SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Artificial Cervical Disc
Device Trade Name:	Mobi-C® Cervical Disc Prosthesis
Applicant's Name and Address:	LDR Spine USA, Inc. 13785 Research Boulevard, Suite 200 Austin, TX 78750 USA
Date of Panel Recommendation:	None
Premarket Approval Application (PMA) No.:	P110009
Date of Notice of Approval:	August 23, 2013

II. INDICATIONS FOR USE

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

III. CONTRAINDICATIONS

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

- Acute or chronic infection, systemic or at the operative site;
- Known allergy or sensitivity to the implant materials (cobalt, chromium, molybdenum, titanium, hydroxyapatite, or polyethylene);
- Compromised vertebral bodies at the index level(s) due to previous trauma to the cervical spine or to significant cervical anatomical deformity or disease (e.g., ankylosing spondylitis, rheumatoid arthritis);

- Marked cervical instability on resting lateral or flexion/extension radiographs demonstrated by translation greater than 3.5mm, and/or > 11° angular difference to that of either level adjacent to the two treated levels;
- Osteoporosis or osteopenia defined as DEXA bone mineral density T-score ≤ -1.5
- Severe facet joint disease or degeneration.

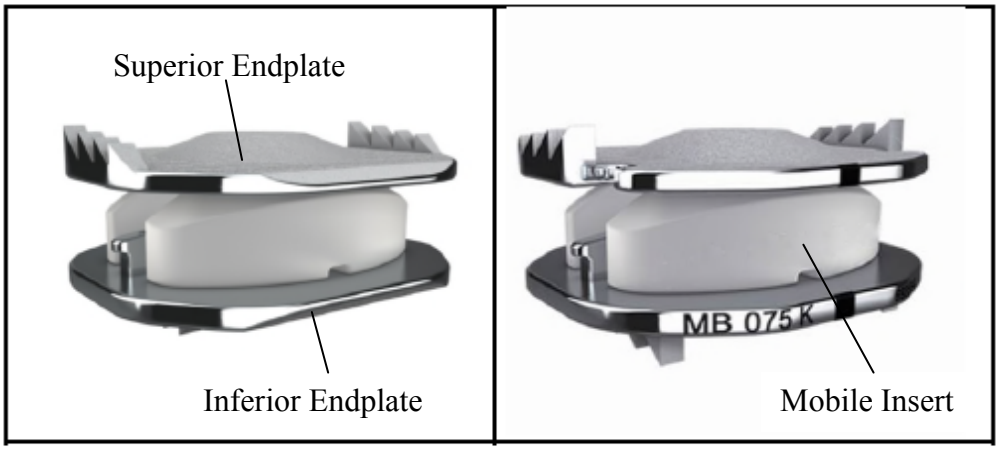
IV. WARNINGS AND PRECAUTIONS

The warnings and precautions may be found in the Mobi-C® Cervical Disc Prosthesis labeling.

V. DEVICE DESCRIPTION

The Mobi-C® is a weight-bearing implant comprised of an ultra-high-molecular-weight polyethylene (UHMWPE per ISO 5832-4) mobile insert sandwiched between two spinal plates consisting of cobalt, chromium, molybdenum (CoCrMo per ISO 5832-12) alloy with a titanium (per ASTM F1580) and hydroxyapatite (per ISO 13779) plasma spray coating. Multiple vertebral body footprint sizes and mobile insert heights are available to conform to the individual patient's anatomy. The components are pre-assembled to create a range of implant configurations. Illustrations of the device are provided below. A set of instruments suitable for cervical spinal interbody surgery, are needed for implantation.

Figure 1. Assembled Mobi-C® (Posterior and Anterior Views)



A. Device Components

The Mobi-C® endplates consist of CoCrMo alloy with a titanium and hydroxyapatite plasma spray coating. Both the superior and inferior spinal endplates incorporate two rows of serrated teeth that are located laterally on each plate. The teeth sink into the bone to facilitate endplate fixation and do not require any bone removal or chiseling prior to insertion. The Mobi-C® has a bone sparing design and technique. The inner surfaces of the endplates that contact the mobile insert feature highly polished surfaces to permit articulation on the mobile insert while enabling a limited amount (approximately 1mm) of translation in the X-Y plane for the mobile insert within the endplates.

The Mobi-C® endplates are available in seven footprint sizes to address individual patient anatomy and maximize endplate coverage. These sizes are illustrated in the table below.

Table 1. Mobi-C® Device Configurations

Depth x Width (mm)	**Inferior/Superior Plate & Mobile Insert Sizes Combinations**							**Height (mm)**
Endplates	13 x 15	14 x 15	15 x 15	13 x 17	14 x 17	15 x 17	15 x 19	H5 H6 H7
Mobile Insert	11 x 12	11 x 12	11 x 12	11 x 12	11 x 12	13 x 14	13 x 14	

