IMPORTANT INFORMATION
ON THE CENTINEL
prodisc™-C TOTAL DISC REPLACEMENT

CENTINEL
Spine

01/24 **IFU003**

CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician (or properly licensed practitioner) that has appropriate training or experience.

DEVICE DESCRIPTION

The pro**disc**-C Total Disc Replacement is made up of three components. The first is the inferior CoCrMo (cobalt chromium molybdenum) alloy plate with a midline keel orientated anterior-posterior that is anchored into the endplate of the inferior vertebral body. The second component is an Ultra High Molecular Weight Polyethylene (UHMWPE) insert that is pre-assembled snap-locked into a tray detail in the inferior CoCrMo alloy plate and provides the inferior convex bearing surface. The third component is a CoCrMo alloy plate with a midline keel that anchors to the superior vertebral body and has a highly polished concave bearing surface that articulates with the convex UHMWPE spherical dome.

The endplate footprints range from 15-19 mm wide (medial-lateral) x 12-18 mm deep (anterior-posterior). Each endplate size is available in three disc heights: 5, 6, and 7 mm. This allows for a wide range of sizing to accommodate individual patient anatomy.

The bone contacting surfaces of the inferior and superior plates as well as both keels are titanium plasma spray coated, which may provide additional fixation through bony ingrowth.

The maximum range of motion allowed by the pro**disc**-C Total Disc Replacement device design is 20° in flexion/extension (17.5° for the 5mm Large, Large Deep, Extra Large, and Extra Large Deep implants), 20° in lateral bending (17.5° for the 5mm Large, Large Deep, Extra Large, and Extra Large Deep implants), and the device is unconstrained in axial rotation as measured through *in vitro* testing.

Magnetic Resonance Imaging

The pro**disc**-C Total Disc Replacement is labeled MR Conditional, where it has been demonstrated to pose no known hazards in a specified MR environment with specified conditions of use. For more information, please refer to the section MRI Information.

The device is provided pre-assembled in the following configurations:

Dimensions – Endplates			
Size	A/P (mm)	Lateral (mm)	Disc Heights (mm)
Implant – Medium	12	15	5, 6, 7
Implant – Medium Deep	14	15	5, 6, 7
Implant – Large	14	17	5, 6, 7
Implant – Large Deep	16	17	5, 6, 7
Implant – Extra Large	16	19	5, 6, 7
Implant – Extra Large Deep	18	19	5, 6, 7

Catalog Number	Component Description
09.820.025S	ProDisc-C Implant, medium 5mm, sterile
09.820.026S	ProDisc-C Implant, medium 6mm, sterile
09.820.027S	ProDisc-C Implant, medium 7mm, sterile
09.820.035S	ProDisc-C Implant, medium Deep 5mm, sterile
09.820.036S	ProDisc-C Implant, medium Deep 6mm, sterile
09.820.037S	ProDisc-C Implant, medium Deep 7mm, sterile
09.820.045S	ProDisc-C Implant, large 5mm, sterile
09.820.046S	ProDisc-C Implant, large 6mm, sterile
09.820.047S	ProDisc-C Implant, large 7mm, sterile
09.820.055S	ProDisc-C Implant, large deep 5mm, sterile
09.820.056S	ProDisc-C Implant, large deep 6mm, sterile
09.820.057S	ProDisc-C Implant, large deep 7mm, sterile
09.820.065S	ProDisc-C Implant, extra large 5mm, sterile
09.820.066S	ProDisc-C Implant, extra large 6mm, sterile
09.820.067S	ProDisc-C Implant, extra large 7mm, sterile
09.820.075S	ProDisc-C Implant, extra large Deep 5mm, sterile
09.820.076S	ProDisc-C Implant, extra large Deep 6mm, sterile
09.820.077S	ProDisc-C Implant, extra large Deep 7mm, sterile

Indications for Use

The pro**disc**-C Total Disc Replacement is indicated in skeletally mature patients for reconstruction of a single disc from C3-C7 following discectomy for intractable symptomatic cervical disc disease (SCDD). Symptomatic cervical disc disease is defined as neck or arm (radicular) pain and/or a functional/neurological deficit with at least one of the following conditions confirmed by imaging (CT, MRI, or X-rays): herniated nucleus pulposus, spondylosis (defined by the presence of osteophytes), and/or loss of disc height. The pro**disc**-C Total Disc Replacement is implanted via an open anterior approach. Patients receiving the pro**disc**-C Total Disc Replacement should have failed at least six weeks of non-operative treatment prior to implantation of the pro**disc**-C Total Disc Replacement.

Contraindications

The pro**disc**-C Total Disc Replacement should not be implanted in patients with the following conditions:

- Active systemic infection or infection localized to the site of implantation

- Osteoporosis defined as DEXA bone density measured T-score ≤ -2.5
- Marked cervical instability on neutral resting lateral or flexion/extension radiographs; translation > 3mm and/or > 11° of rotational difference to either adjacent level
- Allergy or sensitivity to the implant materials (cobalt, chromium, molybdenum, polyethylene, titanium)
- Severe spondylosis characterized by bridging osteophytes or a loss of disc height > 50% or an absence of motion (<2°), as this may lead to limited range of motion and may encourage bone formation (e.g., heterotopic ossification, fusion)
- Clinically compromised vertebral bodies at the affected level due to current or past trauma (e.g., by radiographic appearance of fracture callus, malunion, or nonunion)

Warnings

Correct placement of the device is essential to optimal performance. Use of the pro**disc**-C Total Disc Replacement should only be undertaken after the surgeon has become thoroughly knowledgeable about spinal anatomy and biomechanics, has had experience with anterior cervical spinal surgeries, and has had hands-on training in the use of this specific device. A lack of adequate experience and/or training may lead to a higher incidence of adverse events, including neurological complications.

The safety and effectiveness of this device has not been studied in the pediatric or adolescent age group (<22 years old).

Due to the proximity of vascular and neurological structures to the implantation site, there are risks of serious or fatal hemorrhage and risks of neurological damage with the use of this device. Care should be taken to identify and protect these structures during surgery.

