration of adjacent discs; nerve damage possibly resulting in paralysis or pain, and surrounding soft tissue damage, vascular damage; spinal stenosis; and spondylolysis.
3. Risks associated with any implants in the spine are early or late loosening of the components; disassembly; bending or breakage of any or all of the components; implant migration; loss of purchase; implant fracture; bone fracture; foreign body reactions to the implant including allergic reaction; infection; possible tissue reaction; bone absorption; tumor formation or graft rejection; bone resorption; development of new radiculopathy; myelopathy or pain; cessation of bone growth of the operated portion of the spine; decreased strength of extremities; decreased reflexes; appearance of cord or nerve

root injury; pseudoarthrosis; fracture of the vertebral body. Additionally, there is the possibility of misdiagnosis or missed diagnosis with radiographic imaging of the spine when implants are present.

4. Early or late loosening or movement of the device.
5. Implant migration.
6. Breakage of any or all of the components or instruments.
7. Foreign body reaction to the implants including possible tumor formation, auto immune disease, metallosis, and/or scarring.
8. Pressure on the surrounding tissues or organs, possibly resulting in oesophagas or trachea breakdown from component parts where there is inadequate tissue coverage over the implant. Implant or graft extrusion can lead to fistular complications.
9. Loss of proper spinal curvature, correction, height, and/or reduction.
10. Infection.
11. Bone fracture or stress shielding at, above, or below the level of surgery.
12. Loss of neurological function, appearance of radiculopathy, dural tears, and/or development of pain. Neurovascular compromise including paralysis or other types of serious injury. Cerebral spinal fluid leakage.
13. Hemorrhage and/or hematomas.
14. Discitis, arachnoiditis, and/or other types of inflammation.
15. Deep venous thrombosis, thrombophlebitis, and/or pulmonary embolus.
16. Inability to resume activities of normal daily living.
17. Death.

NOTE: Additional surgery may be necessary to correct some of the adverse effects.

I. Summary of Nonclinical Laboratory Studies

1. Mechanical Studies

Biomechanical tests were conducted to characterize the mechanical performance of the PRESTIGE® Cervical Disc prosthesis under static and dynamic loads.

The biomechanical properties of the PRESTIGE® Cervical Disc prosthesis were assessed in a series of preclinical

experiments. When applicable, all tests were performed on the worst-case size device. The testing information and results are presented in the following table. The tests in this table represent those applicable to the current product line.

Table 3. Mechanical Testing.

Description	# of Samples	Methods	Results
Subluxation	5 repetitions with 1 sample	Implants were held in 10° of flexion and extension, 10° up and down medial/lateral, and in neutral position. The inferior component was translated until the implant was completely dislocated. Maximum subluxation force and force-displacement graphs were recorded for five repetitions of each test.	Results exceeded clinically acceptable values
Wear testing LB/AR followed by FE	3	F/E: 10 million cycles with 148 N axial load and 19.4° of motion. LB-AR: 5 million cycles of coupled motion. 10.4° lateral bend and 7.6° of axial rotation under a 49 N load.	Characterization test only.
Wear testing FE followed by LB/AR	3	F/E: 10 million cycles with 148 N axial load and 19.4° of motion. LB-AR: 5 million cycles of coupled motion. 10.4° lateral bend and 7.6° of axial rotation under a 49 N load.	Characterization test only.
Pushout	5	100 N preload is applied to assembly while an axial force is applied at 25 mm/min until 10 mm is reached. Load and displacement were recorded.	Results exceeded clinically acceptable values
Pullout	5 repetitions with 1 sample	Male and female components were screwed to foam blocks and a static axial load applied. Load was applied at 25 mm/min, and load/displacements were recorded for 5 repetitions of the test.	Results exceeded clinically acceptable values
Pullout	5	Male and female components from fatigue testing (TS00-059) were screwed to foam blocks and a static axial load applied. Load was applied at 25 mm/min and load/displacements were recorded.	Results exceeded clinically acceptable values

