IMPORTANT INFORMATION ON THE SECURE®-C CERVICAL ARTIFICIAL DISC

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GLOBUS MEDICAL DI104A

CAUTION: Federal (U.S.A.) Law Restricts this Device to Sale by or on the order of a Physician

How Supplied

Implant Components – Sterile
Surgical instruments – Non-Sterile (unless otherwise noted on the package label)

DESCRIPTION

The SECURE®-C Cervical Artificial Disc (SECURE®-C) is an articulating intervertebral device comprised of two endplates and a central core, and is inserted using an anterior cervical approach. The superior and inferior cobalt-chrome alloy (CoCrMo per ISO 5832-12, ASTM F1537) endplates feature multiple serrated keels and a commercially pure titanium plasma spray coating (per ISO 5832-2, ASTM F1580, F1978, F1147, and C-633) on the bone contacting surfaces. The sliding core is composed of ultra-high molecular weight polyethylene (UHMWPE per ISO 5834-2, ASTM F648), with a spherical superior interface and a cylindrical inferior interface articulating with the endplates.

SECURE®-C implants are offered in a variety of configurations to accommodate varied patient anatomy. Implant footprints are as follows (AP depth x ML width): 11x12mm, 13x14mm, and 14x16mm. SECURE®-C provides 0° or 6° lordosis options in its neutral position. Implant heights range from 7mm to 12mm, in 1mm increments. A list of SECURE®-C implants is provided in **Table 1**.

The SECURE®-C Cervical Artificial Disc is designed to allow motion in flexion and extension up to 30° (±15°), and in lateral bending to 20° (±10°). The design is intended to also allow unlimited axial rotation, and is constrained by ligaments and posterior elements. The device is also designed to permit translation of ±1.25mm in the sagittal plane.

Table 1. SECURE®-C Cervical Artificial Disc Implants

Part #	Description	Part #	Description
414.107S	SECURE®-C Core, 11x12, 7mm	414.307S	SECURE®-C Core, 14x16, 7mm
414.108S	SECURE®-C Core, 11x12, 8mm	414.308S	SECURE®-C Core, 14x16, 8mm
414.109S	SECURE®-C Core, 11x12, 9mm	414.309S	SECURE®-C Core, 14x16, 9mm
414.110S	SECURE®-C Core, 11x12, 10mm	414.310S	SECURE®-C Core, 14x16, 10mm
414.111S	SECURE®-C Core, 11x12, 11mm	414.311S	SECURE®-C Core, 14x16, 11mm
414.112S	SECURE®-C Core, 11x12, 12mm	414.312S	SECURE®-C Core, 14x16, 12mm
414.207S	SECURE®-C Core, 13x14, 7mm	714.100S	SECURE®-C Endplate Assembly, 11x12, 0°
414.208S	SECURE®-C Core, 13x14, 8mm	714.106S	SECURE®-C Endplate Assembly, 11x12, 6°
414.209S	SECURE®-C Core, 13x14, 9mm	714.200S	SECURE®-C Endplate Assembly, 13x14, 0°
414.210S	SECURE®-C Core, 13x14, 10mm	714.206S	SECURE®-C Endplate Assembly, 13x14, 6°
414.211S	SECURE®-C Core, 13x14, 11mm	714.300S	SECURE®-C Endplate Assembly, 14x16, 0°
414.212S	SECURE®-C Core, 13x14, 12mm	714.306S	SECURE®-C Endplate Assembly, 14x16, 6°

SECURE®-C devices are implanted using instruments specific to the device, as well as manual surgical instruments. Instruments specifically designed for implanting SECURE®-C consist of trials, milling guides, broaching chisels, keel chisels, chisel endcap, implant holding block, implant holders, and endplate positioners. Manual surgical instruments include instruments for cervical distraction, discectomy preparation, and milling.

INDICATIONS FOR USE

The SECURE®-C Cervical Artificial 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 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 as compared to adjacent levels. The SECURE®-C Cervical Artificial Disc is implanted using an anterior approach. Patients should have failed at least 6 weeks of conservative treatment prior to implantation of the SECURE®-C Cervical Artificial Disc.

CONTRAINDICATIONS

The SECURE®-C Cervical Artificial Disc should not be implanted in patients with the following conditions:

- Active systemic infection or localized infection at the surgical site
- Osteoporosis or osteopenia defined as a DEXA bone mineral density T-score ≤ -1
- Allergy or sensitivity to cobalt, chromium, molybdenum, titanium or polyethylene
- Marked cervical instability on neutral resting lateral or flexion/extension radiographs; translation >3mm and/or >11° rotational difference from that of either adjacent level
- Severe spondylosis at the level to be treated, characterized by bridging osteophytes, loss of disc height >50%, an absence of motion (<2°) as this may lead to a limited range of motion and may encourage bone formation (e.g. heterotopic ossification, fusion)
- Severe facet joint arthropathy
- Significant cervical anatomical deformity or 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) or disease (e.g., ankylosing spondylitis, rheumatoid arthritis)
- Symptoms attributed to more than one vertebral level

WARNINGS

The SECURE®-C Cervical Artificial Disc should only be used by surgeons who are experienced with anterior cervical spinal procedures and have undergone hands-on training in the use of this device. Only surgeons who are familiar with the implant components, instruments, procedure, clinical applications, biomechanics, adverse events, and risks associated with the SECURE®-C Cervical Artificial Disc should use this device. A lack of adequate experience and/or training may lead to a higher incidence of adverse events, including neurological complications.

Correct selection of the appropriate implant size and correct placement of the device are essential to ensure optimal performance and function of the device. Please refer to the SECURE®-C Cervical Artificial Disc Surgical Technique manual for step-by-step instructions on the required surgical technique, including determining the correct implant size.

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.

Heterotopic Ossification (HO) is a potential complication associated with cervical total disc replacement devices, which could result in reduced motion. It is recommended that bone wax is used following removal of osteophytes during surgery, to possibly reduce HO bone formation. The short-term postoperative use of non-steroidal anti-inflammatory drugs (NSAIDs), is recommended to possibly reduce the chance of developing HO.

PRECAUTIONS

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

- Intractable radiculopathy or myelopathy due to pathology at more than one level and/or pathology not localized to the disc space;
- Skeletally immature patients, pediatric or adolescent children (<21 years old), or those over the age of 60;
- Prior fusion at an adjacent vertebral level;
- Prior surgery at the level to be treated;
- 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 involved level;
- Neck or arm pain of unknown etiology;
- Neck pain alone;
- Paget's disease, osteomalacia, or other metabolic bone disease;
- Rheumatoid arthritis or other autoimmune disease;
- Neuromuscular disorders such as muscular dystrophy, spinal muscular atrophy, amyotrophic lateral sclerosis;
- Severe insulin dependent diabetes;
- Systemic disease including AIDS, HIV, and Hepatitis;
- Taking medications known to potentially interfere with bone/soft tissue healing (e.g., steroids);
- Active malignancy (including spinal metastases);
- Acute mental illness or substance abuse; and
- Pregnancy.

Pre-operative

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

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 if the DEXA bone density measured T score is < -1.0, as the patient may be osteoporotic or osteopenic.

The patient should be informed of the potential adverse effects (risks/complications) contained in this insert (see POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH).

Preoperative planning may be used to estimate the required implant size, and to assure that the appropriate range of sizes is available for surgery. The procedure should not take place if the appropriate range of sizes will not be available.

Examine all instruments prior to surgery for wear or damage. Instruments which have been used excessively may be more likely to break. Replace any worn or damaged instruments.

Intra-operative

The SECURE®-C Cervical Artificial Disc implant should not be used with components or instruments of spinal systems from other manufacturers. Refer to the SECURE®-C surgical technique manual for step-by-step instructions.

Use aseptic technique when removing the SECURE®-C Cervical Artificial Disc implants from the innermost packaging. Carefully inspect each component and its packaging for any signs of damage, including damage to the sterile barrier. Do not use SECURE®-C implants if the packaging is damaged or the implant shows signs of damage.

Use care when handling the SECURE®-C Cervical Artificial Disc 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 tissue or other debris is not trapped within the device.

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.

When preparing the disc space, remove anterior or posterior osteophytes as needed, taking care to minimize bone removal. Avoid excessive bone removal as this may weaken the vertebral endplates or vertebral body. Correct positioning of the trial is critical prior to performing chisel cuts. Care should be taken to correctly position the trial during this step. Ensure proper alignment and placement of device components as misalignment may cause excessive wear and/or early failure of the device. Bone wax should be placed into any exposed bleeding bone.

Post-operative
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. Patients are recommended to wear a cervical collar for a few weeks following surgery, follow a therapy program for active range of motion exercises, and to avoid lifting above the shoulders, heavy lifting, repetitive bending and prolonged or strenuous activities. The time period of these recommendations is managed by the treating physician, taking into consideration the individual patient's condition as well as the stability and functioning of the implant. A two week postoperative course of non-steroidal anti-inflammatories (NSAIDs) is recommended to potentially reduce the incidence of heterotopic ossification (HO).

SECURE®-C implants have not been evaluated for safety and compatibility in the MR environment, and have not been tested for heating or migration in the MR environment.

POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

The potential adverse effects (risks/complications) associated with the use of the SECURE®-C Cervical Artificial Disc include: (1) those associated with any surgical procedure; (2) those associated with anterior cervical spine surgery; and (3) those associated with a cervical artificial disc device, including the SECURE®-C Cervical Artificial Disc. However, the cause of these adverse events is not exclusive to these categories. In addition to these 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.

1. Risks associated with any surgical procedure include: abscess; cellulitis; wound dehiscence; wound, local, and/or systemic infection; 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 or genitourinary compromise; seizure, convulsion, or changes to mental status; complications of pregnancy including miscarriage and fetal birth defects; inability to resume activities of daily living; and death.

2. Risks associated with anterior cervical spine surgery include: dysphagia; dysphasia; dysphonia; hoarseness; vocal cord paralysis; laryngeal palsy; sore throat; recurring aspirations; nerve deficits or damage; tracheal, esophageal, or pharyngeal perforation; airway obstruction; external chylorrhea; warmth or tingling in the extremities; deficit or damage to the spinal cord, nerve roots, or nerves possibly resulting in paralysis or pain; dural tears or leaking; cerebrospinal fistula; discitis, arachnoiditis, and 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 a cervical artificial disc device, including the SECURE®-C Cervical Artificial Disc, include: early or late loosening of the components; disassembly; bending or breakage of any or all of the components; implant migration; implant malpositioning; loss of purchase; sizing issues with components; anatomical or technical difficulties; implant fracture; bone fracture; skin penetration, irritation, pain, and/or bursitis resulting from pressure on the skin from component parts in patients with inadequate tissue coverage over the implant; foreign body reaction to the implant including possible tumor formation, autoimmune disease, metallosis, and/or scarring; possible tissue reaction; bone resorption; bone formation (including heterotopic ossification) 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, as well as the possibility of a fragment of a broken instrument remaining in the patient; loss of neurological function; decreased strength of extremities; decreased reflexes; cord or nerve root injury; loss of bowel and/or bladder control or other types of urological system compromise; and interference with radiographic imaging because of the presence of the implant.

For the specific adverse events that occurred in the clinical study of the SECURE®-C Cervical Artificial Disc, please see the Safety Results in the CLINICAL STUDY section below. Some of the most common adverse events experienced by study patients were: neck and/or arm pain, dysesthesia, back and/or leg pain, musculoskeletal events (excluding spinal events), and difficulty swallowing.

CLINICAL STUDY

The clinical investigation of the SECURE®-C Cervical Artificial Disc was conducted under an approved IDE (G050075). The study was a prospective, multi-center, two-arm, randomized, unmasked, concurrently controlled, non-inferiority trial to assess the safety and effectiveness of the SECURE®-C Cervical Artificial Disc compared to anterior cervical discectomy and fusion (ACDF) using a plate and structural allograft for reconstruction of the disc at one level from C3-C7 following single-level discectomy for intractable radiculopathy or myelopathy due to a single-level abnormality localized to the disc space. The first five patients at each site were treated with the SECURE®-C device; subsequent patients were randomized in a 1:1 ratio at each site to receive either the SECURE®-C or control treatment. The purpose of the study was to determine whether the SECURE®-C Cervical Artificial Disc was non-inferior to the control.

Patients were treated between July 7, 2005 and April 25, 2008. A total of 380 patients were enrolled at 18 sites. Of these patients, 89 were non-randomly assigned to SECURE®-C. Of the randomized patients, 151 patients were randomized to SECURE®-C and 140 to control ACDF treatment. Final analysis was

conducted after all patients had reached the two year time point. The database for this PMA reflected data collected through January 31, 2011.

Clinical Inclusion and Exclusion Criteria
Patients were enrolled in the study according to the following inclusion/exclusion criteria:

Clinical Inclusion Criteria
Enrollment in the SECURE®-C study was limited to patients who met the following inclusion criteria:

- Symptomatic cervical disc disease (SCDD) in one vertebral level between C3-C7, defined as neck or arm (radicular) pain, or functional or neurological deficit and radiographic confirmation (by CT, MRI, X-ray, etc.) of any of the following:
  - Herniated nucleus pulposus;
  - Radiculopathy or myelopathy;
  - Spondylosis (defined by the presence of osteophytes); or
  - Loss of disc height.
- Age between 18 and 60 years
- Failed at least 6 weeks of conservative treatment
- Neck Disability Index (NDI) Questionnaire score of at least 30 (as percentage of 50 point total)
- Able to understand and sign informed consent form
- Psychosocially, mentally and physically able to fully comply with this protocol including adhering to follow-up schedule and filling out forms
- Able to meet the proposed follow-up schedule at 6 weeks, 3 months, 6 months, 12 months and 24 months
- Able to follow postoperative management program

Clinical Exclusion Criteria
Patients were not permitted to enroll in the SECURE®-C study if they met any of the following exclusion criteria:

- More than one vertebral level requiring treatment
- Prior fusion surgery adjacent to the vertebral level being treated
- Prior surgery at the level to be treated
- Clinically compromised vertebral bodies at the affected level(s) due to current or past trauma
- Radiographic confirmation of facet joint disease or degeneration, defined as apparent sclerosis and/or hypertrophy of the facets demonstrated on AP radiographs as a disruption of the normally smooth facet curve
- Marked cervical instability on resting lateral or flexion/extension radiographs:
  - Translation greater than 3mm, and/or
  - More than 11° of rotational difference from that of either adjacent level.
- Severe spondylosis at the level to be treated as characterized by any of the following:
  - Bridging osteophytes;
  - A loss of disc height greater than 50%; or
  - Absence of motion (<2°)
- Neck or arm pain of unknown etiology
- Osteoporosis, osteopenia, Paget's disease, osteomalacia or any other metabolic bone disease
- Pregnant or interested in becoming pregnant in the next 2 years
- Active systemic or local infection
- Known allergy to titanium, polyethylene, cobalt, chromium or molybdenum
- Taking medications or any drug known to potentially interfere with bone/soft tissue healing (e.g., steroids)

- Rheumatoid arthritis or other autoimmune disease
- Systemic disease including AIDS, HIV, Hepatitis
- 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 has been no clinical signs or symptoms of the malignancy for at least 5 years
- Neuromuscular disorders such as muscular dystrophy, spinal muscular atrophy, amyotrophic lateral sclerosis, etc.
- Acute mental illness or substance abuse
- Use of bone growth stimulator within past 30 days
- Participation in other investigational device or drug clinical trials within 30 days of surgery
- Prisoners

Postoperative Care

The recommended postoperative care included use of an external orthosis for 3 weeks postoperatively, followed by physical therapy program for active range of motion exercises. Patients were instructed to avoid lifting above shoulders for 3 months, and to avoid athletic activities and repetitive bending or lifting for 6 months. Smokers were encouraged not to smoke. Patients were not treated with NSAIDs postoperatively in either treatment group. Some reports in the literature show that short-term postoperative use of NSAIDs may reduce the incidence of heterotopic ossification in some total disc replacement patients.

Follow-up Schedule

All patients were scheduled to return for follow-up examinations at 6 weeks (±2 weeks), 3 months (±2 weeks), 6 months (±1 month), 12 months (±2 months), 24 months (±2 months), and annually thereafter (±2 months), as shown in **Table 2**. All adverse events (device-related or not) were monitored over the course of the study and radiographic assessments were done by an independent core laboratory. All adverse events were independently adjudicated (for adverse event code, severity, and relationship to the device and/or procedure) by a Clinical Events Committee comprised of two practicing spine surgeons. At each evaluation time point, the following clinical and radiographic outcomes were evaluated per the clinical evaluation schedule below: the Neck Disability Index (NDI) to assess pain and function, Visual Analog Scale (VAS) to assess neck and arm pain, neurologic status, general health status as assessed based on the SF-36, medication usage, patient satisfaction with surgery, radiographic parameters, and overall success. Radiographic parameters evaluated included range of motion (angulation and translation), disc height, device displacement, radiolucency, fusion status, and heterotopic ossification. Overall success was determined based on data collected during the initial 24 months of follow-up.