Precautions

Patient selection is extremely important. In selecting patients for a total disc replacement the following factors can be of importance to the success of the procedure: the patient's occupation or activity level, a condition of senility, mental illness, alcoholism, or drug abuse. In addition, certain degenerative diseases (i.e., degenerative scoliosis or ankylosing spondylitis) may be so advanced at the time of implantation that the expected useful life of the device is substantially decreased.

Furthermore, correct selection of the appropriate implant size is extremely important to assure the placement and function of the device. Please refer to the pro**disc**-C Total Disc Replacement Technique Guide for step by step instructions on the required surgical technique, including determining the correct implant size.

The safety and effectiveness of this device has not been established in patients with the following conditions:

- skeletally immature patients, pediatric or adolescent children (<22 years old), or those over the age of 60
- more than one vertebral level with SCDD

- prior fusion surgery at an adjacent vertebral level
- prior surgery at the level to be treated
- when implanted at more than one cervical spinal level and/or adjacent to an anterior cervical discectomy and fusion (ACDF)
- patients with progressive symptoms and signs of spinal cord/nerve root compression with less than six weeks of conservative treatment
- facet joint disease or degeneration at the level to be treated
- neck or arm pain of unknown etiology
- Paget's disease, osteomalacia, or other metabolic bone disease
- pregnancy
- taking medications known to potentially interfere with bone/soft tissue healing (e.g., steroids)
- rheumatoid arthritis or other autoimmune disease
- severe diabetes mellitus requiring daily insulin treatment
- systemic disease including AIDS, HIV, and Hepatitis
- active malignancy

In order to minimize the risk of periprosthetic vertebral fractures, surgeons must consider all co-morbidities, past and present medications, previous treatments, etc. A screening questionnaire for osteopenia or osteoporosis, SCORE (Simple Calculated Osteoporosis Risk Estimation), may be used to screen patients to determine if a DEXA bone mineral density measurement is necessary. If DEXA is performed, the patient should be excluded from receiving the device (per the contraindications listed above) if the DEXA bone density measured T score is ≤ -2.5, as the patient may be osteoporotic. It may also be advisable to exclude patients with a T score ≤ -1.0 as the patient may be osteopenic.

Use aseptic technique when removing the pro**disc**-C Total Disc Replacement implant from the innermost packaging.

Use care when handling the pro**disc**-C Total Disc Replacement implant to ensure that it does not come in contact with objects that could damage the implant. Exercise care to ensure that implantation instruments do not contact the highly polished articulating surfaces of the endplates. Damaged implants are no longer functionally reliable.

To prevent unnecessary damage to the bearing surfaces, ensure that blood or other debris is not trapped within the device.

pro**disc**-C Total Disc Replacement implant should not be used with components or instruments of spinal systems from other manufacturers. See the surgical technique manual for step by step instructions.

Surgical implants must never be re-used or re-implanted. Even though the device appears undamaged, it may have small defects and internal stress patterns that may lead to early breakage.

Patients should be instructed in postoperative care procedures and should be advised of the importance of adhering to these procedures for successful treatment with the device including the avoidance of heavy lifting, repetitive bending, and prolonged or strenuous

activity initially and for a period of weeks to months depending on the individual patient's progress and the stability and functioning of the implant.

Adverse Events

The pro**disc**-C Total Disc Replacement was implanted in 103 investigational subjects and compared to 106 control subjects who received an anterior cervical discectomy and fusion (ACDF) in a multi-center, prospective, randomized, non-inferiority clinical trial. The number of patients who experienced one or more adverse events was not statistically different (p = 1.0000).

The following adverse events were reported during the clinical study comparing pro**disc**-C Total Disc Replacement to ACDF.