Description	# of Samples	Methods	Results
Subsidence	5 repetitions with 1 sample	Implants were assembled to mating foam blocks and axial load was applied at 0.1 mm/sec until the blocks contacted. Load/displacements were recorded for 5 repetitions of the test.	Results exceeded clinically acceptable values
Compressive Fatigue	7	Load was applied at 10 Hz until failure or until 10 million cycles.	Runout
Compressive Fatigue	2	Implants were loaded with 225 N at 10 Hz for 10 million cycles or until failure.	Runout
Cadaver Biomechanics	6	Cadaveric spines were tested in four motions (flexion, extension, left lateral bend and right lateral bend) with and without the artificial disc.	No significant differences between motion and rotational stiffness values at the superior, target, or inferior motion segment units for implanted vs. unimplanted spines

2. Animal Testing

An animal test was conducted to characterize the reaction to wear debris particles generated from the PRESTIGE® Cervical Disc. In addition, characterization tests were performed on both the *in vitro* wear particles and the injected particles.

Summary data for the most relevant tests are provided in the following table.

Table 4. Animal Testing.

Test Description	Tested Component	Sample size	Methods	Results
Animal injection study	ASTM F-138 stainless steel particulate	20 animals total, 2 investigational dose levels + control	Rabbit model tested up to 24 wks. Pathology of spinal and various tissues.	Stainless steel particles tolerated at both low and high doses.
Particle analysis	Serum from <i>in vitro</i> simulator wear tests	5 stainless steel samples obtained at various cycle counts and 1 control sample	Centrifuging and ashing followed by SEM and EDS.	Classification of particles.
Particle analysis	ASTM F-138 stainless steel particulate (purchased for injection study)	2 lots of material (same lots as injected)	Scanning electron microscopy.	Classification of particles.

Further support for the use of this material is found in a published study by Cunningham in which a 4 mg bolus of 316 LVM stainless steel particles was directly applied to the epidural space in an open procedure.[†]

J. Summary of Clinical Study

1. Study Background

The goals of the IDE clinical study of the PRESTIGE® Cervical Disc System were to evaluate the safety and effectiveness of the anterior cervical spinal use of the device in the treatment of patients with symptomatic cervical disc disease. The assessments of safety and effectiveness of the PRESTIGE® Cervical Disc were through direct clinical data comparisons between data collected from patients

[†] Cunningham B.W. Basic scientific considerations in total disc arthroplasty. *The Spine Journal*, 4, 219S-230S, 2004.

implanted with the PRESTIGE® device to an equivalent group of patients who received a surgical fusion utilizing bone graft and plate stabilization. The investigational and control treatments were randomized in a 1:1 manner.

The effectiveness of the PRESTIGE® device was based primarily on a patient having Neck Disability Index (NDI) pain/disability improvement. In addition, neck pain, arm pain, patient gait, general health status, patient satisfaction, and radiographic parameters were evaluated. Safety was based primarily on the nature and frequency of adverse events and second surgeries. The maintenance or improvement in neurological status following surgery was also a safety measurement.

The primary endpoint for the clinical investigation was a composite variable termed “overall success.” Overall success was comprised of NDI and neurological results. Success for these factors as well as the patient not having a serious adverse event classified as implant- or implant/surgical procedure-associated or having a second surgery classified as a “failure” determined whether the patient was an overall success. An alternate overall success assessment was made using functional spinal unit (FSU) height maintenance or improvement along with the aforementioned criteria. Investigational treatment success was based on the 24-month overall success rate being statistically non-inferior to the control group rate.

2. Inclusion Criteria

The indication studied was degenerative disc disease (DDD) accompanied by neck pain of discogenic origin at a single

level between C3 and C7 confirmed by history and radiographic studies. DDD was determined to be present if a herniated disc and/or osteophyte formation were noted.

The following additional inclusion criteria had to be present:

- At least 6 weeks unsuccessful conservative treatment or signs of progression or spinal cord/nerve root compression with continued non-operative care;
- No previous surgical intervention at involved level or planned procedures at involved or adjacent levels;
- ≥ 18 years of age;
- Preoperative Neck Disability Index score of ≥ 30 ;
- Preoperative neck pain score of ≥ 20 on Neck and Arm Pain Questionnaire;
- Not pregnant;
- Willing to sign informed consent and comply with protocol.