Table 2. Clinical Evaluation Schedule

Evaluation	Pre-op	Surgery/ Hospital Discharge	6 wks	3 mo	6 mo	12 mo	24 mo & annually
Neck Disability Index	X		X	X	X	X	X
Neck and Arm Pain (VAS)	X		X	X	X	X	X
Health Status (SF-36)	X		X	X	X	X	X
Neurological Status	X				X	X	X
Adverse Events*	X	X	X	X	X	X	X
Demographic/Baseline Data	X						
Operative Data		X					
Medication Use	X				X	X	X

Evaluation	Pre-op	Surgery/ Hospital Discharge	6 wks	3 mo	6 mo	12 mo	24 mo & annually
Imaging Studies:							
AP & lateral	X	X	X	X	X	X	X
Lateral flex/extension	X				X	X	X
CT and/or MRI	X						
Radiographic Outcomes:							
Range of motion	X				X	X	X
Disc height	X				X	X	X
Device migration			X	X	X	X	X
Fusion status					X	X	X
Radiolucency					X	X	X
Patient Satisfaction						X	X

*Adverse events and complications were recorded at all visits (both scheduled and unscheduled).

Clinical Endpoints

The safety of the SECURE®-C was assessed by comparing the nature and frequency of adverse events (overall and in terms of severity and relationship to the device and/or procedure) and secondary surgical procedures as well as maintenance or improvement in neurological status to the ACDF control group.

The effectiveness of the SECURE®-C was assessed by evaluating improvement in the Neck Disability Index (NDI), neck and arm pain based on a Visual Analog Scale (VAS), and quality of life using the short-form 36 questionnaire (SF-36) as well as patient satisfaction compared to the ACDF control group.

In addition, several radiographic endpoints were considered in evaluating both safety and effectiveness, including range of motion, disc height, device displacement or migration, radiolucency, spinal fusion status, and heterotopic ossification.

Per the protocol, an individual patient was considered a success if the following criteria were met at 24 months:

- Pain/disability improvement of at least 25% in NDI compared to baseline;
- No device failures requiring revision, removal, reoperation, or supplemental fixation;
- Absence of major complications defined as major vessel injury, neurological damage, or nerve injury; and
- For control fusion patients only, radiographic fusion, as defined by the presence of bridging trabecular bone, without evidence of pseudarthrosis (defined radiographically as no apparent bridging trabecular bone and range of motion >3mm in translation and >2° in rotation).

In addition, FDA requested an additional analysis in which an individual patient was considered a success if the following criteria were met at 24 months:

- Pain/disability improvement of at least 15 points in NDI compared to baseline;
- No secondary surgery at the index level including revision, removal, reoperation or supplemental fixation;
- No potentially device-related adverse events;
- Maintenance or improvement in all components of neurologic status; and
- No SECURE®-C intraoperative changes in treatment.

Overall study success criteria were based on a comparison of individual patient success rates, such that the patient success rate for the SECURE®-C investigational group must be non-inferior to that of the ACDF fusion control group. The IDE study was approved using a non-inferiority margin (delta) of 15%

with an advisory that a non-inferiority margin of 10% would be required to demonstrate a reasonable assurance of the device's effectiveness. According to the statistical analysis plan, if non-inferiority was demonstrated, then superiority would be evaluated as defined more specifically in the analysis plan. Of note, the statistical analysis plan pre-specified that the analysis technique would involve predicting 24 month outcomes for those without them, based on interim 6 month and 12 month observed outcomes, and integrating over the predictions to obtain posterior probabilities of non-inferiority and superiority.

Secondary effectiveness evaluations specified in the protocol included comparisons of the following:

- Components of the primary
  - Pain/Disability Improvement (NDI)
  - No device failures requiring revision, re-operation or removal
  - Absence of major complications
- Neck Disability Index: 25% improvement from baseline
- VAS pain scales (neck, right, and left arm): 20mm improvement from baseline
- Health Status Survey SF-36 (mental and physical composite scores): 15% improvement from baseline
- Neurological status (maintenance, worsening, or improvement): proportion of patients maintained or improved
- Mean range of motion (angulation and translation)
- Disc height on standard lateral radiograph: 2mm changes compared to baseline
- No significant radiolucency for the SECURE®-C device: proportion of patients
- Spinal fusion in the control arm
- Patient satisfaction (definitely/mostly): proportion of patients
- Device displacement or migration (>3mm)
- Operative time
- Operative blood loss
- Return to work

Accountability of PMA Cohort

A total of 380 patients at 18 sites were enrolled and treated in the IDE clinical trial; 236 received SECURE®-C (88 non-randomized, 148 randomized) and 144 received control treatment. At the time of database lock, of the 380 patients enrolled in the PMA study, all had reached the 24 month post-operative visit and 331 (87.1%) had data available for analysis at the completion of the study. Complete primary endpoint data (including fusion status for control group patients) was available for 215 investigational (77 non-randomized, 138 randomized) and 98 control patients at 24 months. A total of 5 investigational (2 non-randomized and 3 randomized) and 10 control patients had failures at or prior to the 24 month visit. 36 month follow-up data was also provided in the PMA for some of the study patients. A summary of patient accountability data for 12 month, 24 month, and 36 month follow-up is provided in **Table 3.**

Table 3. Patient Accountability (based on treatment assignment*)

Number of Patients	12 Months (±2 Months)			24 Months (±2 Months)			36 Months (±2 Months)		
	NR SEC	R SEC	R ACDF	NR SEC	R SEC	R ACDF	NR SEC	R SEC	R ACDF
Enrolled	89	151	140	89	151	140	89	151	140
Theoretical	89	151	140	89	151	140	89	151	140
Deaths[1]	1	0	0	1	0	0	1	0	0
Failures[1]	1	1	6	2	3	10	2	4	11
Not yet overdue	0	0	0	0	0	0	1	15	8
Expected[2]	87	150	134	86	148	130	85	132	121
Actual, efficacy[3] (% Follow-up)	82 (94.3%)	140 (93.3%)	114 (85.1%)	77 (89.5%)	138 (93.2%)	98 (75.4%)	60 (70.6%)	60 (45.5%)	38 (31.4%)

Number of Patients	12 Months (±2 Months)			24 Months (±2 Months)			36 Months (±2 Months)		
	NR SEC	R SEC	R ACDF	NR SEC	R SEC	R ACDF	NR SEC	R SEC	R ACDF
Actual, efficacy in window[4] (% Follow-up)	81 (93.1%)	127 (84.7%)	99 (73.9%)	70 (81.4%)	110 (74.3%)	83 (63.8%)	38 (44.7%)	43 (32.6%)	26 (21.5%)
Actual, any data[5] (% Follow-up)	82 (94.3%)	140 (93.3%)	121 (90.3%)	78 (90.7%)	138 (93.2%)	115 (88.5%)	60 (70.6%)	60 (45.5%)	47 (38.8%)

NR SEC=Non-randomized SECURE®-C; R SEC=Randomized SECURE®-C; R ACDF=Control

* A total of 380 patients at 18 sites were enrolled and treated in the IDE clinical trial; 236 received SECURE®-C (88 non-randomized, 148 randomized) and 144 received control treatment. Four patients intended to be treated with SECURE®-C (1 non-randomized and 3 randomized) were intraoperatively treated by the investigator with ACDF; one was due to a randomization error by the site, one was due to inability to visualize the disc space due to the patient's large shoulders, and two were due to small patient anatomy.

1 Deaths and failures are cumulative

2 Theoretical patients minus the number of deaths, failures, and not yet overdue

3 Patients with complete efficacy data

4 Patients with complete efficacy data within the specified visit window

5 Patients with any information recorded at the visit

The as-treated population is used for safety analyses (88 non-randomized SECURE®-C, 148 randomized SECURE®-C, 144 ACDF) and the as-randomized population is used for efficacy analyses (89 non-randomized SECURE®-C, 151 randomized SECURE®-C, 140 ACDF). Statistical comparisons for efficacy are made between randomized groups, for patients as they were intended to be treated, referred to as the "As-Randomized" population. Safety comparison such as adverse events and radiographic measurements are made between randomized groups, for patients as they were actually treated, referred to as the "As-Treated" population.

Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a cervical artificial disc study performed in the US. Select demographic data and preoperative evaluations for all patients enrolled and treated in the study are included in **Table 4** and **Table 5**. Bayesian Credible Intervals (BCIs) between the randomized groups are presented for all comparison tables. There were no differences in gender, age, race (caucasian vs. other), height, weight or BMI between the two randomized groups, as evidenced by the 95% BCIs all containing zero. In addition, there were no differences in preoperative evaluations (NDI, VAS, SF-36) between the two randomized groups, except for SF-36 PCS which was slightly higher for the SECURE®-C group.

Table 4. Patient Demographics and Baseline Characteristics

Demographic Measure	Non-Randomized SECURE-C (N=89)	Randomized SECURE-C (N=151)	Randomized ACDF (N=140)	95% BCI (Randomized Groups)
Gender				
Male	47 (52.8%)	81 (53.6%)	68 (48.6%)	(-6.4%, 16.3%)
Female	42 (47.2%)	70 (46.4%)	72 (51.4%)	
Age (years)	41.6 ±8.13 Range: 20 – 60	43.4 ±7.50 Range: 24 – 60	44.4 ±7.86 Range: 25 – 59	(-2.7, 0.8)
Race				
Caucasian	79 (88.8%)	136 (90.1%)	126 (90.0%)	(-6.8%, 7.2%)*
Black	6 (6.7%)	10 (6.6%)	10 (7.1%)	
Asian	0	0	0	
Hispanic	2 (2.2%)	2 (1.3%)	3 (2.1%)	
Other	2 (2.2%)	3 (2.0%)	1 (0.7%)	
Height (in)	67.3 ±4.03 Range: 59 – 76	68.1 ±3.68 Range: 60 – 76	67.3 ±4.07 Range: 60 – 77	(-0.1, 1.7)

Demographic Measure	Non-Randomized SECURE-C (N=89)	Randomized SECURE-C (N=151)	Randomized ACDF (N=140)	95% BCI (Randomized Groups)
Weight (lbs)	181.6 ±46.05 Range: 110 – 330	191.6 ±45.87 Range: 104 – 365	187.1 ±40.32 Range: 107 – 320	(-5.5, 14.4)
BMI (kg/m^2)	27.9 ±5.36 Range: 19 – 34	28.9 ±5.53 Range: 18 – 48	29.0 ±5.47 Range: 20 – 45	(-1.4, 1.2)
Current tobacco use (yes)**	21 (23.6%)	51 (33.8%)	53 (37.9%)	(-14.9%, 6.9%)
Symptom duration (mo)	25.4 ±44 Range: 1 – 304	16.6 ±27 Range: 0 – 189	19.8 ±40 Range: 0 – 272	(-11.2, 4.7)
History non-op care (yes) • Narcotics use • Injections • Physical therapy • Brace • Chiropractic • Other	85 (95.5%) • 63 (70.8%) • 47 (52.8%) • 53 (59.6%) • 13 (14.6%) • 20 (22.5%) • 13 (14.6%)	147 (97.4%) • 108 (71.5%) • 57 (37.7%) • 85 (56.3%) • 12 (7.9%) • 35 (23.2%) • 44 (29.1%)	138 (98.6%) • 104 (74.3%) • 62 (44.3%) • 77 (55.0%) • 14 (10.0%) • 44 (31.4%) • 37 (26.4%)	(-5.0%, 2.5%)
History prior surgery (yes) • Discectomy • Other	4 (4.5%) • 0 • 4 (4.5%)	2 (1.3%) • 0 • 2 (1.3%)	4 (2.9%) • 2 (1.4%) • 3 (2.1%)	(-5.6%, 2.1%)
Medication use in prior week for neck/arm pain (yes) • Non-narcotics • Weak narcotics • Strong narcotics • Muscle relaxants	 • 63 (70.8%) • 41 (46.1%) • 25 (28.1%) • 33 (37.1%)	 • 109 (72.2%) • 71 (47.0%) • 50 (33.1%) • 51 (33.8%)	 • 96 (68.6%) • 62 (44.3%) • 44 (31.4%) • 57 (40.7%)	 (-6.8%, 14.0%) (-8.7%, 14.0%) (-9.0%, 12.3%) (-17.9%, 4.2%)
Preoperative pain status: • Arm and neck pain • Arm pain only • Neck pain only	 • 82 (92.1%) • 2 (2.2%) • 4 (4.5%)	 • 144 (95.4%) • 4 (2.6%) • 2 (1.3%)	 • 134 (95.7%) • 5 (3.6%) • 1 (0.7%)	 (-5.3%, 4.8%) (-5.5%, 3.3%) (-2.4%, 3.6%)
Preoperative radiographic findings: • Herniated nucleus pulposus • Spondylosis • Loss of disc height	 • 62 (69.7%) • 55 (61.8%) • 14 (15.7%)	 • 127 (84.1%) • 83 (55.0%) • 16 (10.6%)	 • 123 (87.9%) • 79 (56.4%) • 19 (13.6%)	 (-11.6%, 4.3%) (-12.7%, 9.9%) (-10.6%, 4.5%)

*Caucasian vs. other; **Data on amount and length of tobacco use was not captured.

Table 5. Preoperative Evaluation of Endpoints

Variable	Non-Randomized SECURE-C (N=89)	Randomized SECURE-C (N=149)	Randomized ACDF (N=142)	95% BCI (Randomized Groups)
NDI	50.1 ±15.03	51.8 ±13.84	51.5 ±14.86	(-3.0, 3.7)
VAS Neck Pain*	64.1 ±26.18	65.2 ±26.84	63.4 ±27.34	(-4.8, 8.2)
VAS Left Arm Pain*	38.8 ±35.48	45.1 ±37.35	39.8 ±36.28	(-3.5, 14.1)
VAS Right Arm Pain*	34.9 ±36.71	33.8 ±37.03	37.9 ±37.09	(-12.9, 4.8)
SF-36 PCS	33.8 ±7.71	33.9 ±7.41	32.0 ±6.48	(0.2, 3.4)
SF-36 MCS	42.9 ±11.01	44.0 ±13.16	44.4 ±11.97	(-3.3, 2.5)
Neurological Status (normal) • Motor • Sensory • Reflexes	22 (24.7%) • 50 (56.2%) • 59 (66.3%) • 60 (67.4%)	31 (20.5%) • 68 (45.0%) • 69 (45.7%) • 92 (60.9%)	28 (20.0%) • 68 (48.6%) • 66 (47.1%) • 95 (67.9%)	(-8.8%, 9.7%)

Variable	Non-Randomized SECURE-C (N=89)	Randomized SECURE-C (N=149)	Randomized ACDF (N=142)	95% BCI (Randomized Groups)
• Other assessments	• 58 (65.2%)	• 97 (64.2%)	• 86 (61.4%)	
Baseline ROM angulation (°)	9.5 ±5.2 Range: 0.3 – 23.4	8.5 ±4.8 Range: 0.1 – 23.3	7.2 ±4.3 Range: 0.1 – 19.3	(0.2, 2.4)
Baseline ROM translation (mm)	1.0 ±0.75 Range: 0 – 3.4	0.9 ±0.62 Range: 0 – 3.4	0.8 ±0.59 Range: 0 – 2.7	(0.0, 0.3)

* Per FDA, VAS data excludes one site in which some scores were reported verbally rather than written

Surgery and Hospitalization

Surgical data is provided in **Table 6**. The posterior probability that the mean or proportion is lower in the randomized SECURE®-C group than the ACDF group is included in the table. The most common surgical levels were C5-C6 and C6-C7. Mean surgery time was 15.6 min longer for the randomized investigational SECURE®-C group than for the control ACDF group (statistically different). Mean blood loss was also higher by 9.6 milliliters in the randomized SECURE®-C group, and this was borderline statistically significant although likely not clinically significant Mean return to work time was 6 days shorter for the SECURE®-C group than the ACDF group (not statistically different).

Table 6. Surgical Data

Measure	Non-Randomized SECURE-C (N=89)	Randomized SECURE-C (N=151)	Randomized ACDF (N=140)	Posterior Probability *	Posterior Probability **
Treated Level					
C3-C4 (%)	3 (3.4%)	5 (3.3%)	4 (2.9%)	0.4230	0.5529
C4-C5 (%)	7 (7.9%)	8 (5.3%)	11 (7.9%)	0.8075	0.7977
C5-C6 (%)	48 (53.9%)	75 (49.7%)	70 (50.0%)	0.5226	0.7366
C6-C7 (%)	31 (34.8%)	63 (41.7%)	55 (39.3%)	0.3372	0.1482
Surgery Time (min)	98.4 ±34.80	87.7 ±33.02	72.1 ±25.41	<0.0001	0.9878
Blood Loss (mls)	55.6 ±43.93	55.2 ±44.22	45.6 ±33.21	0.0254	0.4540
Classification					
Inpatient (<23 hrs)	62 (69.7%)	92 (60.9%)	87 (62.1%)	0.5830	0.9878
Outpatient (>23 hrs)	27 (30.3%)	59 (39.1%)	53 (37.9%)		
Hospitalization (days)	1.2 ±0.56	1.0 ±0.46	0.9 ±0.46	0.4058	0.9112
Return to Work Time (days)	46.4 ±32.40	44.0 ±71.47	50.0 ±72.21	0.5545	0.9934

Mean ± standard deviation

*Posterior probability that mean or proportion is lower in the randomized SECURE-C group compared to ACDF

**Posterior probability that mean or proportion is lower in the randomized SECURE-C group compared to the non-randomized SECURE-C group

A total of 236 SECURE®-C devices were implanted during the study. The design, footprint and height of the SECURE®-C devices used are presented in **Table 7**.