Table 1: All Adverse Events

Adverse Event	Intra-Op (0-2 days)		Peri-Op (>2 - 42 days)		Short Term (>42-210 days)		Long Term (>210 days)		ACDF (N=106)		ProDisc-C (N=103)	
	ACDF	PRC	ACDF	PRC	ACDF	PRC	ACDF	PRC	Patients (%)	Events (E/Pt)	Patients (%)	Events (E/Pt)
ALL ADVERSE EVENTS									86 (81.1%)	254 (2.40)	84 (81.6%)	237 (2.30)
Adjacent Level DDD or DJD	0	0	0	0	1	0	3	0	4 (3.8%)	4 (0.04)	0 (0.0%)	0 (0.00)
Burning or Dysesthetic Pain	0	0	0	1	0	0	0	0	0 (0.0%)	0 (0.00)	1 (1.0%)	1 (0.01)
Cancer	0	0	0	0	0	0	0	1	0 (0.0%)	0 (0.00)	1 (1.0%)	1 (0.01)
Cardiovascular	2	2	0	1	3	1	2	1	7 (6.6%)	7 (0.07)	5 (4.9%)	5 (0.05)
DDD Progression, Non-Cervical	0	0	0	0	1	0	0	1	1 (0.9%)	1 (0.01)	1 (1.0%)	1 (0.01)
Dermatological	0	0	1	0	0	0	0	1	1 (0.9%)	1 (0.01)	1 (1.0%)	1 (0.01)
Dizziness	0	0	0	1	0	0	0	0	0 (0.0%)	0 (0.00)	1 (1.0%)	1 (0.01)
Dural Tear	0	1	0	0	0	0	0	0	0 (0.0%)	0 (0.00)	1 (1.0%)	1 (0.01)
Dysphagia	3	2	5	3	0	0	1	1	9 (8.5%)	9 (0.08)	6 (5.8%)	6 (0.06)
Dysphonia	1	0	0	0	0	0	0	0	1 (0.9%)	1 (0.01)	0 (0.0%)	0 (0.00)
Edema	1	2	0	0	0	0	0	0	1 (0.9%)	1 (0.01)	2 (1.9%)	2 (0.02)
Fatigue	0	1	0	0	0	0	0	0	0 (0.0%)	0 (0.00)	1 (1.0%)	1 (0.01)
Fracture - Vertebral	0	0	0	0	0	0	1	0	1 (0.9%)	1 (0.01)	0 (0.0%)	0 (0.00)
Gastrointestinal	11	15	1	1	2	1	2	2	15 (14.2%)	16 (0.15)	16 (15.5%)	19 (0.18)
Genitourinary	2	4	0	1	0	0	1	0	3 (2.8%)	3 (0.03)	5 (4.9%)	5 (0.05)
Headache	1	3	2	4	3	4	8	9	12 (11.3%)	14 (0.13)	18 (17.5%)	20 (0.19)
Infection - Non-Wound	0	1	0	0	2	2	4	0	6 (5.7%)	6 (0.06)	2 (1.9%)	3 (0.03)
Infection - Superficial Wound	0	0	1	0	0	0	0	0	1 (0.9%)	1 (0.01)	0 (0.0%)	0 (0.00)
Insomnia	3	4	0	1	0	0	0	1	3 (2.8%)	3 (0.03)	6 (5.8%)	6 (0.06)
Musculoskeletal	0	1	4	3	2	10	15	7	16 (15.1%)	21 (0.20)	18 (17.5%)	21 (0.20)
Musculoskeletal (Spasms - Back)	0	0	1	0	0	0	0	1	1 (0.9%)	1 (0.01)	1 (1.0%)	1 (0.01)
Musculoskeletal (Spasms - Neck)	1	0	2	0	1	2	1	1	5 (4.7%)	5 (0.05)	3 (2.9%)	3 (0.03)
Musculoskeletal (Spasms - Non-Specific)	2	2	0	0	2	0	0	1	4 (3.8%)	4 (0.04)	3 (2.9%)	3 (0.03)
Narcotics Use	0	0	0	1	0	0	0	0	0 (0.0%)	0 (0.00)	1 (1.0%)	1 (0.01)
Neurological	0	1	0	0	0	1	1	2	1 (0.9%)	1 (0.01)	4 (3.9%)	4 (0.04)
Numbness Index Level	0	0	0	0	0	0	2	0	2 (1.9%)	2 (0.02)	0 (0.0%)	0 (0.00)
Numbness Non-Index Level	0	2	0	1	3	2	4	8	7 (6.6%)	7 (0.07)	11 (10.7%)	13 (0.13)
Ossification	0	0	0	0	0	0	0	1	0 (0.0%)	0 (0.00)	1 (1.0%)	1 (0.01)
Other	1	1	0	2	2	1	4	1	6 (5.7%)	7 (0.07)	4 (3.9%)	5 (0.05)
Pain - Back	0	0	1	2	4	3	3	6	8 (7.5%)	8 (0.08)	11 (10.7%)	11 (0.11)
Pain - Back and Lower Extremeties	0	0	0	1	0	1	2	3	2 (1.9%)	2 (0.02)	4 (3.9%)	5 (0.05)
Pain - Incision Site	0	1	0	0	0	0	1	0	1 (0.9%)	1 (0.01)	1 (1.0%)	1 (0.01)
Pain - Neck	2	1	2	2	10	7	11	6	22 (20.8%)	25 (0.25)	16 (15.5%)	16 (0.16)
Pain - Neck and Other	0	0	0	0	0	0	0	1	0 (0.0%)	0 (0.00)	1 (1.0%)	1 (0.01)
Pain - Neck and Shoulder	0	2	0	1	2	1	4	4	6 (5.7%)	6 (0.06)	7 (6.8%)	8 (0.08)
Pain - Neck and Upper Extremeties	0	0	0	0	1	2	6	1	6 (5.7%)	7 (0.07)	3 (2.9%)	3 (0.03)
Pain - Neck and Upper Ext. with Numbness	0	0	0	1	5	2	2	3	6 (5.7%)	7 (0.07)	6 (5.8%)	6 (0.06)
Pain - Other	6	0	0	0	0	0	3	5	7 (6.6%)	9 (0.09)	5 (4.9%)	5 (0.05)
Pain - Shoulder	0	0	1	1	2	4	6	5	9 (8.5%)	9 (0.08)	9 (8.7%)	10 (0.10)
Pain - Upper Extremeties	0	2	0	0	2	3	3	4	5 (4.7%)	5 (0.05)	8 (7.8%)	9 (0.09)
Pain - Upper Extremeties with Numbness	0	0	1	0	1	1	3	3	5 (4.7%)	5 (0.05)	4 (3.9%)	4 (0.04)
Pseudoarthrosis	0	0	0	0	0	0	2	0	2 (1.9%)	2 (0.02)	0 (0.0%)	0 (0.00)
Psychological	3	3	0	0	0	0	2	1	5 (4.7%)	5 (0.05)	4 (3.9%)	4 (0.04)
Pulmonary Infection	0	0	0	0	0	1	0	0	0 (0.0%)	0 (0.00)	1 (1.0%)	1 (0.01)
Puritis	1	0	1	0	0	0	0	0	2 (1.9%)	2 (0.02)	0 (0.0%)	0 (0.00)
Reflex Change	0	0	0	1	0	0	0	0	0 (0.0%)	0 (0.00)	1 (1.0%)	1 (0.01)
Respiratory	0	2	0	1	2	0	1	1	3 (2.8%)	3 (0.03)	4 (3.9%)	4 (0.04)
Seizures	1	0	0	0	1	0	0	0	2 (1.9%)	2 (0.02)	0 (0.0%)	0 (0.00)
Sore Throat	0	1	0	0	1	0	0	0	1 (0.9%)	1 (0.01)	1 (1.0%)	1 (0.01)
Surgery - Index Level	1	0	1	0	2	1	6	1	10 (9.4%)	10 (0.09)	2 (1.9%)	2 (0.02)
Surgery - Other	0	0	3	3	7	1	17	12	21 (19.8%)	27 (0.25)	12 (11.7%)	16 (0.16)
Wound Issues, Other	0	3	1	1	1	0	0	0	2 (1.9%)	2 (0.02)	3 (2.9%)	4 (0.04)

Patients experiencing adverse events in more than one category are represented in each category in which they experienced an adverse event.