3. Exclusion Criteria

Subjects were excluded if they had any of the following:

- Cervical spinal condition other than symptomatic cervical disc disease requiring surgical treatment at the involved level;
- Documented or diagnosed cervical instability defined by dynamic (flexion/extension) radiographs showing sagittal plane translation > 3.5 mm or sagittal plane angulation $> 20^\circ$;
- More than one cervical level requiring surgical treatment;
- Fused level adjacent to the level to be treated;
- Severe pathology of the facet joints of the involved vertebral bodies;

- Previous surgical intervention at the involved level;
- Previous diagnosis of osteopenia or osteomalacia;
- Has any of the following that may be associated with a diagnosis of osteoporosis (if Yes to any of the below risk factors, a DEXA Scan will be required to determine eligibility):
 - Postmenopausal Non-Black female over 60 years of age and weighs less than 140 pounds.
 - Postmenopausal female that has sustained a non-traumatic hip, spine, or wrist fracture.
 - Male over the age of 70.
 - Male over the age of 60 that has sustained a non-traumatic hip or spine fracture.

If the level of BMD is a T score of -3.5 or a T score of -2.5 with vertebral crush fracture, then the patient is excluded from the study.

- Spinal metastases;
- Overt or active bacterial infection, either local or systemic;
- Severe insulin dependent diabetes;
- Chronic or acute renal failure or prior history of renal disease;
- Fever (temperature > 101°F oral) at the time of surgery;
- Documented allergy or intolerance to stainless steel, titanium, or a titanium alloy;
- Mental incompetence;
- Prisoner;
- Pregnant;
- Alcohol and/or drug abuser currently undergoing treatment;

- Received drugs which may interfere with bone metabolism within two weeks prior to the planned date of spinal surgery;
- History of an endocrine or metabolic disorder known to affect osteogenesis;
- Condition that requires postoperative medications that interfere with the stability of the implant;
- Treatment with an investigational therapy within 28 days prior to implantation surgery or such treatment is planned during the 16 weeks following implantation with the PRESTIGE® device.

4. Post-Operative Care

The recommended post-operative care included avoidance of heavy lifting, repetitive bending, and high-impact exercise or athletic activity for 60 days postoperatively. Avoidance of prolonged NSAID use (beyond 2 weeks postop) was also specified in the postoperative regimen. The use of electrical bone growth stimulators was prohibited during the 24-month follow-up period. Patients who smoked were also encouraged to discontinue smoking.

5. Clinical and Radiographic Effectiveness Parameters

Patients were evaluated preoperatively (within 6 months of surgery), intraoperatively, and postoperatively at 6 weeks, 3, 6, 12, and 24 months, and annually thereafter until the last subject enrolled in the study had been seen for their 24 month evaluation. Complications and adverse events were evaluated over the course of the clinical trial. At each evaluation timepoint, the primary and secondary clinical and radiographic outcome parameters were evaluated. Success was determined from data collected during the initial 24 months of follow-up.

Clinical and radiographic outcome parameters were evaluated for treated subjects at the follow-up evaluation timepoints identified above. Clinical parameters assessed were of pain/disability, neck and arm pain, general health, patient global perceived effect, doctor's perception of results, gait, and foraminal compression test. The radiographic outcome parameters consisted of functional spinal unit height as well as evaluations of motion and fusion at the treated level for the investigational and control group, respectively. Adjacent level motion was also evaluated.

Pain/disability status was measured using the Neck Disability Index Questionnaire. Success was defined as a 15-point improvement in the NDI score from the pre-op baseline score.

Neurological status is based on motor function, sensory function, and reflexes. Neurological status success was defined as maintenance or improvement of the pre-op baseline score for each parameter. Overall neurological status success required that each individual parameter be a success for that subject to be counted as a success.

Functional spinal unit height measurements were based on the radiographs. This parameter was considered to be a success if either the anterior or posterior postoperative height was no more than 2 mm less than the 6-week postoperative height.

6. Patient Demographics and Accountability

The study was limited to 36 investigational sites with 550 total subjects. A total of 276 investigational and 265 control patients were enrolled in the study. For the majority of the

demographic parameters, there were no differences in pre-op demographics between the two populations.

Table 5. Study Patient Demographics.

	Investigational	Control
n	276	265
men/women	128/148	122/143
mean age (range)	43.3 (25.0-72.0)	43.9 (22.0 – 73.0)
mean weight (lbs) (range)	181.7 (103-328)	184.7 (98-328)
worker's comp (%)	32 (11.6)	35 (13.2)
tobacco user (%)	95 (34.4)	92 (34.7)

For some subjects, complete 24 month data for all effectiveness variables were not available, however. In order to “complete” the 24 month dataset for the subjects with missing data, 24 month values were predicted from the existing 12 month data using Bayesian statistical methods.