Table 7. SECURE®-C Implant Sizes/Options

Size/Option	Devices (%)	Size/Option	Devices (%)
Design		*Height*	
0° (Parallel)	54 (22.9%)	7mm	210 (89.0%)
6° (Lordotic)	182 (77.1%)	8mm	25 (10.6%)
Footprint		9mm	1 (0.4%)
11mm x 12mm	69 (29.2%)	10mm	0 (0.0%)
13mm x 14mm	159 (67.4%)	11mm	0 (0.0%)
14mm x 16mm	8 (3.4%)	12mm	0 (0.0%)
Device Combination			
11mm x 12mm footprint and 7mm height			69 (29.2%)

13mm x 14mm footprint and 7mm height	136 (57.6%)
13mm x 14mm footprint and 8mm height	22 (9.3%)
13mm x 14mm footprint and 9mm height	1 (0.4%)
14mm x 16mm footprint and 7mm height	5 (2.1%)
14mm x 16mm footprint and 8mm height	3 (1.3%)

Safety and Effectiveness Results

Safety Results

The analysis of safety was based on the as-treated cohort of 380 total patients (88 non-randomized SECURE®-C patients, 148 randomized SECURE®-C patients, and 144 ACDF patients). A summary of the total number of adverse events, events classified by the Clinical Events Committee (CEC) as device-related, events classified by the CEC as surgery-related, events classified by the CEC as severe or life-threatening, events within 48 hours of the original procedure, and device failures (defined as a revision, removal, reoperation or supplemental fixation) are shown in **Table 8.**

Table 8. Adverse Event Summary

		NR SEC (N=88)	R SEC (N=148)	R ACDF (N=144)	Statistics*
All Adverse Events (AEs)	Patients (%)	60 (68.2%)	107 (72.3%)	114 (79.2%)	(-17.0%, 2.4%)
	Events (E/pt)	130 (1.48)	247 (1.67)	294 (2.04)	0.9978
Device-Related AEs	Patients (%)	2 (2.3%)	4 (2.7%)	14 (9.7%)	(-13.0%, -1.5%)
	Events (E/pt)	2 (0.02)	4 (0.03)	17 (0.12)	0.9990
Surgery-Related AEs	Patients (%)	4 (4.5%)	9 (6.1%)	18 (12.5%)	(-13.3%, 0.2%)
	Events (E/pt)	4 (0.05)	10 (0.07)	20 (0.14)	0.9789
Severe or Life-Threatening AEs	Patients (%)	17 (19.3%)	29 (19.6%)	34 (23.6%)	(-13.6%, 5.3%)
	Events (E/pt)	23 (0.26)	38 (0.26)	44 (0.31)	0.8378
AEs within 48 hrs of surgery	Patients (%)	1 (1.1%)	3 (2.0%)	7 (4.9%)	Not provided
	Events	1 (0.01)	4 (0.03)	8 (0.06)	Not provided
Device Failures (revision, reoperation, removal, or supplemental fixation)		2	4	17	0.9990

NR SEC=Non-randomized SECURE®-C; R SEC=Randomized SECURE®-C; R ACDF=Control

*For patient comparison: 95% BCI (lower, upper) for comparison of the difference (SECURE®-C - control) between randomized groups

*For event comparison: Posterior probability that the event rate (E/pt) is lower in the SECURE®-C group than the ACDF group

Note: For statistical comparisons of only randomized patients, ACDF group excludes 1 non-randomized patient, therefore N=143.

Table 9 provides data on the total number of adverse events in each treatment group stratified by level treated. The percentage of subjects with adverse events was similar for the SECURE®-C and ACDF groups, for all treated levels.

Table 9. Total Adverse Events by Level Treated

Level Treated	NR SEC	R SEC	R ACDF	95% BCI (lower, upper)
C3-4	1/3 (33.3%)	5/5 (100%)	4/4 (100%)	(-35.3%, 42.4%)
C4-5	5/7 (71.4%)	5/8 (62.5%)	11/11 (100%)	(-64.6%, -1.2%)
C5-6	30/47 (63.8%)	56/74 (75.7%)	56/72 (77.8%)	(-16.5%, 10.5%)
C6-7	24/31 (77.4%)	41/61 (67.2%)	43/57 (75.4%)	(-23.8%, 8.2%)

NR SEC=Non-randomized SECURE®-C; R SEC=Randomized SECURE®-C; R ACDF=Control

The adverse events reported in the PMA clinical study from all 236 SECURE®-C patients and 144 ACDF patients are shown in **Table 10**. This table includes adverse events from all patients, randomized and non-randomized, to establish the safety profile of the device. Adverse events are listed in alphabetical

order. Definitions of adverse event categories are provided in **Table 11**. Adverse event rates are based on the number of patients having at least one occurrence of an adverse event, divided by the number of patients in that treatment group. Events per patient are based on the number of adverse events, divided by the number of patients. Note that patients with the same event reported within a window are counted once but may appear in multiple time points for the same event. The overall adverse event profile (percentage of patients experiencing at least one adverse event) is qualitatively lower for the randomized SECURE®-C group (70.8%) than the control ACDF group (79.2%), but is not statistically different. In addition, the overall number of adverse events per patient is lower for the SECURE®-C group(s) than the ACDF group (posterior probability 0.9978). In the SECURE®-C group, the most common adverse events were neck pain, upper extremity pain, back and/or lower extremity pain, and trauma.

One non-randomized SECURE®-C patient died of cardiopulmonary arrest 210 days after surgery. The patient had poor cardiovascular fitness and the event was not considered to be associated with the device by the investigator or the Clinical Events Committee (CEC). One randomized ACDF patient died of unknown causes 1111 days after surgery. No other patients died during the study.

Table 10. Adverse Events in the US IDE Study (All Patients)

Adverse Event	Intra-Op (0-2 days)		Peri-Op (>2days-6wks)		Short Term (>6wks-12mo)		Long Term (>12mo -24mo)		Longer Term (>24mo)		SECURE-C (N=236)		ACDF (N=144)	
	SEC	ACF	SEC	ACF	SEC	ACF	SEC	ACF	SEC	ACF	Patients (%)	Events (E/Pt)	Patients (%)	Events (E/Pt)
All Adverse Events											**167 (70.8%)**	**377 (1.60)**	**114 (79.2%)**	**294 (2.04)**
Cancer[1]	0	0	0	0	1	0	1	0	2	0	4 (1.7%)	4 (0.02)	0 (0.0%)	0 (0.00)
Cardiovascular	0	0	1	0	4	0	4	0	0	1	8 (3.4%)	10 (0.04)	1 (0.7%)	1 (0.01)
Carpal Tunnel Syndrome (CTS)	0	0	1	0	8	5	2	3	1	0	12 (5.1%)	12 (0.05)	8 (5.6%)	8 (0.06)
Cerebrovascular	0	0	1	0	1	0	1	1	0	1	3 (1.3%)	3 (0.01)	2 (1.4%)	3 (0.02)
Compressive Peripheral Neuropathy (Non-CTS)	0	0	2	0	2	0	2	0	1	0	7 (3.0%)	7 (0.03)	0 (0.0%)	0 (0.00)
Death	0	0	0	0	1	0	0	0	0	1	1 (0.4%)	1 (0.01)	1 (0.7%)	1 (0.01)
Dysesthesia - Lower Extremities	0	0	0	0	2	1	0	0	0	0	2 (0.8%)	2 (0.01)	1 (0.7%)	1 (0.01)
Dysesthesia – Other	0	0	2	1	0	2	0	0	0	0	2 (0.8%)	2 (0.01)	3 (2.1%)	3 (0.02)
Dysesthesia - Upper Extremities	1	0	3	5	10	9	3	2	5	1	20 (8.5%)	25 (0.11)	15 (10.4%)	18 (0.13)
Dysphagia	0	4	4	3	1	1	1	0	0	0	6 (2.5%)	6 (0.02)	8 (5.6%)	8 (0.06)
Dysphonia	0	1	0	1	1	0	0	0	0	0	1 (0.4%)	1 (0.01)	2 (1.4%)	2 (0.01)
Gastrointestinal	0	0	0	1	4	0	2	0	0	0	6 (2.5%)	6 (0.02)	1 (0.7%)	1 (0.01)
Headache	0	0	1	2	4	5	1	3	2	1	8 (3.4%)	8 (0.03)	11 (7.6%)	11 (0.08)
Infection – Other	0	0	0	1	2	2	1	0	0	0	3 (1.3%)	3 (0.01)	3 (2.1%)	3 (0.02)
Infection - Superficial Wound	0	0	0	2	0	0	0	0	0	0	0 (0.0%)	0 (0.00)	2 (1.4%)	2 (0.01)
Muscle Spasms	0	0	0	0	0	0	0	1	0	0	0 (0.0%)	0 (0.00)	1 (0.7%)	1 (0.01)
Musculoskeletal	0	0	4	1	16	5	8	2	3	2	30 (12.7%)	36 (0.15)	9 (6.3%)	10 (0.07)
Neurological	0	0	1	1	1	2	0	1	1	0	3 (1.3%)	3 (0.01)	4 (2.8%)	7 (0.05)
Other*	1	1	1	2	5	1	2	1	2	1	11 (4.7%)	11 (0.05)	4 (2.8%)	6 (0.04)
Pain - Back and/or Lower Extremities	0	0	2	3	16	11	8	4	10	7	36 (15.3%)	37 (0.16)	23 (16.0%)	28 (0.20)
Pain - Neck	1	0	13	17	21	21	6	5	12	4	50 (21.2%)	53 (0.22)	41 (28.5%)	51 (0.35)
Pain - Neck and Upper Extremities	0	0	8	7	13	13	4	5	3	3	26 (11.0%)	29 (0.12)	28 (19.4%)	28 (0.19)
Pain - Neck and Upper Extremities with Dysesthesia	0	0	1	0	0	3	0	0	0	0	1 (0.4%)	1 (0.01)	3 (2.1%)	3 (0.02)
Pain - Neck with Dysesthesia	0	0	0	1	2	3	0	0	0	0	2 (0.8%)	2 (0.01)	4 (2.8%)	4 (0.03)
Pain – Other	1	0	0	0	1	0	0	0	0	1	2 (0.8%)	2 (0.01)	1 (0.7%)	1 (0.01)
Pain - Upper Extremities	1	2	10	9	12	8	9	3	6	5	32 (13.6%)	43 (0.18)	24 (16.7%)	28 (0.20)
Pain - Upper Extremities with Dysesthesia	0	0	1	0	3	1	0	1	1	0	5 (2.1%)	5 (0.02)	2 (1.4%)	3 (0.02)

Adverse Event	Intra-Op (0-2 days)		Peri-Op (>2days-6wks)		Short Term (>6wks-12mo)		Long Term (>12mo -24mo)		Longer Term (>24mo)		SECURE-C (N=236)		ACDF (N=144)	
	SEC	ACF	SEC	ACF	SEC	ACF	SEC	ACF	SEC	ACF	Patients (%)	Events (E/Pt)	Patients (%)	Events (E/Pt)
Psychological	0	0	1	0	0	0	0	0	0	1	1 (0.4%)	1 (0.01)	1 (0.7%)	1 (0.01)
Surgery - Adjacent Level	0	0	0	0	2	0	0	0	2	2	4 (1.7%)	4 (0.02)	2 (1.4%)	3 (0.02)
Surgery - Index Level	0	0	1	4	2	4	2	2	2	4	6 (2.5%)	7 (0.03)	14 (9.7%)	17 (0.00)
Surgery - Lumbar Level	0	0	0	2	4	2	1	0	1	1	6 (2.5%)	6 (0.03)	5 (3.5%)	7 (0.05)
Surgery - Other Cervical	0	0	0	0	0	0	0	0	0	1	0 (0.0%)	0 (0.00)	1 (0.7%)	1 (0.00)
Surgery - Thoracic Level	0	0	0	0	1	0	0	0	0	0	1 (0.4%)	1 (0.01)	0 (0.0%)	0 (0.00)
Trauma	0	0	7	3	13	8	6	7	6	2	30 (12.7%)	42 (0.18)	17 (11.8%)	28 (0.20)
Urogenital	0	0	0	0	0	0	0	0	1	0	1 (0.4%)	1 (0.01)	0 (0.0%)	0 (0.00)
Weakness	0	0	0	0	2	1	1	0	0	0	3 (1.3%)	3 (0.01)	1 (0.7%)	1 (0.01)
Wound Issue	0	0	0	4	0	0	0	0	0	0	0 (0.0%)	0 (0.00)	4 (2.8%)	4 (0.03)

SEC = all SECURE®-C Cervical Artificial Disc; ACDF = Anterior Cervical Discectomy and Fusion (Control)

[1] 3 non-randomized SEC: prostate cancer at 692 days, metastatic colon cancer at 959 days, metastatic esophageal cancer at 979 days; 1 randomized SEC: lymphoma at 358 days

*Other: diabetes (SEC, ACDF), thyroid disease (2 SEC, ACDF), hemolytic syndrome (SEC), Wegener's granulomatosis (SEC), CSF leak after lumbar ESI (SEC), corneal abrasion (SEC), allergic reaction to medication (SEC) or to cervical collar material (2 ACDF), lightheadedness (SEC), flu symptoms (ACDF), occasional clicking (ACDF), mild lump in throat without dysphagia (SEC), and snoring (SEC).

Table 11. Adverse Event Categories

Category	Definition
Cancer	A malignancy or malignant tumor/neoplasm
Cardiovascular	Any condition of the heart and/or blood vessels (excluding the blood vessels that supply the brain)
Carpal Tunnel Syndrome (CTS)	Condition with entrapment of the median nerve in the carpal tunnel
Cerebrovascular	Any condition relating to the brain and the blood vessels that supply it
Compressive Peripheral Neuropathy (Non-CTS)	Dysfunction of one or more nerves excluding Carpal Tunnel Syndome
Death	The termination of life
Dysesthesia - Lower Extremities	Dysesthesia in the lower extremities including hips, buttocks, legs, knees, feet, toes
Dysesthesia - Other	Dysesthesia in areas excluding the upper and lower extremities
Dysesthesia - Upper Extremities	Dysesthesia in the upper extremities including include neck, shoulders, arms, elbows, hands, fingers
Dysphagia	Difficulty in swallowing
Dysphonia	Difficulty in speaking
Gastrointestinal	Any condition pertaining to the stomach and intestines
Headache	Pain in various parts of the head, but not confined to the area of distribution of any nerve
Infection - Superficial Wound	An infection near the surface of the surgical incision
Infection - Other	An infection in an area other than the surgical incision
Muscle Spasms	A sudden contraction of muscle(s), excluding neck or upper extremity spasms which are considered to be pain
Musculoskeletal	Any condition pertaining to the muscles and skeleton, such as fracture, ligament tear, arthritis of any kind, and degenerative conditions, excluding muscle spasms and events related to spinal degenerative conditions
Neurological	Any condition pertaining to a disorder of the nervous system, e.g. Multiple Sclerosis, Parkinson's Disease, Alzheimer's
Other	An adverse event not associated with any other term
Pain - Back and/or Lower Extremities	Pain* (including stiffness, strain, tightness) in back, and/or hip, leg, ankle, feet, or buttock; includes pain with or without dysesthesia
Pain - Neck	Pain* in the neck

Category	Definition
Pain - Neck and Upper Extremities	Pain* in the neck *and* shoulder, arm, wrist, or hand
Pain - Neck and Upper Extremities with Dysesthesia	Pain* in the neck *and* shoulder, arm, wrist, or hand w/ dysesthesia
Pain - Neck with Dysesthesia	Pain* in the neck with dysesthesia
Pain - Other	Pain* in an area that is not the back or lower extremities, or the neck or upper extremities
Pain - Upper Extremities	Pain* in the shoulder, arm, wrist or hand
Pain - Upper Extremities with Dysesthesia	Pain* in the shoulder, arm, wrist or hand with dysesthesia
Psychological	Any psychological condition
Surgery - Index Level	A secondary surgical procedure performed at the index level (originally treated) of the cervical spine, which may include an adjacent level if the index level is operated at same time
Surgery - Adjacent Level	A surgical procedure performed at an adjacent level or level(s) to the index surgery only
Surgery - Other Cervical	A surgical procedure performed at a cervical level that is not the index level or adjacent level(s)
Surgery - Thoracic Level	A surgical procedure performed at a thoracic level or levels, that is an adjacent level(s) to the index surgery
Surgery - Lumbar Level	A surgical procedure performed at a lumbar level.
Trauma	Physical injury caused by a physical force or traumatic event (e.g. motor vehicle accident, fall, etc.)
Urogenital	Any condition of, relating to, affecting, treating, or being the organs or functions of excretion and reproduction
Weakness	Any symptom of weakness or fatigue of the neck and/or upper extremities, not associated with pain or dysesthesia
Wound Issue	Any issue of surgical incision, such as hematoma, excluding infection

Bayesian methods were used to analyze the primary endpoint, and were also used to compare adverse events in the randomized groups. The analysis results are provided in **Table 12**, with 95% Bayesian Credible Intervals (BCI) for the difference in adverse event rates (SECURE-C – ACDF). BCIs that include zero indicate no statistical difference in proportions between randomized groups. Based on the BCIs, there were no differences between groups for all adverse events, except neck and upper extremity pain and surgery-index level, which is statistically lower for SECURE®-C, and musculoskeletal (which excludes spinal events), which is statistically higher for SECURE®-C.