Adverse event categories identified as Musculoskeletal are further defined as:

- Musculoskeletal (spasms – back): any event involving muscular spasms in the lumbar spine region

- Musculoskeletal (spasms – neck): any event involving muscular spasms in the cervical spine region
- Musculoskeletal (spasms – non-specific): any event involving general complaints of muscular spasms not related to the lumbar or cervical spine
- Musculoskeletal: classifies all events related to muscles, tendons, ligaments, cartilage, bones, joints and surrounding tissues that do not fall into one of the categories above.

Adverse event category "Neurological" broadly includes AEs related to the nervous system. Any specific episodes of numbness or reflex changes are further classified in the following categories: Numbness Index Level, Numbness Non-Index Level, and Reflex Change.

***Other –** the following 5 adverse events in 4 pro**disc**-C patients: Keratitis, diagnosed with Dry Eye Syndrome, IV Infiltrated, Left leg weakness and heavy, and Horner's Syndrome as well as the following 7 adverse events in 6 ACDF patients: diagnosed with early Diabetes, Radiographic films show no evidence of a solid fusion, worsening of Diabetes, Wegener's disease, Polycythemia, Ringing bilateral ears, and Ringing ears.

The table below shows all adverse events that were considered implant related and the time-course of their occurrence:

Table 2: Implant Related Adverse Events

Adverse Event	Intra-Op (0-2 days)		Peri-Op (>2 - 42 days)		Short Term (>42-210 days)		Long Term (>210 days)		Total	
	ACDF	PRC	ACDF	PRC	ACDF	PRC	ACDF	PRC	ACDF	PRC
Dysphagia	0	0	1	0	0	0	0	0	1	0
Infection - Superficial Wound	0	0	1	0	0	0	0	0	1	0
Musculoskeletal	0	0	1	0	0	0	0	0	1	0
Pain - Neck	0	0	1	0	0	0	0	0	1	0
Surgery - Index Level	1	0	1	0	2	0	1	2	5	2

There were nine (9) implant related AEs in seven (7) ACDF patients and two (2) implant related AEs in two (2) pro**disc**-C patients. All "Surgery – Index Level" AEs were considered severe or life threatening as well as the "Infection – Superficial Wound" AE in the ACDF group. The relationship of an adverse event to the implant was determined by the treating physician.

The following secondary surgical procedures at the index level were reported during the study:

Table 3: Secondary Surgical Procedures – Index Level

Tx Group	Cause	Action	Days Post-op
ACDF	Worsening Cervical Radiculopathy	Plate Removal - (C5-6), ACDF (C6-7)	1079
ACDF	MVA	Supplemental Fixation C6-7 and L4-5 PSF	420
ACDF	Adjacent Level Disease	Plate Removal - (C5-6), ACDF (C6-7)	732
ACDF	C5-6 Pseudoarthrosis;	C5-6 Supplemental Fixation	377
ACDF	Allograft Subsidence At C6-7	Revision C6-7 ACDF	296
ACDF	Dysphagia	Revision C6-7 ACDF	14
ACDF	Neck Pain	Revision C6-7 ACDF	425
ACDF	Adjacent Level Disease	Plate Removal - (C5-6), ACDF (C6-7)	826
ACDF	Neck Pain	Revision C4-5 ACDF	644
ACDF	Non Union C6-7	Supplemental Fixation C6-7	637
ACDF	Stenosis C6-7, Subsidence C6-7	Re-operation C6-7, Bone Fortification	300
PRC	Pt Had Worsening Pain	Removal of TDR with Fusion	499
PRC	Neck Pain	Removal of TDR with Fusion	492

One ACDF patient underwent a second revision surgery at the index level at 917 days post-op in response to ongoing pain and weakness.

Table 4: Secondary Surgical Procedures – Index Level – Time Course (Randomized)

	Prior to Discharge		6 wks		3 mo		6 mo		12 mo		18 mo		24 mo		>24 mo		Total	
	ACDF	ProDisc-C	ACDF	ProDisc-C	ACDF	ProDisc-C	ACDF	ProDisc-C	ACDF	ProDisc-C	ACDF	ProDisc-C	ACDF	ProDisc-C	ACDF	ProDisc-C	ACDF	ProDisc-C
Removals	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	2
Reoperations	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	0
Revisions	0	0	1	0	0	0	1	0	1	0	1	0	1	0	3	0	8	0
Supplemental Fixation	0	0	0	0	0	0	0	0	1	0	1	0	1	0	0	0	3	0

There were no statistically significant differences between the pro**disc**-C and ACDF treatment groups for the percentage of patients experiencing at least one adverse event in the following categories:

- All Adverse Events (p=1.0000)
- Device-related Adverse Events (p=0.1706)
- Surgery-related Adverse Events (p=0.4113)

A statistically significant difference in favor of pro**disc**-C was detected for the percentage of patients experiencing at least one severe or life-threatening adverse event (p=0.0137).

Unintended fusion (i.e., heterotopic ossification resulting in bridging trabecular bone and a loss of motion (<2°)), occurred in three pro**disc**-C patients in the randomized clinical trial.

Potential Risks

Potential risks associated with the use of pro**disc**-C Total Disc Replacement 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 pro**disc**-C Total Disc Replacement. However, the causality of these adverse events is not exclusive to these categories. 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 were observed in the clinical study and therefore have been previously reported in the adverse events table.