An analysis was performed to assess the ability to pool data across sites and to compare data across the study arms. These analyses evaluated the primary clinical outcome variables as well as overall success and found no differences that would prevent pooling of the data across the sites within a given group of subjects.

7. Surgical Results and Hospitalization

The mean operative times and mean hospitalization times were statistically different for the investigational and control groups. However, these slight differences are considered to have no clinical significance and were likely due to the large sample sizes.

Table 6. Surgical Results.

	Investigational	Control
mean operative time (hrs)	1.6	1.4
mean EBL (ml)	60.1	57.5
hospitalization (days)	1.1	1.0
spinal level treated		
C ₃₄ (%)	7 (2.5)	10 (3.8)
C ₄₅ (%)	14 (5.1)	15 (5.7)
C ₅₆ (%)	143 (51.8)	149 (56.2)
C ₆₇ (%)	112 (40.6)	91 (34.3)

8. Clinical and Radiographic Effectiveness Evaluation

Individual subject success (i.e. overall success) was defined in the study protocol as success in certain clinical outcome parameters. Success for these parameters included:

1. An improvement of at least 15 points from the baseline Neck Disability Index score;
2. Maintenance or improvement in neurological status;
3. No serious adverse event classified as implant-associated or implant/surgical procedure-associated; and
4. No additional surgical procedure classified as "Failure."

In addition, an alternate overall success determination was made based on the above criteria with the addition of functional spinal unit (FSU) height maintenance. FSU height was considered maintained if it did not decrease more than 2 mm after 6 weeks following surgery.

Study success was expressed as the number of individual subjects categorized as a success divided by the total number of subjects evaluated. The table below describes

the success rates for individual outcome parameters and overall success. All success rates were based on the data from the 24-month follow-up evaluation and posterior probabilities of success were calculated using Bayesian statistical methods. The conclusions were based on an interim analysis which was pre-defined in the protocol.

Table 7. Posterior Probabilities of Success at 24 Months.

Primary Outcome Variable	Investigational	Control
	Posterior Mean (95% HPD Credible Interval)	Posterior Mean (95% HPD Credible Interval)
NDI	80.8% (74.7%, 87.0%)	80.8% (74.1%, 86.7%)
Neurological	92.1% (87.6%, 96.2%)	84.7% (78.6%, 90.5%)
FSU Height	95.4% (91.5%, 98.7%)	93.7% (89.2%, 97.8%)
Overall Success (without FSU)	78.8% (72.1%, 85.0%)	70.0% (62.7%, 77.4%)
Overall Success (with FSU)	80.1% (73.1%, 87.4%)	64.0% (55.3%, 72.8%)

Bayesian statistical analyses yielded a posterior probability of non-inferiority at 24 months of approximately 100%. The posterior probability of superiority was found to be 95.9%.

With FSU height included in the overall success criteria, the probability (also called the posterior probability) that the 24-month overall success rate for the investigational group was equivalent to the 24-month success rate for the control group was 100%. The posterior probability of superiority was 99.7%.

When a patient receives the PRESTIGE® Cervical Disc, the chance (predictive probability) of overall success[‡] at 24 months is 78.8%. Given the results of the trial, there is a 95% probability that the chance of success ranges from 72.1% to 85.0%. When a patient receives the control

[‡] Without FSU height.

treatment, the chance of overall success at 24 months is 70.0%. Given the results of the trial, there is a 95% probability that the chance of success ranges from 62.7% to 77.4%.

K. Conclusion

The scientific evidence that has been presented here supports the safety and effectiveness of the PRESTIGE® Cervical Disc in the treatment of cervical degenerative disc disease from C3 to C7. The study demonstrated that the treatment of DDD with the PRESTIGE® Cervical Disc was as effective as the control treatment (fusion with bone graft and plate stabilization). The results for the primary effectiveness outcome parameters for the investigational group were equivalent to the control group. The PRESTIGE® Cervical Disc was able to achieve comparable clinical performance while maintaining motion at the involved cervical level.

L. Panel Recommendation

To be determined.

M. CDRH Decision

To be determined.

N. Approval Specifications

To be determined.