Table 12. Statistical Comparison of Adverse Events (Randomized Patients As Treated)

Adverse Event	Patients Experiencing Adverse Events (%)		95% BCI (lower, upper)
	SEC (N=148)	ACDF (N=144)	
Any Adverse Event	**107 (72.3%)**	**114 (79.7%)**	**(-17.0%, 2.4%)**
Cancer	1 (0.7%)	0 (0.0%)	(-1.6%, 3.2%)
Cardiovascular	2 (1.4%)	1 (0.7%)	(-2.3%, 3.7%)
Carpal Tunnel Syndrome (CTS)	10 (6.8%)	8 (5.6%)	(-4.9%, 6.9%)
Cerebrovascular	1 (0.7%)	2 (1.4%)	(-3.9%, 2.2%)
Compressive Peripheral Neuropathy	4 (2.7%)	0 (0.0%)	(-0.2%, 6.2%)
Death	0 (0.0%)	1 (0.7%)	(-3.3%, 1.5%)
Dysesthesia - Lower Extremities	2 (1.4%)	1 (0.7%)	(-2.3%, 3.7%)
Dysesthesia – Other	2 (1.4%)	3 (2.1%)	(-4.4%, 2.7%)
Dysesthesia - Upper Extremities	13 (8.8%)	15 (10.5%)	(-8.7%, 5.2%)
Dysphagia	4 (2.7%)	8 (5.6%)	(-7.9%, 1.9%)
Dysphonia	1 (0.7%)	2 (1.4%)	(-3.9%, 2.2%)

Adverse Event	Patients Experiencing Adverse Events (%)		95% BCI (lower, upper)
	SEC (N=148)	ACDF (N=144)	
Gastrointestinal	3 (2.0%)	1 (0.7%)	(-1.8%, 4.7%)
Headache	7 (4.7%)	11 (7.7%)	(-8.8%, 2.7%)
Infection – Other	3 (2.0%)	3 (2.1%)	(-3.9%, 3.7%)
Infection - Superficial Wound	0 (0.0%)	2 (1.4%)	(-4.4%, 1.0%)
Muscle Spasms	0 (0.0%)	1 (0.7%)	(-3.3%, 1.5%)
Musculoskeletal	20 (13.5%)	9 (6.3%)	(0.3%, 14.1%)
Neurological	1 (0.7%)	4 (2.8%)	(-5.9%, 1.2%)
Other*	7 (4.6%)	4 (2.8%)	(-2.7%, 6.7%)
Pain - Back and/or Lower Extremities	20 (13.5%)	23 (16.1%)	(-10.8%, 5.6%)
Pain - Neck	35 (23.6%)	41 (28.7%)	(-15.0%, 5.1%)
Pain - Neck and Upper Extremities	16 (10.8%)	28 (19.6%)	(-17.0%, -0.5%)
Pain - Neck and Upper Extremities with Dysesthesia	1 (0.7%)	3 (2.1%)	(-4.9%, 1.7%)
Pain - Neck with Dysesthesia	0 (0.0%)	4 (2.8%)	(-6.4%, 0.1%)
Pain - Other	2 (1.4%)	1 (0.7%)	(-2.3%, 3.7%)
Pain - Upper Extremities	25 (16.9%)	24 (16.8%)	(-8.5%, 8.7%)
Pain - Upper Extremities with Dysesthesia	4 (2.7%)	2 (1.4%)	(-2.4%, 5.1%)
Psychological	1 (0.7%)	1 (0.7%)	(-2.8%, 2.7%)
Surgery - Adjacent Level	2 (1.4%)	2 (1.4%)	(-3.4%, 3.2%)
Surgery - Index Level	4 (2.7%)	14 (9.8%)	(-13.0%, -1.5%)
Surgery - Lumbar Level	4 (2.7%)	5 (3.5%)	(-5.3%, 3.5%)
Surgery - Other Cervical	0 (0.0%)	1 (0.7%)	(-3.5%, 1.5%)
Trauma	18 (12.2%)	17 (11.9%)	(-7.3%, 7.8%)
Weakness	3 (2.0%)	1 (0.7%)	(-1.8%, 4.7%)
Wound Issue	0 (0.0%)	4 (2.8%)	(-6.4%, 0.1%)

SEC = all SECURE®-C Cervical Artificial Disc; ACDF = Anterior Cervical Discectomy and Fusion (Control)
*Other previously defined in Table 2

Table 13 provides a higher level comparison of all pain adverse events that occurred in the study. There were no statistical differences between randomized groups for all pain categories listed. Rates were higher for ACDF than for SECURE®-C in all categories, but the differences were not statistically significant.

Table 13. Pain Adverse Events (All Treated Subjects)

Category	NR SEC (N=88)	R SEC (N=148)	R ACDF (N=144)	95% BCI (lower, upper)*
Subjects with ≥1 pain AE	39 (44.3%)	78 (52.7%)	88 (61.1%)	(-19.9%, 2.5)
Total pain AEs	58	122	157	--
Subjects with ≥1 cervical spine related pain AE	30 (34.1%)	68 (45.9%)	81 (56.3%)	(-21.8%, 0.8%)
Total cervical spine related pain AEs	41	100	128	--
Pain AEs by location:				
• Neck	• 26 (29.5%)	• 51 (34.5%)	• 63 (43.8%)	• (-20.5%, 1.6%)
• Arm	• 17 (19.3%)	• 44 (29.7%)	• 50 (34.7%)	• (-15.8%, 5.5%)
• Neck and arm	• 30 (34.1%)	• 67 (45.3%)	• 76 (52.8%)	• (-19.1%, 3.6%)
• Headache	• 1 (1.1%)	• 7 (4.7%)	• 11 (7.6%)	• (-8.8%, 2.7%)
• Back and/or LE	• 16 (18.2%)	• 20 (13.5%)	• 23 (16.0%)	• (-10.8%, 5.6%)
• Other	• 0	• 2 (1.4%)	• 1 (0.7%)	• (-2.3%, 3.7%)

NR SEC=Non-randomized SECURE®-C; R SEC=Randomized SECURE®-C; R ACDF=Control
*For statistical comparisons of only randomized patients, ACDF group excludes 1 non-randomized patient, therefore N=143.

Some adverse events resulted in surgical intervention at the index level, subsequent to the initial surgery. Secondary surgical interventions, classified as revisions, removals, reoperations or supplemental fixations at the index level, are study failures and are reported in **Table 14**, with details provided in **Table 15**. The percentage of patients experiencing secondary surgery at the index level was lower for the SECURE®-C group (2.5%) than the ACDF group (9.7%), and was statistically superior between randomized groups at 24 months (95% BCI: 0.3%, 10.8%).

Table 14. Secondary Surgical Interventions at the Index Level (All Patients As Treated)

Adverse Event	Intra-Op (0-2 days)		Peri-Op (>2days-6wks)		Short Term (>6wks-12mo)		Long Term (>12mo-24mo)		Longer Term (>24mo)		TOTAL Patients (%)	
	SEC	ACDF	SEC	ACDF	SEC	ACDF	SEC	ACDF	SEC	ACDF	SEC (N=236)	ACDF (N=144)
Revision	0	0	0	1	0	2	0	2	0	1	0 (0.0%)	6 (4.2%)
Removal	0	0	0	0	2	2	1	2	1	3	4 (1.7%)	7 (4.9%)
Reoperation	0	0	0	0	0	1	1	0	1	0	2 (0.8%)	1 (0.7%)
Suppl Fixation	0	0	0	0	0	0	0	0	0	0	0 (0.0%)	0 (0.0%)
Total	0	0	0	1	2	5	2	4	2	4	6 (2.5%)	14 (9.7%)

SEC = all SECURE®-C Cervical Artificial Disc; ACDF = Anterior Cervical Discectomy and Fusion (Control)
Note: 1 SECURE®-C and 4 ACDF secondary surgeries occurred beyond the 24 month visit window (24 + 6 months) and therefore do not count as 24 month failures.

Table 15. Secondary Surgical Procedure Details

Group	Cause/Adverse Event	Action	Postop Days
NR SEC	Arm and parascapular pain	Removal C5-6, fusion same level	880
NR SEC	Neck and shoulder pain	Removal C5-6, fusion same level	183
R SEC	Neck pain	Removal C5-6, fusion C5-7	507
R SEC	C5-6 stenosis	Posterior decompression C5-6	942
R SEC	C5-7 radiculopathy	Posterior decompression C5-7	575
R SEC	Neck pain	Removal C6-7, fusion same level	310
ACDF	C5-6 degenerated disc	Removal C4-5, cervical arthroplasty inserted at C5-6	1576
ACDF	Continued neck pain, numbness	Removal C5-6, plate and spacer inserted same level	441
ACDF	Neck pain and right arm pain	Removal C5-6, plate and cage inserted C6-7	266
ACDF	Right shoulder pain	Removal C6-7, plate and autograft inserted same level	400
ACDF	Neck pain	Removal C5-6 (no replacement)	776
ACDF	Left C5 radiculopathy	Removal C5-6, 2-level plate/1 spacer inserted C4-6	54
ACDF	C4-5, C6-7 disc herniation	Removal C5-6, 3-level plate/spacers inserted C4-7	623
ACDF	C4-5 degenerated disc	Removal C5-6, plate and spacer inserted C4-5	1216
ACDF	Neck pain, C5-6 disc herniation	Removal C4-5, plate and allograft inserted C5-6	1058
ACDF	Neck pain and thumb paresthesia	Posterior decompression C6-7 *(non-study surgeon)*	418
ACDF	Myelopathy	Removal C4-5, plate same level *(non-study surgeon)*	263
ACDF	Left arm pain, numbness	Removal C6-7, plate and allograft at C5-6	1162
ACDF	*Unknown (non-study surgeon)*	Removal C4-5, 2-level plate inserted	215
ACDF	Neck and left arm pain	Removal C6-7, plate and cage inserted C5-6	735

NR SEC=Non-randomized SECURE®-C; R SEC=Randomized SECURE®-C; ACDF=Control

The number and percentage of patients who experienced a device-related adverse event as determined by the Clinical Events Committee (CEC) is provided in **Table 16**. Device-related events were identified as having etiology, temporal association, or cause, that is related to the device, such as: revision, removal, reoperation, or supplemental fixation at the index level, surgery at the index level to remove or alter the device, fracture or mechanical failure of device(s), pseudarthrosis, radiolucency around device(s),

migration, subsidence, loosening, etc. The CEC felt that it was not appropriate to broadly classify events such as neck or arm pain as potentially device related, as these are commonly reported symptoms for patients entering a study with preoperative neck and/or arm pain.

Based on the CEC's classification, the device-related adverse event profile is lower for the randomized SECURE®-C (2.5%) group than the ACDF (9.7%) group because there were less secondary surgeries at the index level in the SECURE®-C group.

Table 16. Device-Related Adverse Events

Adverse Event	Intra-Op (0-2 days)		Peri-Op (>2-42 days)		Short Term (>42-210 days)		Long Term (>210-900 d)		Longer (>900 days)		Patients (%)	
	SEC	ACDF	SEC	ACDF	SEC	ACDF	SEC	ACDF	SEC	ACDF	SEC (N=236)	ACDF (N=144)
Surgery – Index Level	0	0	1	3	1	2	4	5	0	4	6 (2.5%)	14 (9.7%)

SEC = all SECURE®-C Cervical Artificial Disc; ACDF = Anterior Cervical Discectomy and Fusion (Control)

The change in neurologic status at each study timepoint is provided in **Table 17** for all patient groups. If any one of the four neurologic assessments deteriorated, then the overall neurologic status is considered deteriorated. For overall neurologic status and for each of the four individual assessments, the percentage of patients with stable or improved status was similar for both groups. The randomized SECURE®-C group demonstrated numerically greater percentages of patients with stable/improved neurologic status than the control ACDF group at each time point, with statistical significance at 6 and 36 months; statistical comparisons of 24 month neurologic status success demonstrate non-inferiority with a posterior probability of 100%.

Table 17. Neurological Status

Timepoint	Status	Non-Randomized SECURE-C (N=88)	Randomized SECURE-C (N=148)	Randomized ACDF (N=144)	95% BCI# (lower, upper)
6 months	Improved	49/83 (59.0%)	81/139 (58.3%)	71/130 (54.6%)	(0.7%, 12.6%)
	Stable	29/83 (34.9%)	54/139 (38.8%)	47/130 (36.2%)	
	Deteriorated	5/83 (6.0%)	4/139 (2.9%)	12/130 (9.2%)	
12 months	Improved	47/81 (58.0%)	78/136 (57.4%)	67/124 (54.0%)	(-1.6%, 11.1%)
	Stable	28/81 (34.6%)	52/136 (38.2%)	46/124 (37.1%)	
	Deteriorated	6/81 (7.4%)	6/136 (4.4%)	11/124 (8.9%)	
24 months	Improved	45/75 (60.0%)	73/123 (59.3%)	57/101 (56.4%)	(-2.9%, 9.2%)
	Stable	26/75 (34.7%)	46/123 (37.4%)	38/101 (37.6%)	
	Deteriorated	4/75 (5.3%)	4/123 (3.3%)	6/101 (5.9%)	
36 months	Improved	34/52 (65.4%)	35/53 (66.0%)	23/43 (53.5%)	(0.9%, 20.6%)
	Stable	14/52 (26.9%)	18/53 (34.0%)	16/43 (37.2%)	
	Deteriorated	4/52 (7.7%)	0/53 (0%)	4/43 (9.3%)	

#95% Credible Interval on difference (SECURE-C randomized – ACDF) between proportions of improved/stable vs. deteriorated

Effectiveness Results

Primary Effectiveness Analysis

The analysis of effectiveness was based on the as-randomized cohort of 380 total patients (89 non-randomized SECURE®-C patients, 151 randomized SECURE®-C patients, and 144 ACDF patients). The individual patient success rate was defined as the number of patients classified as success divided by the number of patients evaluated at 24 months. The success rates for each of the individual success components and the overall success is provided in **Table 18** for both randomized groups at 24 months.

Posterior probabilities of non-inferiority and superiority were calculated using Bayesian statistical methods. The statistical analysis plan pre-specified that the analysis technique would involve predicting 24 month outcomes for those without them, based on interim 6 month and 12 month observed outcomes, and integrating over the predictions to obtain posterior probabilities of non-inferiority and superiority.

The study was approved using a non-inferiority margin (delta) of 15%; FDA advised that additional analysis be performed with a margin of 10% at the time of PMA. Only the 10% delta analysis is presented; 15% non-inferiority is always met for all variables demonstrating non-inferiority at 10%. According to the statistical analysis plan, if non-inferiority was determined, then superiority would be evaluated; these results are also presented.

In addition to the protocol-defined overall success criteria, FDA requested an additional alternative definition of overall success to include improvement in NDI of 15 points, maintenance or improvement in neurologic status, absence of device-related adverse events, exclusion of fusion criteria, and no intraoperative changes in SECURE®-C treatment (i.e., intraoperative conversion to fusion). Analysis using the alternative FDA-defined endpoint is provided in **Table 19**.