1. Risks associated with any surgical procedure are those such as: abscess; cellulitis; wound dehiscence; wound necrosis; edema; hematoma; heart and vascular complications; hypertension; thrombosis; ischemia; embolism; thromboembolism; hemorrhage; thrombophlebitis; adverse reactions to anesthesia; pulmonary complications; organ, nerve or muscular damage; gastrointestinal compromise; seizure, convulsion, or changes to mental status; and complications of pregnancy including miscarriage and fetal birth defects;
2. Risks associated with anterior interbody surgery of the cervical spine include: dysphagia; dysphasia; dysphonia; hoarseness; vocal cord paralysis; laryngeal palsy; sore throat; recurring aspirations; nerve deficits or damage; tracheal, esophageal; and pharyngeal perforation; airway obstruction; external chylorrhea; warmth or tingling in the extremities; deficit or damage to the spinal chord, nerve roots, or nerves possibly resulting in paralysis or pain; dural tears or leaking; cerebrospinal

fistula; discitis, arachnoiditis, and/or other types of inflammation; loss of disc height; loss of proper curvature, correction, height or reduction of the spine; vertebral slipping; scarring, herniation or degeneration of adjacent discs; surrounding soft tissue damage, spinal stenosis; spondylolysis; otitis media; fistula; vascular damage and/or rupture; and headache;

3. Risks associated with implants in the spine, including the pro**disc**-C Total Disc Replacement device, are: early or late loosening of the components; disassembly; bending or breakage of any or all of the components; implant migration; malpositioning of the implant; loss of purchase; sizing issues with components; anatomical or technical difficulties; implant fracture; bone fracture; skin penetration; irritation, pain, bursitis resulting from pressure on the skin from component parts in patients with inadequate tissue coverage; foreign body reaction to the implants including possible tumor formation, autoimmune disease, metallosis, and/or scarring; possible tissue reaction; bone resorption; bone formation 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 and placement of implants or instruments; loss of neurological function; decreased strength of extremities; decreased reflexes; appearance of cord or nerve root injury; loss of bowel and/or bladder control; and interference with radiographic imaging because of the presence of the implant;
4. Wound, local and/or systemic infections;
5. Inability to resume activities of normal daily living;
6. Death

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

Death, a potential adverse event, did not occur during the randomized clinical trial. There was one death reported in the continued access cohort of the study that was due to a methadone overdose approximately one and a half weeks postoperatively and was not considered to be associated with the implant or the implantation procedure.

Clinical Study

Clinical data were collected to evaluate the safety and effectiveness of the pro**disc**-C Total **Disc** Replacement as compared to the control device, an anterior cervical discectomy and fusion (ACDF) surgery with the use of allograft bone (cortical ring) and an anteriorly applied plating system in patients undergoing single-level **disc**ectomy for intractable SCDD. The purpose of the study was to determine whether the pro**disc**-C Total Disc Replacement was non-inferior to ACDF. A total of 209 subjects were enrolled, randomized and treated (103 patients in the investigational pro**disc**-C treatment group and 106 patients in the control group). To qualify for enrollment in the study, patients met all the inclusion criteria and none of the exclusion criteria listed in the following table:

Inclusion	Exclusion
1. Symptomatic cervical **disc** disease (SCDD) in only one vertebral level	1. More than one vertebral level requiring treatment.

between C3-C7 defined as:

- Neck or arm (radicular) pain; and/or a functional / neurological deficit with at least one of the following conditions confirmed by imaging (CT, MRI or X-rays)
- Herniated nucleus pulposus;
- Spondylosis (defined by the presence of osteophytes); and/or
- Loss of disc height

2. Age between 18 and 60 years.
3. Unresponsive to non-operative treatment for approximately six weeks or has the presence of progressive symptoms or signs of nerve root/spinal cord compression in the face of conservative treatment.
4. NDI score greater than or equal to 15/50 (30%) (Considered moderate disability).
5. Psychosocially, mentally and physically able to fully comply with this protocol including adhering to follow-up schedule and requirements and filling out forms.
6. Signed informed consent.

2. Marked cervical instability on resting lateral or flexion/extension radiographs:
    a. translation greater than 3 mm and/or
    b. greater than 11 degrees of rotational difference to that of either adjacent level .
3. Has a fused level adjacent to the level to be treated.
4. Radiographic confirmation of severe facet joint disease or degeneration.
5. Known allergy to cobalt, chromium, molybdenum, titanium or polyethylene.
6. Clinically compromised vertebral bodies at the affected level(s) due to current or past trauma, e.g., by the radiographic appearance of fracture callus, malunion or nonunion.
7. Prior surgery at the level to be treated.
8. Severe spondylosis at the level to be treated as characterized by any of the following:
    a. Bridging osteophytes;
    b. A loss of disc height greater than 50%; or
    c. Absence of motion (<2°).
9. Neck or arm pain of unknown etiology.
10. Osteoporosis: A screening questionnaire for osteoporosis, SCORE[1] (Simple Calculated Osteoporosis Risk Estimation), will be used to screen patients who require a DEXA bone mineral density measurement. If DEXA is required, exclusion will be defined as a DEXA bone density measured T score ≤ -2.5 (The World Health Organization definition of osteoporosis.[2])
11. Paget's disease, osteomalacia or any other metabolic bone disease (excluding osteoporosis which is addressed above).
12. Severe diabetes mellitus requiring daily insulin management
13. Pregnant or interested in becoming pregnant in the next 3 years.
14. Active infection - systemic or local.

[1] Lydick E, Cook K, Turpin J, et al. Development and validation of a simple questionnaire to facilitate identification of women likely to have low bone density. Am J Man Care 1998; 4:37-48.
[2] The WHO Study Group: Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Geneva, World Health Organization, 1994.

15. Taking medications or any drug known to potentially interfere with bone/soft tissue healing (e.g., steroids).
16. Rheumatoid arthritis or other autoimmune disease.
17. Systemic disease including AIDS, HIV, hepatitis.
18. Active malignancy: A patient with a history of any invasive malignancy (except non-melanoma skin cancer), unless he/she has been treated with curative intent and there have been no clinical signs or symptoms of the malignancy for at least 5 years.

Following surgery, investigators were advised to prescribe the appropriate rehabilitation program and manage patient progress on an individual basis. They were given certain guidelines to follow irrespective of the subject's treatment group. The guidelines included a hard or soft collar at the surgeon's discretion. Direction was given to the patient regarding standard wound care procedures. Limitations were placed on patients in regard to prolonged or strenuous activity initially and for a period of weeks to months depending on the individual patient's progress. The patients were instructed not to resume heavy physical activity until the surgeon had reviewed postoperative radiographs and was confident that the implant was stable and functioning. In addition, patients were instructed to immediately report any change in their pain or neurologic status to their doctor.