Table 18. Overall Success at 24 Months Using Protocol-Specified Definition

Component	Non-Randomized SECURE-C (N=89)	SECURE-C (N=151)	ACDF (N=140)	Posterior Probability		95% BCI# (lower, upper)
				Non-Inferiority	Superiority	
NDI (≥25% impr)	67/78 (85.9%)	127/139 (91.4%)	101/116 (87.1%)	100.0%	87.8%	(-3.2%, 12.6%)
No removals etc.	84/86 (97.7%)	142/145 (97.9%)	123/133 (92.5%)	100.0%	98.2%	(0.3%, 10.8%)
N complications	85/85 (100%)	143/143 (100.0%)	127/127 (100.0%)	100.0%	52.9%	(-2.0%, 2.3%)
Fusion (control)	N/A	N/A	90/101 (89.1%)	N/A	N/A	N/A
Overall Success	**67/79 (84.8%)**	**127/141 (90.1%)**	**81/114 (71.1%)**	**100.0%**	**100.0%**	**(8.2%, 27.0%)**

#BCI for difference in proportions (SECURE-C – ACDF), using Bayesian methods

Table 19. Overall Success at 24 Months Using FDA-Defined Criteria

Component	Non-Randomized SECURE-C (N=89)	SECURE-C (N=151)	ACDF (N=140)	Posterior Probability		95% BCI# (lower, upper)
				Non-Inferiority	Superiority	
NDI (≥15pt impr)	64/78 (82.1%)	124/139 (89.2%)	98/116 (84.5%)	100.0%	88.6%	(-3.3%, 13.8%)
Neuro success	72/76 (94.7%)	120/125 (96.0%)	93/98 (94.9%)	100.0%	69.0%	(-4.1%, 7.3%)
No removals etc.	84/86 (97.7%)	142/145 (97.9%)	123/133 (92.5%)	100.0%	98.2%	(0.3%, 10.8%)
No device AEs	84/86 (97.7%)	141/145 (97.2%)	120/131 (91.6%)	100.0%	96.0%	(-0.6%, 10.2%)
No change in tx	88/89 (98.9%)	148/151 (98.0%)	N/A	N/A	N/A	N/A
Overall Success	**60/78 (76.9%)**	**109/130 (83.8%)**	**82/112 (73.2%)**	**100.0%**	**98.1%**	**(0.6%, 20.2%)**

#BCI for difference in proportions (SECURE-C – ACDF), using Bayesian methods

As specified in the analysis plan, the threshold for establishing success for non-inferiority or superiority is a posterior probability of 95.4%. Therefore, overall success results demonstrate non-inferiority of the SECURE®-C group to the control group. In addition, all components of overall success of the SECURE®-C group were non-inferior to the control group. **Superiority of the SECURE®-C investigational group to the control was established for overall success, with a posterior probability of 100% for the protocol-specified definition of overall success and 98.1% for the alternative FDA-defined overall success.**

The timecourse of overall success for each treatment group is shown in **Table 20.**

Table 20. Timecourse of Overall Success

		6 mo	12 mo	24 mo	36 mo	48 mo
Protocol – Specified Definition	**NR SEC (N=89)**	76/84 (90.5%)	75/83 (90.4%)	67/79 (84.8%)	54/62 (87.1%)	21/26 (80.8%)
	R SEC (N=151)	133/142 (93.7%)	126/140 (90.0%)	127/141 (90.1%)	54/63 (85.7%)	8/14 (57.1%)
	R ACDF (N=140)	20/129 (15.5%)	76/123 (61.8%)	81/114 (71.1%)	33/49 (67.3%)	1/16 (6.3%)
FDA Defined Alternative Definition	**NR SEC (N=89)**	67/84 (79.8%)	68/83 (81.9%)	60/78 (76.9%)	42/55 (76.4%)	19/25 (76.0%)
	R SEC (N=151)	122/142 (85.9%)	122/140 (87.1%)	109/130 (83.8%)	49/61 (80.3%)	7/13 (53.8%)
	R ACDF (N=140)	104/128 (81.3%)	98/123 (79.7%)	82/112 (73.2%)	34/50 (68.0%)	1/16 (6.3%)

NR SEC=Non-randomized SECURE®-C; R SEC=Randomized SECURE®-C; R ACDF=Control

Overall success for each treatment group stratified by level treated is presented in **Table 21**. There were no statistical differences in overall success between the randomized groups at C3-4 and C4-5 for either definition of success, and at C5-6 and C6-7 for the FDA definition. However, at C5-6 and C6-7, the proportion of SECURE®-C patients achieving overall success was statistically higher than ACDF patients, using the protocol-specified definition.

Table 21. Overall Success by Level Treated

Overall Success	Non-Randomized SECURE-C (N=89)	Randomized SECURE-C (N=151)	ACDF (N=140)	95% BCI# (lower, upper)
Protocol-specified:				
• C3-4	• 2/2 (100%)	• 5/5 (100%)	• 4/4 (100%)	• (-35.3%, 42.5%)
• C4-5	• 5/6 (83.3%)	• 8/8 (100%)	• 7/10 (70.0%)	• (-8.4%, 54.4%)
• C5-6	• 35/42 (83.3%)	• 60/69 (87.0%)	• 38/55 (69.1%)	• (3.2%, 32.1%)
• C6-7	• 25/29 (86.2%)	• 54/59 (91.5%)	• 32/45 (71.1%)	• (5.4%, 35.2%)
FDA defined:				
• C3-C4	• 2/2 (100%)	• 5/5 (100%)	• 4/4 (100%)	• (-35.4%, 42.4%)
• C4-C5	• 3/6 (50.0%)	• 7/8 (87.5%)	• 7/10 (70.0%)	• (-22.7%, 47.4%)
• C5-C6	• 29/41 (70.7%)	• 51/62 (82.3%)	• 40/55 (72.7%)	• (-5.5%, 24.4%)
• C6-C7	• 26/29 (89.7%)	• 46/55 (83.6%)	• 31/43 (72.1%)	• (-4.8%, 27.9%)

#BCI for difference in proportions (SECURE-C randomized – ACDF), using Bayesian methods

Various post-hoc sensitivity analyses were conducted to assess the robustness of the study conclusions. Additional analyses were provided on overall success stratified by: preoperative radiographic findings, pain status, neurologic status, instability, motion, duration of neck symptoms, and history of conservative care; without Bayesian predictions, without 6 month data in the predictions, and with missing interim outcomes set to worst case values; with ACDF patients with adjacent level subsequent surgery in which the device was removed but not replaced were considered successes rather than failures; using only in-window data; with imputations for missing values including a last observation carried forward analysis, a worst case analysis, and a tipping point analysis; and excluding subjects with major protocol violations. Non-inferiority was established for nearly all of these scenarios for both the protocol-specified and FDA-defined alternate endpoints except the most extreme case in which all missing investigational outcomes are considered failures and all missing control outcomes are considered successes where non-inferiority was only established for the protocol-specified endpoint.

Additional data was provided which stratified outcomes by patient race as shown in **Tables 22** and **23**.

Table 22. Overall Success by Patient Race

Overall Success	Randomized SECURE-C		ACDF		95% BCI[#] (lower, upper)	
	Caucasian (N=136)	Non-Caucasian (N=15)	Caucasian (N=126)	Non-Caucasian (N=14)	Randomized SECURE-C	ACDF
Protocol-specified:	118/127 (92.9%)	9/14 (64.3%)	75/105 (71.4%)	6/9 (66.7%)	(8.1%, 54.3%)	(-18.5%, 37.5%)
FDA defined:	100/116 (86.2%)	9/14 (64.3%)	77/103 (74.8%)	5/9 (55.6%)	(0.9%, 47.9%)	(-8.4%, 49.2%)

[#]BCI for difference in proportions (Caucasian – Non-Caucasian), without predictions

Table 23. Overall Success by Patient Race with Treatment Comparison

Overall Success	Caucasian		Non-Caucasian		95% BCI[#] (lower, upper)	
	Randomized SECURE-C (N=136)	ACDF (N=126)	Randomized SECURE-C (N=15)	ACDF (N=14)	Caucasian	Non-Caucasian
Protocol-specified:	118/127 (92.9%)	75/105 (71.4%)	9/14 (64.3%)	6/9 (66.7%)	(11.7%, 31.1%)	(-35.9%, 35.0%)
FDA defined:	100/116 (86.2%)	77/103 (74.8%)	9/14 (64.3%)	5/9 (55.6%)	(0.9%, 21.8%)	(-28.3%, 44.0%)

[#]BCI for difference in proportions (SECURE-C randomized – ACDF), without predictions

For patients randomized to SECURE®-C, the Caucasian group had higher success rates than the non-Caucasian group for both overall success definitions whereas for patients randomized to ACDF, there was no difference between the Caucasian and non-Caucasian groups particularly for the protocol-specified definition of overall success. Within the Caucasian group, those treated with the SECURE®-C have higher success rates than those treated with ACDF, whereas within the non-Caucasian group, the outcomes are more similar. Due to the relatively small number of non-Caucasians treated in the IDE, this potential variability in outcomes based on race will be evaluated further as part of an Enhanced Surveillance Study the applicant will conduct for 10 years postmarket.

Secondary Effectiveness Analysis

In addition to the components of primary success, secondary effectiveness variables were assessed including VAS Neck and Arm Pain, SF-36 Health Status Survey, Patient Satisfaction, Return to Work, Radiographic, and Neurologic Status. The threshold for establishing non-inferiority or superiority for secondary objectives was 95%.

The following secondary endpoint success definitions were specified:

- NDI success: improvement of both ≥25% and ≥15 points from baseline
- VAS pain success: improvement of ≥20mm
- SF-36 success: improvement of ≥15%
- Satisfaction: response of definitely or mostly satisfied

Success rates at 24 months based on these definitions are presented in **Table 24**. SECURE®-C was non-inferior to ACDF for all measures, except right arm pain, as discussed below. An additional post-hoc analysis for neck, right arm and left arm pain was performed in which success was defined as either 20mm improvement or zero (0mm) pain at the postoperative visit. In this analysis, SECURE®-C is non-inferior to ACDF at 24 months for VAS neck, left arm and right arm pain improvement.

Table 24. Secondary Effectiveness Endpoints – Function, Health, and Satisfaction

Component	Randomized SECURE-C (N=151)	ACDF (N=140)	Posterior Probability		95% BCI# (lower, upper)
			Non-Inferiority	Superiority	
Neck Disability Index (≥25% improvement)	127/139 (91.4%)	101/116 (87.1%)	100.0%	87.8%	(-3.2%, 12.6%)
Neck Disability Index (≥15pt improvement)	124/139 (89.2%)	98/116 (84.5%)	100.0%	88.6%	(-3.3%, 13.8%)
VAS Neck Pain	104/133 (78.2%)	76/108 (70.4%)	100.0%	95.1%	(-1.7%, 19.9%)
VAS Left Arm Pain	74/133 (55.6%)	55/108 (50.9%)	99.7%	85.6%	(-5.5%, 18.4%)
VAS Right Arm Pain	57/133 (42.9%)	49/108 (45.4%)	83.8%	25.5%	(-15.9%, 7.9%)
VAS Neck Pain*	108/133 (81.2%)	78/108 (72.2%)	100.0%	98.4%	(0.9%, 21.0%)
VAS Left Arm Pain*	101/133 (75.9%)	73/108 (67.6%)	99.9%	88.6%	(-3.7%, 15.6%)
VAS Right Arm Pain*	98/133 (73.7%)	76/108 (70.4%)	99.9%	82.7%	(-4.6%, 13.4%)
SF-36 PCS	109/138 (79.0%)	89/114 (78.1%)	98.8%	62.6%	(-8.5%, 12.0%)
SF-36 MCS	70/138 (50.7%)	48/114 (42.1%)	99.9%	94.0%	(-2.5%, 21.2%)
Satisfaction	133/139 (95.7%)	98/115 (85.2%)	100.0%	99.7%	(2.9%, 17.8%)

#BCI for difference in proportions (Randomized SECURE-C – ACDF)

*Alternate definition of VAS success defined post hoc as either 20mm pain improvement or 0mm pain at the postoperative visit.

For patients receiving the SECURE®-C device, the mean angular range of motion values at 12 months and 24 months postoperative were 9.5° and 9.3°, respectively, compared to 8.5° at the preoperative evaluation. The mean translational range of motion values at both 12 months and 24 months postoperative was 1.3mm and 1.2mm, respectively, compared to 0.9mm preoperatively.

The average angulation range of motion (flexion-extension) and range of results for all SECURE®-C patients at the preoperative, 6 month, 12 month and 24 month visit are shown in **Figure 1**.

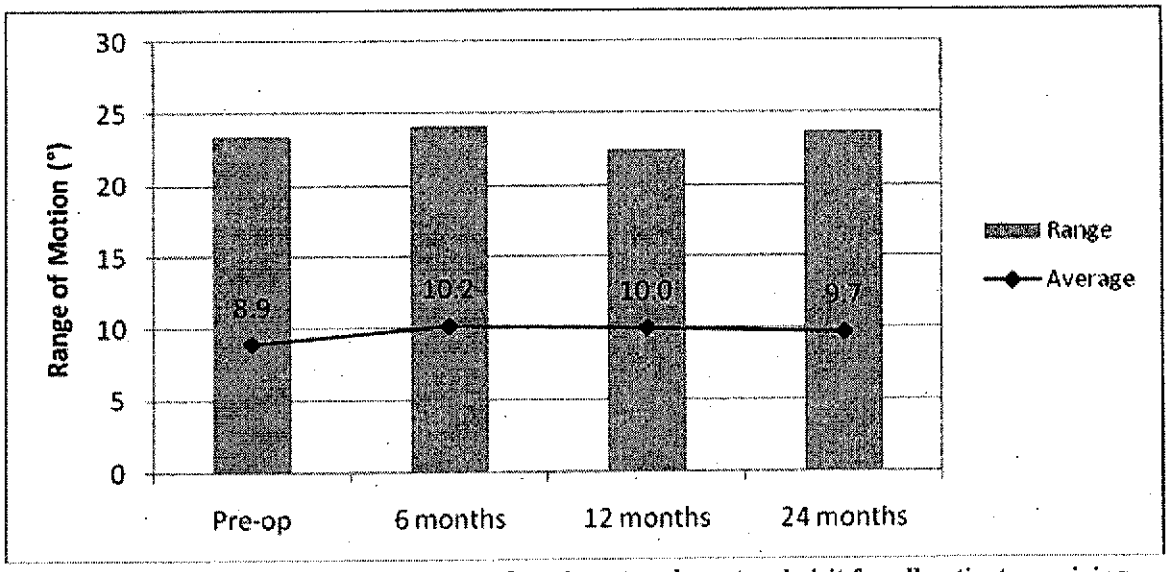


Figure 1. Average flexion/extension range of motion at each protocol visit for all patients receiving SECURE®-C.

Range of motion success for the SECURE®-C group was defined as ≥4° of motion in flexion-extension or maintenance of motion relative to preoperative baseline. Of the 165/195 (84.6%) SECURE®-C patients

who were considered range of motion successes at 24 months (including both non-randomized and randomized patients), 160/165 (97.0%) achieved ≥4° of motion in flexion-extension, 101/165 (61.2%) maintained motion from preoperative baseline, and 96/165 (58.1%) were successes under both criteria. Only 5/165 (3.0%) maintained motion from preoperative baseline but had <4° of motion.

Table 25 presents data on change in range of motion from preoperative baseline for each timepoint by treatment group.

Table 25. Radiographic Change in Range of Motion for SECURE®-C

		6 mo	12 mo	24 mo
NR SEC	Increased (>2°)	36/74 (48.6%)	35/73 (47.9%)	34/68 (50.0%)
	No change (-2 to 2)	17/74 (23.0%)	20/73 (27.4%)	12/68 (17.6%)
	Decreased (<-2)	21/74 (28.4%)	18/73 (24.7%)	22/68 (32.4%)
R SEC	Increased (>2°)	55/130 (42.3%)	53/128 (41.4%)	48/112 (42.9%)
	No change (-2 to 2)	52/130 (40.0%)	36/128 (28.1%)	27/112 (24.1%)
	Decreased (<-2)	23/130 (17.7%)	39/128 (30.5%)	37/112 (33.0%)
All SEC	Increased (>2°)	91/204 (44.6%)	88/201 (43.8%)	82/180 (45.6%)
	No change (-2 to 2)	69/204 (33.8%)	56/201 (27.9%)	39/180 (21.7%)
	Decreased (<-2)	44/204 (21.6%)	57/201 (28.4%)	59/180 (32.8%)

NR SEC=Non-randomized SECURE®-C; R SEC=Randomized SECURE®-C; All SEC=Both Non-randomized and Randomized SECURE®-C

A histogram of angular range of motion on flexion/extension radiographs at 24 months for all patients treated with SECURE®-C is provided in **Figure 2** (values are rounded to the nearest integer).

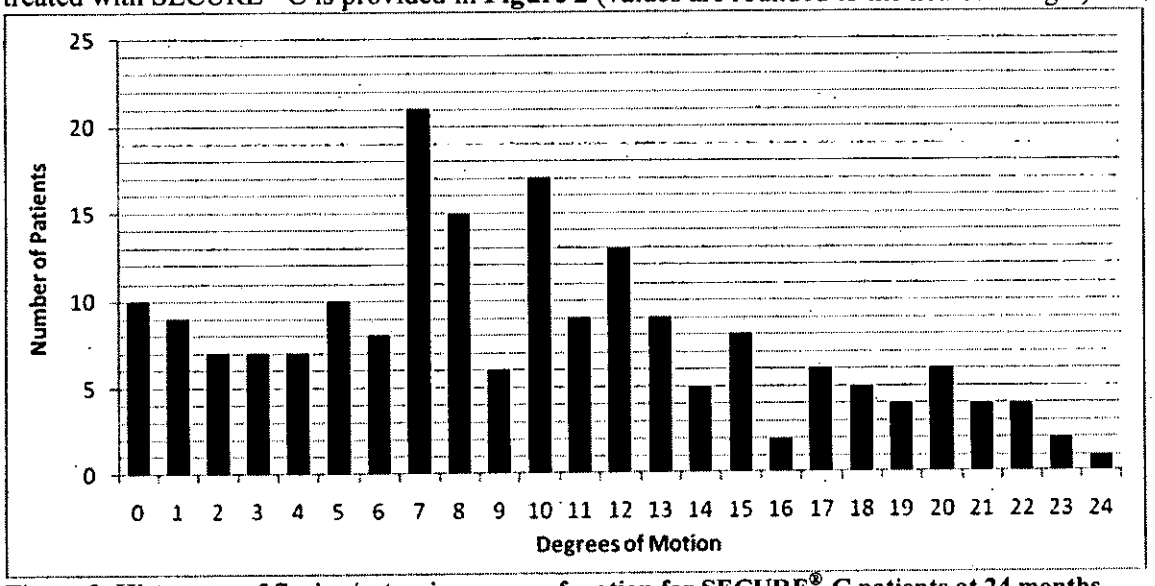


Figure 2. Histogram of flexion/extension range of motion for SECURE®-C patients at 24 months.