Patients were not treated with NSAIDs postoperatively in either treatment group despite some reports in the literature that short-term postoperative use of NSAIDs may reduce the incidence of heterotopic ossification in total disc replacement patients.

Subjects were evaluated pre-operatively, intra-operatively, and immediately post-operatively followed by evaluations at 6 weeks, 3 months, 6 months, 12 months, 18 months and 24 months. Complications and adverse events, device-related or not, were evaluated over the course of the clinical trial. At each evaluation time-point, the primary and secondary clinical and radiographic outcome parameters were evaluated.

Safety and effectiveness was assessed in all randomized subjects.

The safety of the pro**disc**-C Total Disc Replacement was assessed by monitoring intra-operative and post-operative adverse events. Radiographs were used to monitor the occurrence of some of the adverse events, including device subsidence, migration, and breakage as well as heterotopic ossification and unintended fusion in the investigational group.

All radiographic endpoints were evaluated independently by a core laboratory (Medical Metrics, Inc., Houston, TX) and reviewed by an independent radiologist.

The overall success analysis using the composite primary endpoint, as described in the IDE, is presented. FDA requested that in addition to the IDE overall success criteria (presented herein as Overall Success), analysis of Overall Success be presented using an improvement in NDI of ≥15 points relative to the pre-operative baseline (presented herein as Additional Analysis). FDA also requested that a non-inferiority delta of 10% be applied to the analyses. Sensitivity analyses for both definitions used a non-inferiority delta of 10%.

Table 5: Overall Success Definitions

Overall Success	Additional Analysis
The patient's NDI score improves by at least 20% over baseline value	The patient's NDI score improves by at least 15 points over baseline value
The patient's neurologic parameters, i.e. motor sensory, and relexes are maintained or improved	The patient's neurologic parameters, i.e. motor sensory, and relexes are maintained or improved
No removals, revisions, re-operations or additional fixation were required to modify any implant	No removals, revisions, re-operations or additional fixation were required to modify any implant
No adverse events occur which are related to the treatment, ProDisc-C or its implantation or ACDF surgery or its associated implants or graft material	No adverse events occur which are related to the treatment, ProDisc-C or its implantation or ACDF surgery or its associated implants or graft material

The secondary endpoints assessed were quality of life measured with the SF-36 questionnaire, improvement on a Visual Analog Scale (VAS) for neck and arm pain intensity and frequency, and several radiographic assessments (device migration, subsidence, disc height, range of motion, heterotopic ossification and fusion status). Other outcomes measured included VAS subject satisfaction, willingness to have the same surgery again, employment status, and medication use.

Clinical Patient Population

Thirteen (13) sites treated patients in the pivotal study with a total of two hundred and nine (209) subjects enrolled, randomized, and treated; 103 subjects in the investigational treatment arm (pro**disc**-C Total Disc Replacement) and 106 subjects in the control arm (ACDF) were treated.

Subject Demographics

The table below shows select demographics and baseline characteristics of the investigational and control groups.

Table 6: Demographic and Baseline Characteristics

	ProDisc-C (N Trtd=103)	ACDF (N Trtd=106)	Two-Sided p-value
Implant Level			**0.4764**
C3-C4	3 (2.9%)	1 (0.9%)	
C4-C5	10 (9.7%)	6 (5.7%)	
C5-C6	58 (56.3%)	61 (57.5%)	
C6-C7	32 (31.1%)	38 (35.8%)	
Age at Surgery (years)			**0.2025**
Mean	42.1	43.5	
STD	8.42	7.15	
Age Group [N (%)]			**0.5810**
<=42 years	52 (50.5%)	49 (46.2%)	
>42 years	51 (49.5%)	57 (53.8%)	
Gender [N (%)]			**0.8897**
Female	57 (55.3%)	57 (53.8%)	
Male	46 (44.7%)	49 (46.2%)	
Race [N (%)]			**0.1000**
Caucasian	88 (85.4%)	97 (91.5%)	
African-American	4 (3.9%)	1 (0.9%)	
Hispanic	3 (2.9%)	5 (4.7%)	
Asian American	5 (4.9%)	0 (0.0%)	
Other	3 (2.9%)	3 (2.8%)	
Smoking Status			**0.9159**
Never	51 (49.5%)	49 (46.2%)	
Former	18 (17.5%)	20 (18.9%)	
Current	34 (33.0%)	37 (34.9%)	
Height (in)			**0.2839**
Mean	67.23	67.77	
STD	3.703	4.106	
Weight (lbs)			**0.0943**
Mean	171.04	180.27	
STD	41.797	47.331	
Body Mass Index (kg/m^2)			**0.0896**
Mean	26.44	27.34	
STD	5.319	5.54	
NDI Score (%)			**0.4560**
Mean	53.93	52.28	
STD	15.096	14.544	
Duration of Neck/Arm Pain			**0.9645**
<6 weeks	3 (2.9%)	3 (2.8%)	
6 weeks to a year	44 (42.7%)	44 (41.5%)	
>1 year	56 (54.4%)	59 (55.7%)	

Surgical and Hospitalization Information

The mean intra-operative time in the pro**disc**-C Total Disc Replacement group was 107.2 minutes whereas it was 98.7 minutes in the ACDF group ($p<0.0078$). The mean estimated blood loss (EBL) in the pro**disc**-C Total Disc Replacement group was 83.5cc whereas it was 63.5cc in the ACDF group ($p<0.0094$). The length of hospital stay was analogous in both groups; 1.4 days pro**disc**-C and 1.3 days ACDF, $p<0.7882$. While the differences in the means for estimated blood loss and operative time were statistically significant, in each case the ranges were similar so the statistical significance may not be clinically significant.

The table below describes the implant sizes used in the pro**disc**-C patients:

Table 7: Implant Sizes Used

Inlay	Medium	Medium Deep	Large	Large Deep	Extra Large	Extra Large Deep
5 mm	23 (22.3%)	16 (15.5%)	25 (24.3%)	6 (5.8%)	1 (1.0%)	0 (0.0%)
6 mm	7 (6.8%)	6 (5.8%)	14 (13.6%)	4 (3.9%)	0 (0.0%)	0 (0.0%)
7 mm	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)

Clinical Effectiveness Evaluation

The primary effectiveness endpoint of this study was the difference in proportion of Overall Success between the two treatment groups at 24 months post-operatively. The success status of subjects was summarized by treatment group.

The population which was used to assess these endpoints consisted of all randomized subjects in the pivotal study who completed all evaluations at the 24-month time point, regardless of when the 24-month measurements occurred.

Table 8: Components of Overall Success

Component of Overall Success	ProDisc-C	ACDF	Fisher's Exact Test p-value (One-Sided)
NDI Success (IDE)* (≥20% Improvement from Baseline)	84/ 99 (84.9%)	79/ 92 (85.9%)	0.6561
NDI Success (FDA)* (≥15 Point Improvement from Baseline)	79/ 99 (79.8%)	72/ 92 (78.3%)	0.4665
Neurological Success* (Maintenance or Improvement from Baseline)	90/ 99 (90.9%)	81/ 92 (88.0%)	0.3407
Absence of Revisions, Removals, Re-operations or Supplemental Fixation at the Index Level	101/103 (98.1%)	97/106 (91.5%)	0.0327
Absence of Adverse Events Related to the Implant or Implantation	100/103 (97.1%)	99/106 (93.4%)	0.1779
Analysis	**ProDisc-C**	**ACDF**	
Overall Success (IDE) (20% NDI)	78/101 (77.2%)	75/101 (74.3%)	0.3715
Additional Analysis (FDA) (15 point NDI)	73/101 (72.3%)	69/101 (68.3%)	0.3222

* Denominators for NDI and Neurological Success (92 ACDF, 99 pro**disc**-C) reflect only patients that completed the study. Denominators for Re-operations and Adverse Events (106 ACDF, 103 pro**disc**-C) include all patients treated in the study. Denominators for Overall Success reflect all patients with known outcomes at month 24. The relationship of adverse events to the implant or its implantation was determined by the treating physician.

The results of both overall success analyses indicate that the pro**disc**-C Total Disc Replacement is statistically non-inferior to the ACDF control group. As stated in the IDE protocol, "The test of the sole, primary hypothesis that pro**disc**-C Total Disc Replacement is non-inferior to ACDF is based on an exact 95% one-sided, upper confidence bound for the difference in success probabilities, PA-PB, where A denotes the fusion (ACDF) arm and B denotes the pro**disc**-C Total Disc Replacement arm. If the upper bound is delta = 0.15 or less, then pro**disc**-C Total Disc Replacement is considered non-inferior to ACDF." The Overall Success upper bound of the exact 95% one-sided confidence interval was 7.10%. This result is below the 15% delta needed to establish non-inferiority under the IDE protocol and below the 10% delta needed to establish non-inferiority under the FDA's

requested analysis. Using the Additional Analysis criteria for overall success, the upper bound of the exact 95% one-sided confidence interval was 7.0%. This result is below the 10% delta needed to establish non-inferiority. To assess the impact on the conclusion of non-inferiority of patients with unknown outcomes at Month 24 (5 ACDF, 2 pro**disc**-C) a number of sensitivity analyses were conducted. The following conditions were applied for all patients with unknown outcomes at Month 24 for both Overall Success and the Additional Analysis:

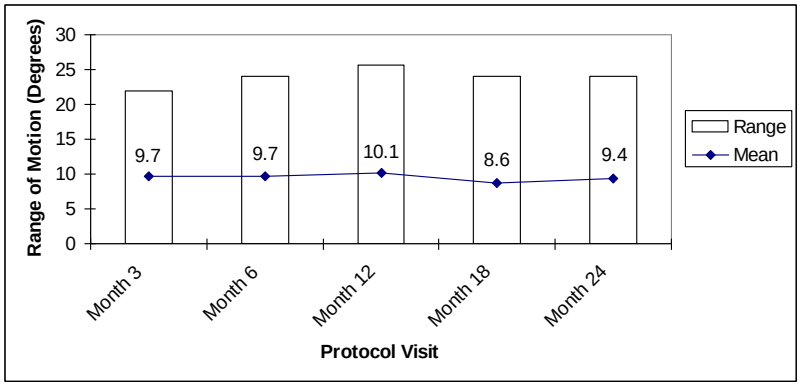
- All Failures (all designated as failure regardless of treatment group)
- All Success (all designated as success regardless of treatment group)
- Last observation carried forward (LOCF), if there were no outcomes for a patient for any post-operative time-point the patient was removed from analysis
- Modified LOCF using only Month 12 or Month 18 results, if a patient had no known outcomes at Month 12 or beyond they were designated as success if ACDF and failure if pro**disc**-C Total Disc Replacement
- Worst Case (all ACDF designated as success, all pro**disc**-C Total Disc Replacement designated as failure)

Under all sensitivity analyses the pro**disc**-C Total Disc Replacement remained non-inferior, with the upper bound of the exact 95% one-sided confidence intervals under worst case analysis falling below the 15% non-inferiority delta for Overall Success and below the 10% non-inferiority delta for FDA's requested Additional Analysis.