Analysis of the correlation between range of motion and overall success (both definitions) as well as NDI and VAS pain scores was done by evaluating the percentage of patients successful on each outcome stratified by range of motion status (≥4° or <4° on flexion/extension) as well as by evaluating correlation plots. No meaningful correlations were found between range of motion and overall success or NDI or VAS pain outcomes for absolute values or changes from baseline.

Radiographic evaluation of mean disc height for the treated level at the preoperative and 24 month time points are shown in **Table 26** for all subjects. Change in disc height success (>2mm) for the treatment groups is shown below in **Table 27**.

Table 26. Radiographic Disc Height

Component	Preoperative			24 months		
	NR SEC	R SEC	ACDF	NR SEC	R SEC	ACDF
Disc Height	3.7 ±0.77	3.8 ±0.75	3.7 ±0.72	5.8 ±0.81	5.7 ±0.99	4.3 ±1.32

NR SEC=Non-randomized SECURE®-C; R SEC=Randomized SECURE®-C; ACDF=Control

Table 27. Secondary Effectiveness Endpoints – Radiographic Measurements

Component	Non-Randomized SECURE-C	Randomized SECURE-C	ACDF	Posterior Probability# Superiority	95% BCI# (lower, upper)
Disc Height Change (>2mm)	42/71 (59.2%)	47/118 (39.8%)	14/94 (14.9%)	100.0%	(12.9%, 35.5%)

#Comparison on the difference (SECURE-C - control) between proportions in randomized groups

Radiolucencies around the implant of more than 25% were evaluated; none (0%) of the SECURE®-C patients and 4/104 (3.8%) ACDF patients demonstrated radiolucencies around the implant at 24 months. There were no device migrations or displacements, including superior or inferior subsidence observed in any SECURE®-C patients.

Radiographic fusion for control patients was defined by the presence of bridging trabecular bone, without evidence of pseudarthrosis, and flexion-extension range of motion ≤2° in rotation and ≤3mm in translation. At 24 months, 89.1% (90/101) of control ACDF patients demonstrated radiographic fusion.

Available radiographs for all treated SECURE®-C patients were assessed by an independent radiographic evaluator for heterotopic ossification (HO) grade, based on the Mehren[1] classification system, as well as to determine the number of patients with stable or "worsening" (progressing by at least one grade) HO from visit to visit. **Table 28** shows 24 month HO results.

Table 28. Heterotopic Ossification for All SECURE®-C Subjects at 24 months

Time Period/ Grade	Non-Randomized SECURE-C	Randomized SECURE-C	ALL SECURE-C
Grade 0	21/76 (27.6%)	30/122 (24.6%)	51/198 (25.8%)
Grade I	18/76 (23.7%)	22/122 (18.0%)	40/198 (20.2%)
Grade II	26/76 (34.2%)	43/122 (35.2%)	69/198 (34.8%)
Grade III	9/76 (11.8%)	16/122 (13.1%)	25/198 (12.6%)
Grade IV	2/76 (2.6%)	11/122 (9.0%)	13/198 (6.6%)
Stable	44/75 (58.7%)	69/116 (59.5%)	113/191 (59.2%)
Worsening	31/75 (41.3%)	47/116 (40.5%)	78/191 (40.8%)

[1] Mehren C, et al. Heterotopic Ossification in Total Cervical Artificial Disc Replacement. Spine 31(24):2802-2806, 2006.

The percentage of patients with range of motion ≥4° at 24 months for each HO grade is shown in **Table 29**. Overall, 82.1% of SECURE®-C patients have ≥4° motion at 24 months.

Table 29. Range of Motion (ROM) ≥4° at 24 months by HO Grade for All SECURE®-C Subjects

Variable	Grade 0 (N=51)	Grade I (N=40)	Grade II (N=69)	Grade III (N=25)	Grade IV (N=13)	Total
Patients w/ ROM ≥4°	50/51	37/40	59/67	14/24	0/13	160/195
% Patients ROM ≥4°	98.0%	92.5%	88.1%	58.3%	0.0%	82.1%

Conclusions Drawn from the Study Data

The clinical data support the reasonable assurance of safety and effectiveness of the SECURE®-C device when used in accordance with the indications for use. Based on the clinical study results, it is reasonable

to conclude that the clinical benefits of the use of the SECURE®-C device in terms of improvement in pain and disability, and the potential for motion preservation, appear to outweigh the risks associated with the device and surgical procedure when used in the indicated population in accordance with the directions for use.

PACKAGING

SECURE®-C implants are supplied pre-packaged and sterile, using gamma irradiation. The integrity of the sterile packaging should be checked to ensure that sterility of the contents is not compromised. Packaging should be carefully checked for completeness and all components should be carefully checked to ensure that there is no damage prior to use. Damaged packages or products should not be used, and should be returned to Globus Medical. During surgery, after the correct size has been determined, remove the implants from the packaging using aseptic technique.

The instrument sets are provided non-sterile and are steam sterilized prior to use, as described in the STERILIZATION section below. Following use or exposure to soil, instruments must be cleaned, as described in the CLEANING section below.

HANDLING

All instruments and implants should be treated with care. Improper use or handling may lead to damage and/or possible malfunction. Instruments should be checked to ensure that they are in working order prior to surgery. All instruments should be inspected prior to use to ensure that there is no unacceptable deterioration such as corrosion, discoloration, pitting, cracked seals, etc. Non-working or damaged instruments should not be used, and should be returned to Globus Medical.

CLEANING

All instruments that can be disassembled must be disassembled for cleaning. The Narrow Implant Holder is disassembled by unthreading the handle/sleeve and removing it from the working end. The Single Endplate Positioner is disassembled by unthreading the adjustable stop. All handles must be detached. Instruments may be reassembled following sterilization. The instruments should be cleaned using neutral cleaners before sterilization and introduction into a sterile surgical field or (if applicable) return of the product to Globus Medical.

Cleaning and disinfecting of instruments can be performed with aldehyde-free solvents at higher temperatures. Cleaning and decontamination must include the use of neutral cleaners followed by a deionized water rinse. Note: certain cleaning solutions such as those containing formalin, glutaraldehyde, bleach and/or other alkaline cleaners may damage some devices, particularly instruments; these solutions should not be used.

The following cleaning methods should be observed when cleaning instruments after use or exposure to soil, and prior to sterilization:

1. Immediately following use, ensure that the instruments are wiped down to remove all visible soil and kept from drying by submerging or covering with a wet towel.
2. Disassemble all instruments that can be disassembled.
3. Rinse the instruments under running tap water to remove all visible soil. Flush the lumens a minimum of 3 times, until the lumens flush clean.
4. Prepare Enzol® (or a similar enzymatic detergent) per manufacturer's recommendations.
5. Immerse the instruments in the detergent and allow them to soak for a minimum of 2 minutes.
6. Use a soft bristled brush to thoroughly clean the instruments. Use a pipe cleaner for any lumens. Pay close attention to hard to reach areas.
7. Using a sterile syringe, draw up the enzymatic detergent solution. Flush any lumens and hard to reach areas until no soil is seen exiting the area.

8. Remove the instruments from the detergent and rinse them in running warm tap water.
9. Prepare Enzol® (or a similar enzymatic detergent) per manufacturer's recommendations in an ultrasonic cleaner.
10. Completely immerse the instruments in the ultrasonic cleaner and ensure detergent is in lumens by flushing the lumens. Sonicate for a minimum of 3 minutes.
11. Remove the instruments from the detergent and rinse them in running deionized water or reverse osmosis water for a minimum of 2 minutes.
12. Dry instruments using a clean soft cloth and filtered pressurized air.
13. Visually inspect each instrument for visible soil. If visible soil is present, then repeat cleaning process starting with Step 3.

STERILIZATION

SECURE®-C Cervical Artificial Disc implants are provided STERILE. Re-sterilization of the implants is not recommended. The polyethylene components may not be re-sterilized for any reason. No implant should be re-used once it comes into contact with human tissue or body fluid.

Sterile SECURE®-C implants are sterilized by gamma radiation using a standard medical device sterilization dose of 25-40kGy. This dose was validated using the VD_{MAX} method according to ANSI/AAMI/ISO 11137-2:2006 Sterilization of Healthcare Products. Sterilization validation was performed to assure a Sterility Assurance Level (SAL) of 10^{-6}. Sterile implants are packaged in a heat sealed, double foil pouch. The expiration date is provided on the package label. Do not use if expired. These implants are considered sterile unless the packaging has been opened or damaged. Carefully inspect each component and its packaging for any damage. Do not use if the packaging or the implant is damaged.

All instruments used in surgery must be sterilized by the hospital prior to use. Remove all packaging materials prior to sterilization. Prior to sterilization, confirm that all instruments that can be disassembled remain disassembled and any handles remain detached, as described above in the CLEANING section. (Instruments may be reassembled following sterilization.) Only sterile products should be placed in the operative field.

The Cervical Instruments used with the SECURE®-C Cervical Artificial Disc are provided non-sterile, and have been validated following ANSI/AAMI/ISO 17665-1:2006 Guidelines for Steam Sterility Validation to assure a Sterility Assurance Level (SAL) of 10^{-6}. The use of an FDA cleared wrap is recommended, per the Association for the Advancement of Medical Instrumentation (AAMI) ST79, *Comprehensive Guide to Steam Sterilization and Sterility Assurance in Health Care Facilities*.

The Cervical Instruments used with the SECURE®-C Cervical Artificial Disc are supplied NONSTERILE. Sterilization is recommended as follows:

Method	Cycle	Temperature	Exposure Time	Drying Time
Steam	Pre-vacuum (wrapped)	132°C (270°F)	4 minutes	30 minutes
Steam	Gravity displacement (wrapped)	132°C (270°F)	15 minutes	45 minutes

Always immediately clean and re-sterilize instruments that have been used in surgery. This process must be performed before handling or (if applicable) returning to Globus Medical.

These parameters are validated to sterilize these instruments. The autoclave must be properly installed, maintained, and calibrated.

CONFORMANCE TO STANDARDS

The SECURE®-C endplates are manufactured from cobalt-chrome-molybdenum alloy, CoCrMo, as specified in ASTM F1537 (and ISO 5832-12). The superior and inferior surfaces of the SECURE®-C endplates are plasma sprayed with commercially pure titanium, as specified in ASTM F1580, F1978, F1147 and C-633 (and ISO 5832-2). The SECURE®-C cores are manufactured from ultra-high molecular weight polyethylene, UHMWPE, as specified in ASTM F648 (and ISO 5834-2).

CONTACT INFORMATION

Globus Medical may be contacted at 1-866-GLOBUS1 (456-2871) or at www.globusmedical.com. A complete Summary of Safety and Effectiveness (SSED), surgical technique, and labeling information for SECURE-C may be obtained at www.fda.gov by searching PMA number P100003.

PRODUCT COMPLAINTS

Any health care professional (e.g., customer or user of this system), who has any complaints or who has experienced any dissatisfaction in the product quality, identity, durability, reliability, safety, effectiveness and/or performance, should notify Globus Medical. Further, if any of the implanted system component(s) ever "malfunctions," (i.e., does not meet any of its performance specifications or otherwise does not perform as intended), or may have caused or contributed to the death or serious injury of a patient, Globus Medical should be notified immediately by telephone, fax or written correspondence. When filing a complaint, please provide the component(s) name and number, lot number(s), your name and address, and the nature of the complaint. Complaints may also be reported directly to Medwatch at http://www.fda.gov/medwatch. You will be contacted by Globus Medical to provide specific information for an Enhanced Surveillance Study, for specific information regarding your clinical experience regarding the complaint and overall experience with the device. In the event that the SECURE®-C device requires removal for any reason, follow the instructions provided below in the DEVICE RETRIEVAL section.

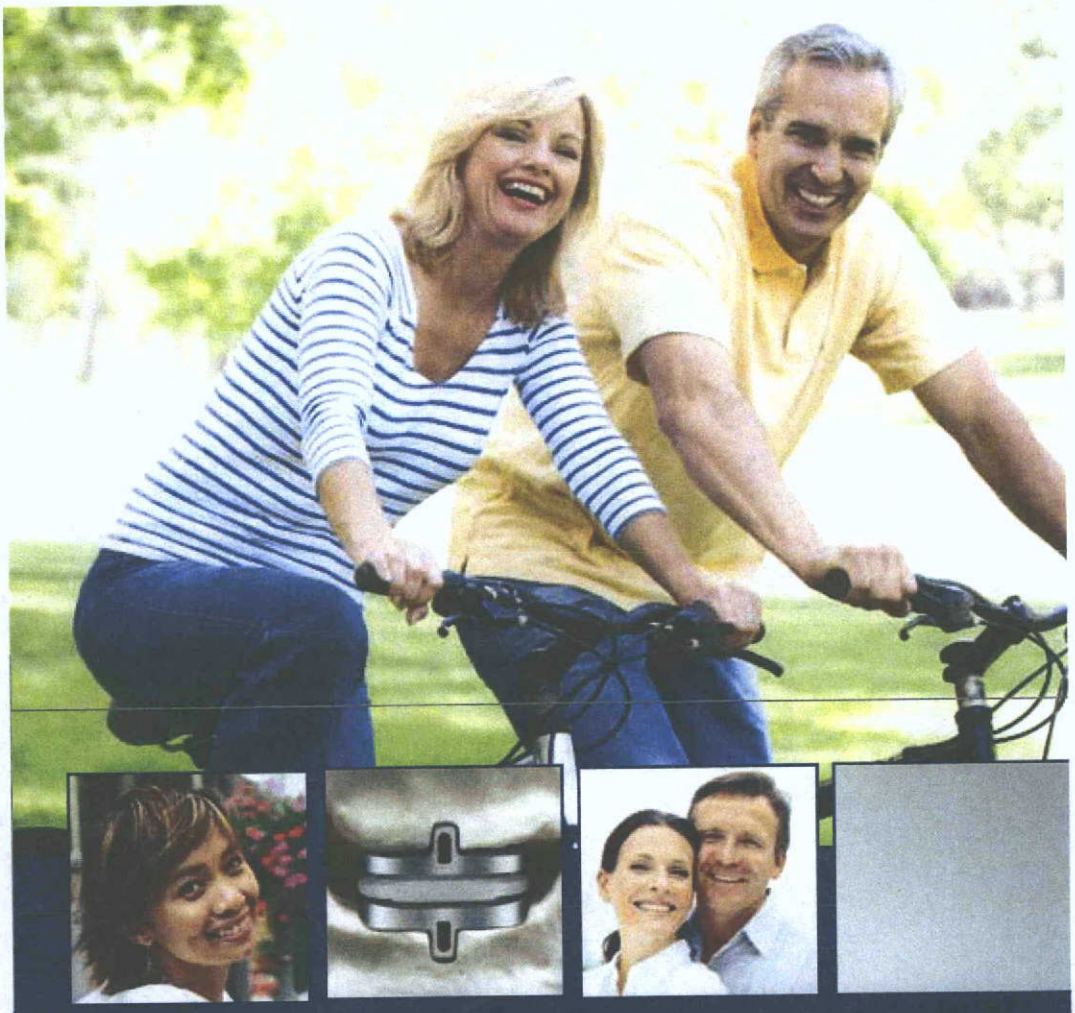
DEVICE RETRIEVAL

Should it be necessary to explant a SECURE®-C Cervical Artificial Disc device, please contact Globus Medical to receive instructions regarding data collection, including histopathological, mechanical, patient and adverse event information. Please refer to the SECURE®-C Cervical Artificial Disc Surgical Technique for step-by-step instructions on the required surgical technique for device retrieval. All explanted devices must be returned to Globus Medical for analysis, in a leakproof container, with the date of explantation, explanting surgeon, and any known information regarding initial implantation, reasons for removal, and adverse event information. Please note that the explanted SECURE®-C 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. Globus Medical will request additional information regarding the reason for removal, patient information and associated clinical outcomes.

NOTE: All implant removals must be reported immediately to Globus Medical.

Limited warranty and disclaimer: Globus Medical products are sold with a limited warranty to the original purchaser against defects in workmanship and materials. Any other express or implied warranties, including warranties of merchantability or fitness, are hereby disclaimed.

CAUTION: Federal (U.S.A) Law Restricts this Device to Sale by or on the order of a Physician.



SECURE®-C

Cervical Artificial Disc

Patient Information

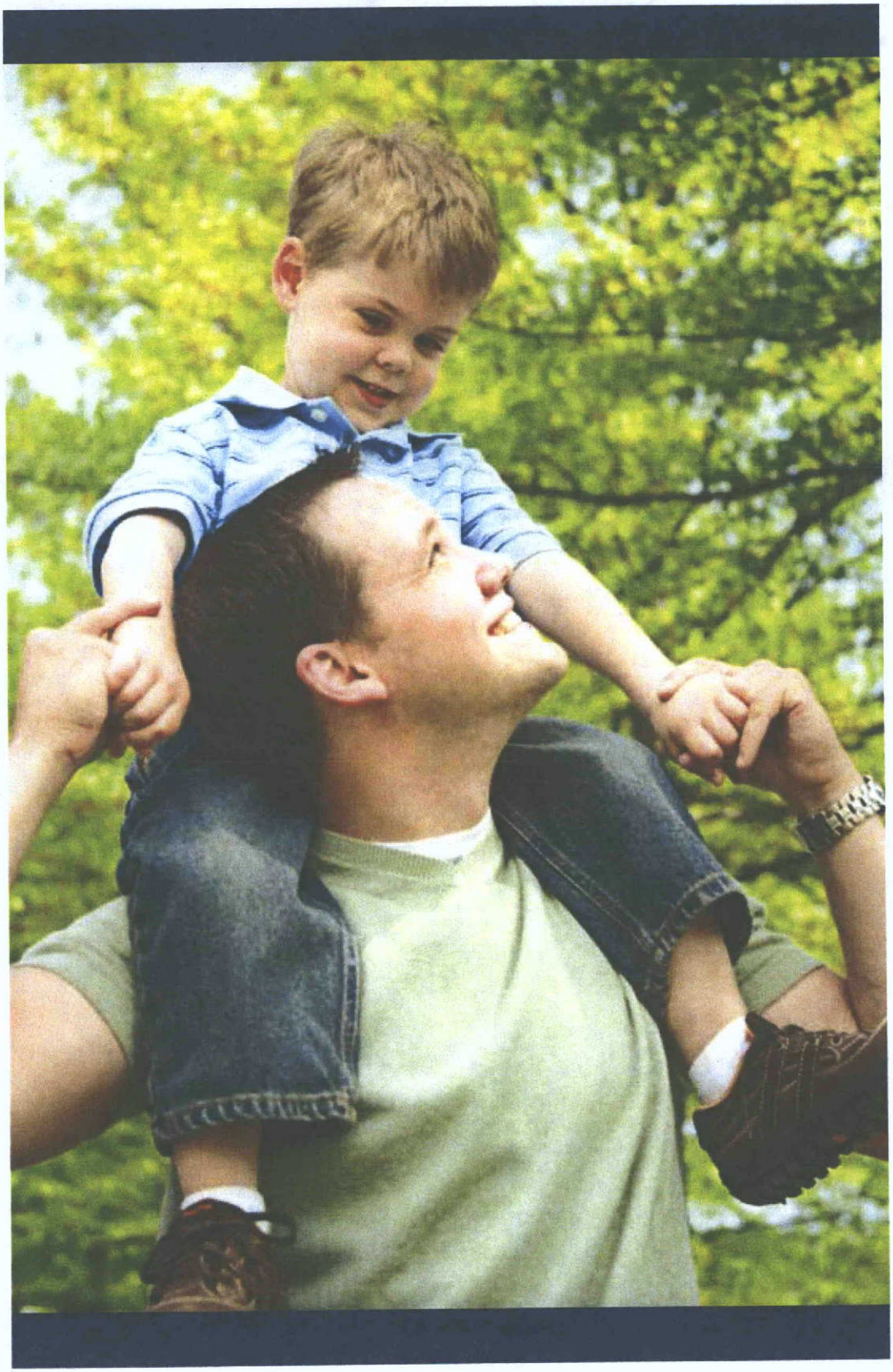


Table of Contents

Glossary

Alleviate:	To make something less severe or more bearable, especially pain
Anterior:	Front of the body
Axial Rotation:	(In the neck) Turning the head side to side
Bone Graft:	A transplant of bone taken from one area to another area
Cobalt Chromium Molybdenum Alloy (CoCrMo):	A metallic material used in implants
CT:	Computerized tomography (CT), which is an x-ray procedure that combines many x-ray images to create cross-sectional images (like slices) of the body
Degeneration:	Deterioration of tissue, which may include loss of function
Disc:	The soft tissue found between the bones of the spinal column that help cushion the spine
Discectomy:	A surgical procedure in which the central portion of a disc is removed
Extension:	(In the neck) Bending the head backward
Facet Joint:	Joints that connect the vertebrae together in the back of the spine and slide against one another during motion
Flexibility:	Motion or movement in a joint
Flexion:	(In the neck) Bending the head forward
Fusion:	Joining two bones together so that they no longer move
Herniated Disc:	A disc that, due to use, injury or disease, bulges outside its normal area, potentially causing pain and limiting function
Heterotopic Ossification:	Unintended bone formation around or across the disc space between the spinal bones (vertebrae)
Incision:	A surgical cut made in skin

Glossary

Lateral Bending:	(In the neck) Bending the head side to side (ear to shoulder)
MRI:	Magnetic Resonance Imaging (MRI), which is a radiographic (like an X-ray) procedure that uses magnets to create cross-sectional images (like slices) of the body
Myelopathy:	Disease of the spinal cord
Osteoporosis:	A condition in which the bones are thin or weak and become brittle and fragile
Osteopenia:	A condition in which the bones are somewhat thin or weak, which may develop into osteoporosis
Polyethylene:	A hard plastic material used in implants
Radiculopathy:	Disease of the nerves in or near the spine as a result of pressure from a disc, or irritation of the nerves due to disc or spinal joint disease
Rehabilitation:	The process of recovery from surgery to a more normal condition
Spondylosis:	A degenerative disease in which the vertebral joints of the spine become stiff and then fused
Synthetic Spacer:	Implant made of an artificial material (such as metal or plastic) that is commonly used in fusion surgeries to hold open the disc space
Systemic:	Pertaining to or affecting a particular body system
Vertebrae:	The bones of the spine that make up the spinal column, with a hole for the spinal cord to pass through
X-Ray:	An image produced by the use of radiation waves, showing bone and other tissues in the body

SECURE®-C
Cervical Artificial Disc

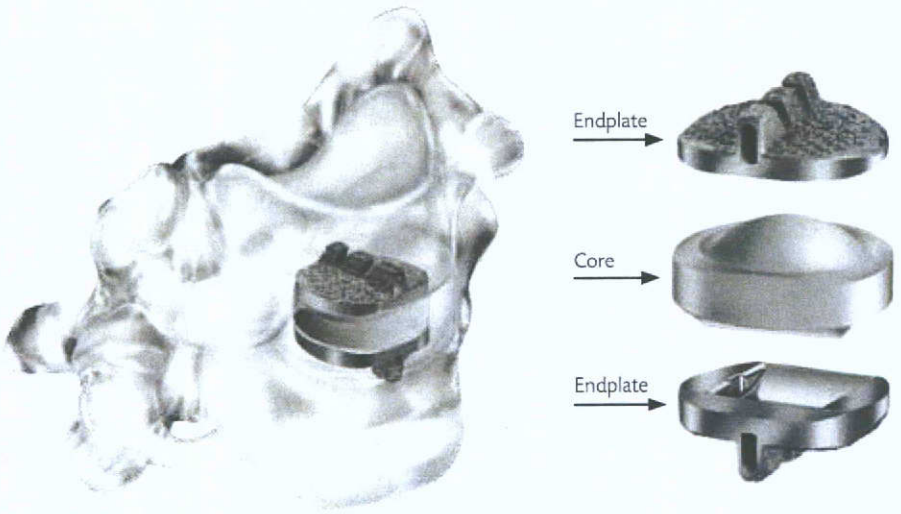
Patient Information

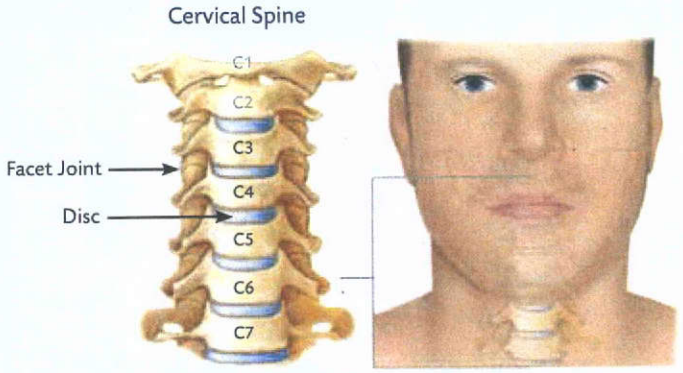
This brochure is intended to provide you with information about a treatment option for your arm pain and/or neurologic symptoms (such as weakness or numbness). After reviewing and discussing your medical history, x-rays, and the results of other evaluations you have completed, you and your doctor have determined that an option for improving your condition would be to undergo cervical spine (neck) surgery using the SECURE®-C Cervical Artificial Disc made by Globus Medical, Inc.

What is the SECURE®-C Cervical Artificial Disc?

The SECURE®-C Cervical Artificial Disc consists of two metallic endplates (cobalt chromium molybdenum alloy, CoCrMo) and a polyethylene (plastic) inner core. The materials used in the device are commonly used in orthopedic implants. The two endplates are secured to the top and bottom surfaces of the involved vertebrae (the bones in the spine) and the core fits between them. The implanted device is designed to allow motion at the treated level as the plastic core moves against the metallic endplates.

Specifically, SECURE®-C's design is intended to allow the neck to move in flexion/extension (bending the neck forward and backward), lateral bending (bending the neck side to side) and axial rotation (turning the head side to side). SECURE®-C is intended to treat a disc in the cervical spine (neck) between the C3 and C7 vertebral bodies. The device is provided in different sizes to fit different patients.

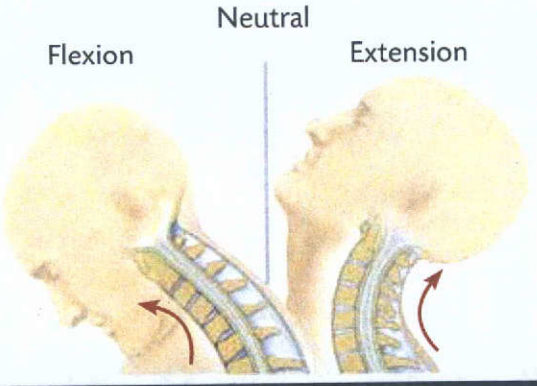




What is the cervical spine and how does it normally move?

Your spine is one of the most important parts of your body. It gives your body structure, support, stability, flexibility (motion or movement in a joint) and provides protection for your spinal cord. A normal spine allows you to move about freely and to bend with flexibility. Your neck, or cervical spine, is composed of seven bones (vertebrae) which are numbered C1 to C7 and are stacked on top of each other to form a column. Each vertebrae has a hole for the spinal cord which contains nerves that carry signals from your brain to the rest of your body. There is a disc between each vertebra which acts as a shock absorber and has a thick outer layer (annulus) that surrounds a soft gel-like center (nucleus).

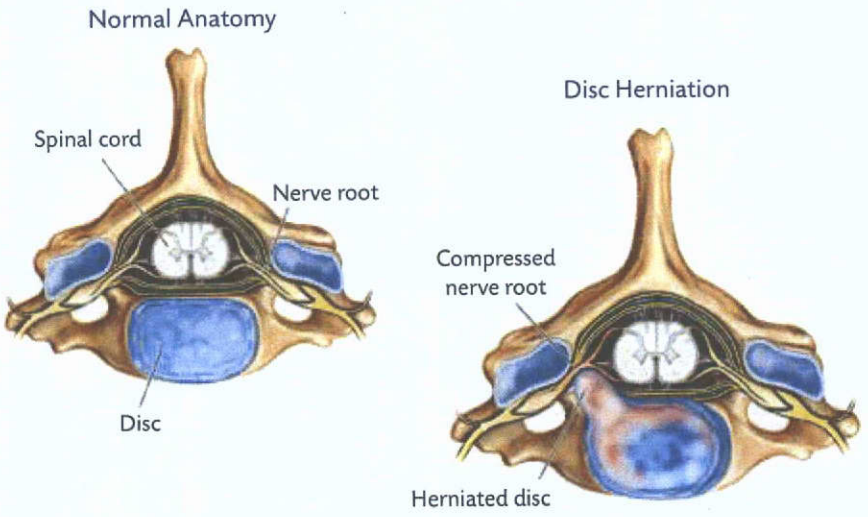
The natural motion of the spine involves movement between each bone, compression of the disc, and sliding of the facet joints (contact areas between the bones). The motion of the cervical spine is: flexion-extension (bending the head forward and backward), lateral bending (bending the head side-to-side) and axial rotation (turning the head). As an example, the image below illustrates flexion-extension motion in the cervical spine.



What is causing my arm and neck symptoms?

Age, genetics, injury, and everyday wear and tear caused by routine activities can contribute to damage and deterioration (degeneration) of the discs in your neck. Degeneration commonly causes pain that radiates toward the shoulders and arms and/or weakness and numbness and may also cause neck pain. Your doctor has probably taken X-rays and an MRI or CT of your neck and may have found a herniated disc (a disc bulge as shown in the illustration below), spondylosis (degeneration of the vertebral joint causing stiffness), or narrowing of the disc as compared to your other discs. Your doctor may diagnose your condition as radiculopathy (disease or irritation of the nerves) or myelopathy (disease of the spinal cord) at one level.

Normal Disc Compared to Herniated Disc



Why may I need surgery?

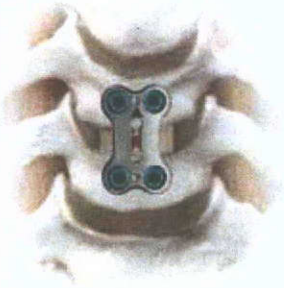
Non-surgical treatment, such as physical therapy, injections, and possibly a neck brace, will be prescribed first by your doctor. If these treatments do not relieve your pain or dysfunction, you and your doctor may determine that you are a candidate for cervical disc replacement. If this option is selected, your surgeon will remove the diseased cervical disc and insert a disc replacement, such as the SECURE®-C Cervical Artificial Disc.

The SECURE®-C design permits motion in flexion and in extension.

How is surgery with the SECURE®-C Cervical Artificial Disc different from a fusion?

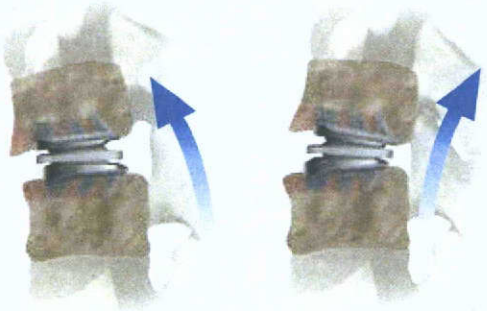
The current standard of care for the surgical treatment of cervical disc disease is fusion (joining of two bones together), which is known as anterior cervical discectomy and fusion (ACDF). In both an ACDF and a SECURE®-C Cervical Artificial Disc procedure, the unhealthy disc is removed and the height at that level is restored to relieve pressure on the nerves and/or spinal cord. In an ACDF, after the unhealthy disc is removed, it is replaced with a bone graft (bone taken from one area and moved to another) or synthetic spacer (artificial implant designed to hold open the disc space), and a cervical plate with screws is used for stabilization. The goal of this procedure is to permanently fuse two or more vertebrae together so they cannot move except as a single unit. This may alleviate (lessen or make more bearable) pain and other symptoms but has potential disadvantages, including loss of motion and flexibility.

Fusion



Restricts normal motion

SECURE®-C



Flexion (forward bending)

Extension (backward bending)

How is surgery with the SECURE®-C Cervical Artificial Disc different from a fusion? *(cont'd)*

The SECURE®-C Cervical Artificial Disc has been developed to provide pain relief while potentially allowing motion of the cervical spine. In a SECURE®-C procedure, after the unhealthy disc is removed, it is replaced with the device alone (no bone graft). The device is designed to provide support for the vertebrae while potentially allowing motion in backward and forward bending, side-to-side bending, and turning.

Who should receive the SECURE®-C Cervical Artificial Disc?

The SECURE®-C Cervical Artificial Disc may be used to treat patients who meet the following requirements:

- 21 to 60 years old
- One diseased disc (C3-C7)
- Arm pain and/or neurological symptoms such as weakness or numbness with or without neck pain for at least six weeks that has not responded to non-surgical care such as medication and physical therapy
- Specific findings on imaging studies such as X-ray, CT, or MRI

In addition, in order to receive this device you must be old enough so that your bones are mature and no longer growing.