Secondary Efficacy Analysis

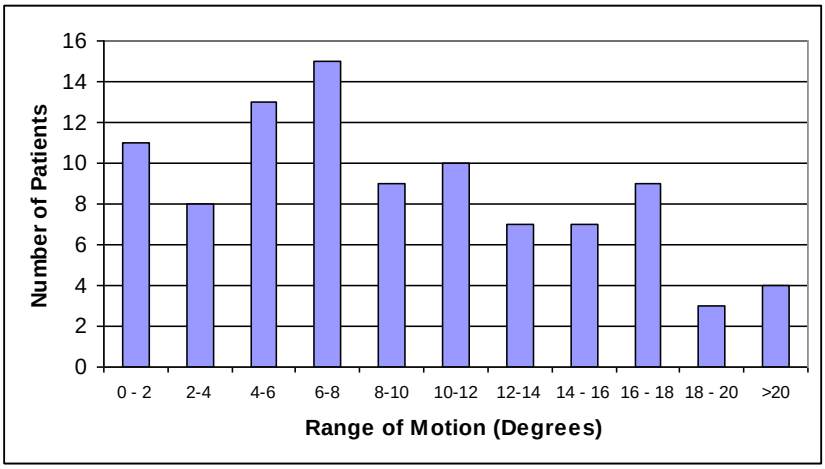
Flexion/extension range of motion (ROM) in degrees at the operative level, determined as the difference in Cobb measurements between dynamic flexion/extension lateral radiographs, was determined at pre-op, 3, 6, 12, 18 and 24 months for pro**disc**-C Total Disc Replacement.

Figure 1: pro**disc**-C Total **Disc** Replacement Time Course of Mean Flexion/Extension Range of Motion



A histogram is provided showing the range of ROM values recorded for all pro**disc**-C Total Disc Replacement subjects at 24 months. This histogram used values obtained by rounding recorded range of motion for each subject to the nearest integer.

Figure 2: Histogram of pro**disc**-C Total **Disc** Replacement Flexion/Extension ROM at 24 Months (N=96 subjects)



Analysis of the range of motion data versus overall success for the pro**disc**-C subjects with available range of motion data at 24 months was also performed. The overall success rates at month 24 of subjects with ≥4° of motion were compared to subjects with <4° of motion using both the IDE Overall Success analysis as well as the Additional Analysis (FDA) success criteria. Neither success criteria demonstrated a statistically significant difference (p=0.7439, p=0.7587 respectively) between the groups.

How Supplied

The pro**disc**-C Total Disc Replacement implants are supplied pre-packaged and sterile. The integrity of the packaging should be checked to ensure that the sterility of the contents is not compromised. Remove the implants from the packaging using aseptic technique, only after the correct size has been determined.

Conformance to Standards

The pro**disc**-C Total Disc Replacement endplates are manufactured from CoCrMo conforming to ISO 5832-12 (1996) "Implants for surgery – Metallic materials – Part 12: Wrought cobalt-chromium-molybdenum alloy. The surfaces of both inferior and superior plates that abut against the bone are plasma sprayed with CPTI conforming to ISO/DIS 5832-2 (1999) "Implants for surgery – Metallic materials– Part 2: Unalloyed titanium". The inlays are manufactured from ultra-high molecular weight polyethylene (UHMWPE) conforming to ISO 5834-2 and ASTM 648.

MRI Information

Centinel pro**disc**-C implants are labeled MR Conditional according to the terminology specified in ASTM F 2503-05, Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment.
Non-clinical testing of the pro**disc**-C demonstrated that the implant is MR Conditional. A patient with a pro**disc**-C implant may be scanned safely under the following conditions:

- **Static magnetic field** of 1.5-Tesla and 3.0-Tesla at Normal Operating Mode or First Level Controlled Mode
- **Highest spatial gradient magnetic field** of 900-Gauss/cm or less
- **Maximum MR system reported** whole body averaged specific absorption rate (SAR) of 2-W/kg for the Normal Operating Mode and 4 W/kg for the First Level Controlled Mode for 15 minutes of scanning

Note:
In non-clinical testing, a Centinel pro**disc**-C implant of largest geometrical volume and mass was tested for heating and results showed a maximum observed heating of 1.1ºC for 1.5T and a maximum observable heating of 1.9°C for 3.0T with a machine reported whole body averaged SAR of 2 W/kg as assessed by calorimetry.

Patients may be safely scanned in the MRI chamber at the above conditions. Under such conditions, the maximal expected temperature rise is less than 2°C. To minimize heating, the scan time should be as short as possible and the SAR as low as possible. Temperature rise values obtained were based upon a scan time of 15 minutes.

The above field conditions tested in a 1.5T and a 3.0T Philips Achieva (Philips Healthcare, Software release 2.6.3 SP4) MR scanner should be compared with those of the user's MR system in order to determine if the item can safely be brought into the user's MR environment. Centinel MR Conditional pro**disc**-C implants may have the potential to cause artifact in the diagnostic imaging.

Artifact Information:

MR image quality may be compromised if the area of interest is in the same area or relatively close to the position of the pro**disc**-C implant and it may be necessary to optimize MR imaging parameters in order to compensate for the presence of the implant.

A representative implant has been evaluated in the MRI chamber and worst case artifact information is provided below. Overall, artifacts created by pro**disc**-C implants may present issues if the MR imaging area of interest is in or near the area where the implant is located.

- For FFE sequence: Scan duration: 3min, TR 100ms, TE 15ms, flip angle 15° worst case artifact will extend approximately 3.5cm from the implant
- For SE sequence: Scan duration: 4min, TR 500ms, TE 20ms, flip angle 70°, worst-case artifact will extend approximately 2.5cm from the implant

Device Retrieval

Should it be necessary to remove a pro**disc**-C Total Disc Replacement, please contact Centinel Spine to receive instructions regarding the data collection, including histopathological, mechanical, and adverse event information. Please refer to the pro**disc**-C Total Disc Replacement Technique Guide for information regarding the required surgical technique for device retrieval and instructions for returning the explanted device to Centinel Spine. All explanted devices must be returned to Centinel Spine for analysis.

Please note that the disc replacement device should be removed as carefully as possible in order to keep the implant and surrounding tissue intact. Also, please provide descriptive information about the gross appearance of the device in situ, as well as descriptions of the removal methods, i.e., intact or in pieces.

Note: All implant removals must be reported immediately to Centinel Spine.

See Directions for Use at www.centinelspine.com/prodisc_reprocessing.php or call 1-484-887-8810.

Centinel Spine
900 Airport Road, Suite 3B
West Chester, PA 19380