Who should not receive the SECURE®-C Cervical Artificial Disc? (Contraindications)

You should avoid having surgery with the SECURE®-C Cervical Artificial Disc if you are experiencing any of the following conditions:

- Active systemic (whole body) infection or an infection at the operating site, as undergoing surgery could interfere with your ability to heal and could increase the chance of spreading or worsening the infection
- Osteoporosis or osteopenia (thin or weak bones resulting from a loss of calcium) because this condition could increase the risk of bone fracture, or could cause the device to loosen
- Allergy to cobalt, chromium, molybdenum, or titanium (metals in the device), or polyethylene (plastic in the device) because this could cause an allergic reaction
- An unstable cervical spine as seen on X-ray and determined by your doctor, because the SECURE®-C surgery involves removal of the disc without the use of a stabilizing plate (as is routinely done for fusion) and may cause further instability
- Advanced spinal arthritis (severe spondylosis) as determined by your doctor, as your disc may have begun to turn into bone, which could severely limit any motion that could be achieved
- Severe facet joint arthropathy (deterioration of the facet joint between each vertebrae) as determined by your doctor, which is not treated by replacement of the disc
- Weakened bones or spinal deformity (abnormal curvature) at the affected level due to current or past trauma or disease as determined by your doctor, which could increase the risk of device loosening
- More than one cervical disc requiring treatment, as the device has only been evaluated in patients with one cervical disc requiring treatment

What are the WARNINGS and PRECAUTIONS associated with the SECURE®-C device?

WARNINGS

There was a clinical study in the United States to evaluate patients treated with the SECURE®-C Cervical Artificial Disc. To participate in the clinical study, patients had to meet certain criteria. For example, patients could not be included in the study if they were taking medications known to interfere with bone healing (such as steroids), if they had a prior surgery at the level being treated, if they had a prior fusion surgery next to the level being treated, or if they were pregnant. *As a result, it is unknown if the device will perform as well in other types of patients compared to those included in the study.*

The device is placed close to major blood vessels (including arteries) and nerves that are located in the cervical spine. There is a risk of nerve damage and/or serious or fatal bleeding if these structures are damaged during or after surgery.

Heterotopic Ossification (HO) is a potential complication associated with cervical total disc replacement devices. HO occurs when bone forms around or across the disc space, which could result in reduced motion. The short-term postoperative use of non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen, may reduce the chance of developing HO, but this has not been proven.

PRECAUTIONS

Because the clinical study evaluated patients that met certain criteria, the safety and effectiveness of the SECURE®-C device has not been established in patients with the following conditions:

- Intractable radiculopathy or myelopathy due to disease at more than one level or disease outside of the disc space;
- Patients whose bones are still growing;
- Under the age of 21 or over the age of 60;
- Prior fusion at an adjacent level of the spine;
- Prior surgery at the level of the spine to be treated;
- Progressive symptoms and signs of spinal cord or nerve compression with less than six weeks of non-surgical treatment;

What are the WARNINGS and PRECAUTIONS associated with the SECURE®-C device? *(cont'd)*

- Disease or degeneration of the facet joint at the level of the spine to be treated;
- Neck or arm pain of unknown cause;
- Neck pain alone;
- Paget's disease (enlarged bones), osteomalacia (weakened bones), or other metabolic bone disease (chemical imbalance);
- Rheumatoid arthritis (chronic joint inflammation) or other autoimmune disease (abnormal body response to normal substances);
- Neuromuscular disorders such as muscular dystrophy (progressive loss of muscle), spinal muscular atrophy(decreased muscle), amyotrophic lateral sclerosis (Lou Gehrig's disease);
- Severe insulin dependent diabetes;
- Systemic disease including AIDS, HIV, and hepatitis;
- Taking medications known to potentially interfere with bone/soft tissue healing (e.g., steroids);
- Active malignancy (cancer), including spinal metastases (spreading of cancer);
- Acute mental illness or substance abuse; and
- Pregnancy.

It is extremely important that you let your doctor know about any medications you are taking, any allergies you have, if you are pregnant (or intend to become pregnant) or if you have any other illnesses or medical conditions that may help your doctor decide if this device is right for you. Failure to fully inform your doctor about your overall state of health and existing medical conditions may create unnecessary complications if you are treated with this device.

What are the potential RISKS and ADVERSE EFFECTS associated with the SECURE®-C Cervical Artificial Disc?

Complications may occur when you are treated with the SECURE®-C Cervical Artificial Disc, as with any surgery. Possible complications may include but are not limited to the following:

- Nerve damage
- Neck and/or arm pain
- Allergic reaction to the implant material
- Implant components bending, breaking, loosening or moving
- Instruments bending or breaking
- Infection of your surgical wound, disc, bone, or surrounding soft tissue
- Systemic infection
- Nerve or spinal cord injury, possibly resulting in paralysis or permanent impairment
- Painful or difficult swallowing, or hoarseness
- Impairment or change in speech
- Injury to your throat or windpipe, or blocking of your airway
- Trauma during surgery (excessive bleeding, fracture, spinal cord or nerve injury)
- Poor implant sizing or placement
- Development or progression of disease at other levels in your cervical spine
- Tingling, numbness or weakening of muscles in your extremities
- Change in the curvature of your neck or the height of your cervical disc(s)
- Loss of motion (unintentional fusion) at the treated level
- Bone growth in your disc space, also called heterotopic ossification
- Bone loss or thinning
- Dural tear (tear in the protective membrane around the spine)
- Leakage of spinal fluid
- Reactions to the anesthesia used in your surgery
- Hematoma (collection of clotted blood)
- Swelling
- Scarring of tissue in or around your surgical wound
- Complications of pregnancy, including miscarriage or fetal birth defects
- Injury or damage to the blood vessels, heart, lungs, stomach, intestines, bowels, bladder, or other organs, during surgery
- Changes in mental status
- Inability to resume activities of normal daily living
- Death

What are the potential RISKS and ADVERSE EFFECTS associated with the SECURE®-C Cervical Artificial Disc? *(cont'd)*

In addition to the risks listed on the previous page, there is also the risk that the surgery may not be effective in relieving your symptoms, or may cause worsening of your symptoms. If this occurs, you may need another surgery in order to help you feel better.

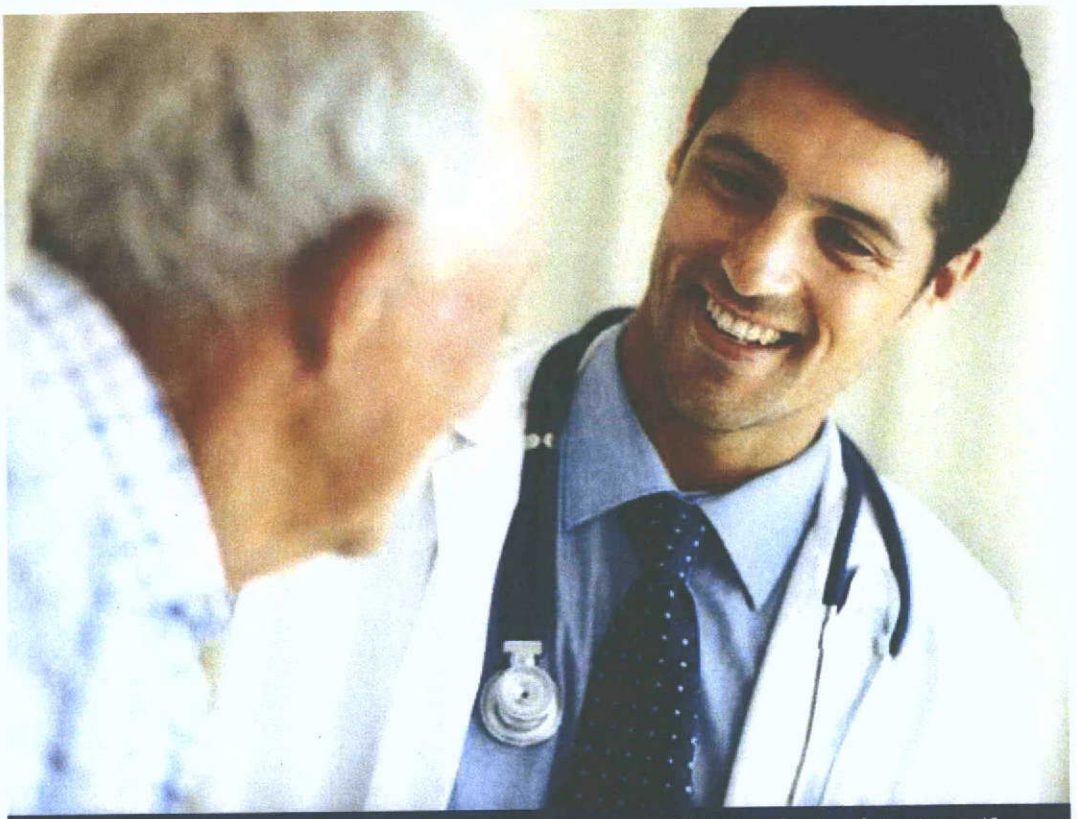
Throughout the course of the U.S. clinical study, patients reported health related problems to their physicians. Some of the events listed on the previous page occurred in the U.S. clinical study. For the patients in the U.S. clinical study treated with the SECURE®-C Cervical Artificial Disc (236 patients) or with ACDF (144 patients), some of the more common events were:

- Neck pain in 50 out of 236 SECURE®-C patients (21.2%), and 41 out of 144 ACDF patients (28.5%);
- Arm pain in 32 out of 236 SECURE®-C patients (13.6%), and 24 out of 144 ACDF patients (16.7%);
- Both neck and arm pain in 26 out of 236 SECURE®-C patients (11.0%), and 28 out of 144 ACDF patients (19.4%);
- Abnormal sensation in the arms (dysesthesia) in 20 out of 236 SECURE®-C patients (8.5%), and 15 out of 144 ACDF patients (10.4%);
- Pain in the back and/or legs in 36 out of 236 SECURE®-C patients (15.3%), and 23 out of 144 ACDF patients (16.0%);
- Other musculoskeletal adverse events (excluding events related to the spine) in 30 out of 236 SECURE®-C patients (12.7%), and 9 out of 144 ACDF patients (6.3%); and
- Difficulty swallowing in 6 out of 236 SECURE®-C patients (2.5%), and 8 out of 144 ACDF patients (5.6%).

What are the potential RISKS and ADVERSE EFFECTS associated with the SECURE®-C Cervical Artificial Disc? *(cont'd)*

Six patients (2.5%) treated with SECURE®-C, and 14 patients (9.7%) treated with ACDF, had additional surgery at the same level within 2 years after their surgery. Four patients (1.7%) treated with SECURE®-C, and 6 patients (4.2%) treated with ACDF, had surgery at an adjacent level within 2 years after surgery. **No mechanical failures of the SECURE®-C device were observed in any study patients.** There may be other risks associated with treatment using SECURE®-C.

Although many of the major risks are covered in this patient brochure, a comprehensive list is provided in the package insert for the device, which your doctor has received. Please ask your doctor for more information about any additional risks that could be related to your planned surgery.



SECURE®-C may help to restore normal everyday motion in some patients

What are the expected outcomes and benefits of the SECURE®-C Cervical Artificial Disc?

The surgery may relieve your symptoms of pain, weakness and/or numbness, and the SECURE®-C Cervical Artificial Disc is designed to allow motion at the treated level. In the U.S. clinical study, 236 patients were treated with SECURE®-C and 144 patients were treated with ACDF. Some of the study results at two years after surgery are described below. The clinical benefit beyond two years has not been measured. Ask your doctor for more details about the clinical study and its results.

Two years after surgery, the overall success rate for SECURE®-C patients in the clinical study using the original success criteria was 90.1%, compared to 71.1% for ACDF patients, which showed that SECURE®-C is statistically superior to ACDF. The overall success rate at two years using the FDA-defined success criteria was 83.8% for SECURE®-C patients, compared to 73.2% for ACDF patients, which also showed that SECURE®-C is statistically superior to ACDF. In the study, 89.2% of SECURE®-C patients demonstrated meaningful improvement in an outcome measure designed to evaluate patient function known as the NDI (Neck Disability Index), compared to 84.5% of ACDF patients, two years after surgery. In addition, 96.0% of SECURE®-C patients in the study had the same or improved neurologic status, compared to 94.9% of ACDF patients, two years after surgery.

Moreover, 96% of SECURE®-C patients in the study were satisfied with the results of their surgery two years after the procedure, compared to 85% of ACDF patients. Eighty-two percent of patients treated with the SECURE®-C had four or more degrees of motion in flexion-extension (bending the head forward and backward), and 67% had either the same or more motion in flexion-extension at two years as before they were treated.

The rates of complications were about the same when comparing the group treated with the SECURE®-C and the group treated with the standard of care, ACDF, in the first two years following surgery. The rate of subsequent surgery at the index level for SECURE®-C patients (2.5%) is statistically superier to the rate for ACDF patients (9.7%), in the first two years after surgery.

What can I expect before surgery?

Review your medical history with your doctor as well as your current condition and all possible options for treatment (including medications, physical therapy and other surgeries such as a fusion). Discuss any medications you are currently taking, including non-prescription drugs, herbal supplements, and vitamins, as well as any allergies you have. You may be asked by your doctor to discontinue the use of certain medications prior to your surgery. Typically you should not eat or drink the night before surgery, but your doctor will give you detailed instructions as to exactly what to do the night before surgery and during your recovery.

You will want to prepare your home life accordingly to ensure a comfortable atmosphere suitable for easy recovery. This includes things like removing safety hazards that may cause you to fall or lose your balance. Place important things within easy reach (phone, etc.) during your recovery. You will want to arrange for someone to help you at home after surgery. Your doctor will also discuss with you any potential risks and benefits of the procedure. *Ensure that you have read and that you understand this entire brochure.*

What can I expect during surgery?

The SECURE®-C Cervical Artificial Disc is implanted by removing your diseased disc and inserting the device. The SECURE®-C device is implanted through an anterior (front) surgical approach to your neck. General anesthesia will be administered and an incision will be made in the anterior (front) part of your neck so that the front of the spine will be exposed. The incision is usually about one inch long. Your diseased disc will be removed. The surgeon will prepare the space from which the disc has been removed, using trials to determine the best implant size for you, and will insert the SECURE®-C Cervical Artificial Disc in that size. The two device endplates are secured to the top and bottom surfaces of the involved vertebrae and the core fits between them. After insertion, your incision will be closed.

What can I expect after surgery?

Ask your doctor about your specific recovery plan. Surgery with the SECURE®-C Cervical Artificial Disc is considered major surgery. You can expect to remain in the hospital for approximately one day. Usually your heart and lung function will continue to be monitored immediately after surgery and there may be a drainage tube in your wound. As with any surgery, you should expect some discomfort and a period of rehabilitation. Your doctor will most likely prescribe medicine to control nausea or pain. After your surgery, it is important to ask your doctor about the proper way to recover. Remember that recovering from pain and surgery is a continuing process. **It is very important to closely follow your doctor's specific post-operative care instructions in order to recover quickly and for the best outcome possible.**

Contact your doctor immediately if you experience any of the following:

- Nausea or vomiting
- Difficulty swallowing or breathing
- Severe pain that does not go away when you take your pain medicine
- Fever
- Trouble urinating
- Loose stitches or an open surgical wound
- Red streaks or pus draining from your wound
- A rash

Your doctor may recommend or discuss the following with you:

- Proper wound care
- Medication to help manage any post-surgical pain
- A cervical collar to wear for a few weeks following surgery
- A therapy program for active range of motion exercises
- Avoiding lifting above the shoulders and repetitive bending
- Avoiding rough or strenuous athletic activities

Frequently asked questions after surgery

When can I drive?

There is a possibility that you will be restricted from driving for a period of time after surgery. If this is the case, your doctor will tell you when you may drive again.

Can I shower after surgery?

You should be able to quickly shower but you will have a bandage on your neck. Try not to soak the dressing while in the shower. Also you should not use a hot tub or take long baths until your doctor tells you its okay to do so.

Will there be a scar?

Typically it's a small incision that will heal with a scar that is not very noticeable. However, this will vary from person to person.

What about traveling with this device?

It is advised that you contact authorities at your local airport prior to traveling after this device has been implanted. This is due to increased security measures. Airport personnel should be able to provide you with guidance and information that will help you pass through security more easily and quickly. Be sure to ask your doctor to provide a patient identification card that will indicate you have a metallic device implanted in your neck.

How can I contact the manufacturer of the device for user assistance?

Globus Medical, Inc. is the manufacture of the device. Contact information is provided below:

Globus Medical, Inc.
2560 General Armistead Avenue
Audubon, PA 19403
1-866-456-2871
www.globusmedical.com

Summary

In order to make the most informed treatment decision for your care, please discuss any questions you may have with your doctor. While discussing the SECURE®-C Cervical Artificial Disc as a possible treatment option for your symptoms, be sure to discuss other possible surgical and non-surgical treatment options for your medical condition. Inform your doctor if you have an active infection, or an allergy to cobalt, chromium, molybdenum, or titanium (metals in the device), or polyethylene (plastic in the device). Also, please inform your doctor if you have been diagnosed with osteoporosis, osteopenia, or if you have any other health issues.

Globus Medical
Valley Forge Business Center
2560 General Armistead Avenue
Audubon, PA 19403
www.globusmedical.com

LIMITED WARRANTY AND DISCLAIMER:
Globus Medical products are sold with a limited warranty to the original purchaser against defects in materials and workmanship. Any other express or implied warranties, including warranties of merchantability or fitness, are hereby disclaimed.

WARNING: In the United States, this product has labeling limitations. Refer to the package insert for complete information.

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

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