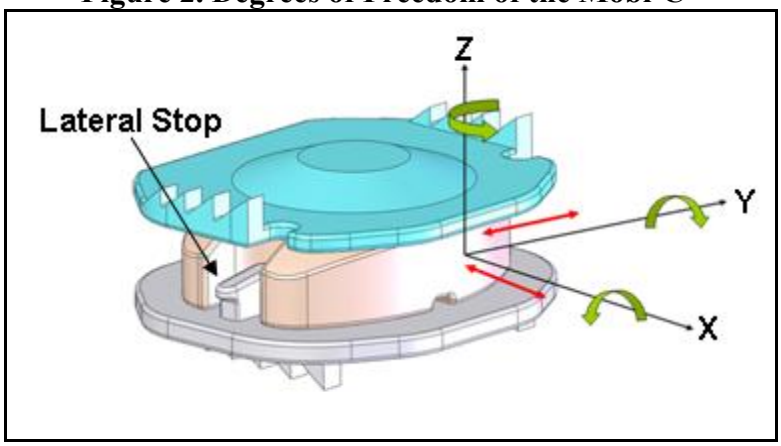
Product Scope		
Part Number	Footprint (mm)	Height (mm)
MB 3355	13×15	H5
MB 3356	13×15	H6
MB 3357	13×15	H7
MB 3455	14×15	H5
MB 3456	14×15	H6
MB 3457	14×15	H7
MB 3555	15×15	H5
MB 3556	15×15	H6
MB 3557	15×15	H7
MB 3375	13×17	H5
MB 3376	13×17	H6
MB 3377	13×17	H7
MB 3475	14×17	H5
MB 3476	14×17	H6
MB 3477	14×17	H7
MB 3575	15×17	H5
MB 3576	15×17	H6
MB 3577	15×17	H7
MB 3595	15×19	H5
MB 3596	15×19	H6
MB 3597	15×19	H7

The Mobi-C® UHMWPE mobile insert consists of a standard (symmetric) convex spherical dome that is radiolucent. The mobile insert articulates with both the superior and inferior device endplates, the inner contact surfaces of which are spherical and flat, respectively. The bottom of the mobile insert contains a grooved feature to enhance lubrication of the mobile insert and inferior endplate surfaces with bodily fluids. The mobile insert is self-centering on the inferior endplate. Each movement of the superior plate induces the mobile insert to re-position on the inferior spinal plate, which maintains the superior versus inferior vertebral alignment.

The mobile insert is available in three different heights that result in a total prosthesis height of 5 mm (H5), 6 mm (H6) or 7 mm (H7), to better accommodate individual patient anatomy. In addition, each of the three insert heights is available in two different footprints to accommodate the range of device endplate sizes.

The purpose of the Mobi-C® device is to provide pain relief and restore normal biomechanical function to a diseased spine level after disc excision. The mobile insert articulates between the superior and inferior spinal plates, which allows for multiaxial motion, including five independent degrees of freedom that include two translational and three rotational. The five independent degrees of freedom are illustrated below. The kinematic principle behind the Mobi-C® design is to allow for normal range of motion in the cervical spine and to enable or re-establish the physiological mobility of the targeted disc space through the mobile insert design. This biomechanical and kinematic concept (the mobile insert design) is designed to preserve the instantaneous axis of rotation of the affected disc space.

Figure 2. Degrees of Freedom of the Mobi-C®



The inferior endplate includes two lateral stops that control and limit the translation and rotation of the mobile insert. The lateral stops also prevent the potential for migration of the mobile insert. Mobi-C® is designed to control the amount of translation by the mobile insert in the X and Y plane to ± 1 mm. The device is also designed to allow for ± 8° of mobile insert rotation about the Z axis. The superior endplate is unconstrained in Z axis rotation. Rotation in flexion/extension about the Y axis is designed to be at least ± 10°, while rotation in lateral bending about the X axis is also designed to be at least ± 10°. This combination of controlled mobility allows the mobile insert to be self-centering on the inferior plate. Each movement of the superior plate induces the mobile insert to re-position on the inferior plate which maintains the superior versus inferior vertebral alignment. For the product scope, these design parameters are met.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the treatment of intractable radiculopathy or myelopathy due to a multi-level abnormality localized to the level of the disc space at two contiguous levels.

- Nonoperative alternative treatments include, but are not limited to, physical therapy, medications, braces, chiropractic care, bed rest, spinal injections, or exercise programs.
- Surgical alternatives include, but are not limited to, surgical decompression and/or fusion using various bone grafting techniques or interbody fusion devices, which may or may not be used in conjunction with anterior cervical plating (e.g., plate and screws), or

posterior spinal systems (e.g., rods, hooks, wires). Anterior cervical discectomy and fusion (ACDF) with an interbody graft or spacer is the most commonly used method for decompression and fusion[1].

Each alternative has advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician.

VII. MARKETING HISTORY

The Mobi-C® received CE Mark approval in 2004 and is currently distributed in 24 countries in Europe, Africa, Asia, Australia, and the Americas. The device has not been withdrawn from the market for any reason relating to safety and effectiveness. The Mobi-C® is available in: Argentina, Australia, Austria, Belgium, Brazil, China, Denmark, France, Germany, Greece, Italy, Korea, Malaysia, Mexico, Portugal, Singapore, South Africa, Spain, Switzerland, Taiwan, Thailand, Turkey, United Kingdom, and Venezuela.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) identified from the Mobi-C® Cervical Disc Prosthesis clinical study results, approved device labeling for other cervical total disc replacement devices, and published scientific literature including: (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 Mobi-C® Cervical Disc Prosthesis. In addition to the risks listed below, there is also the risk that surgery may not be effective in relieving symptoms, or may cause worsening of symptoms. Additional surgery may be required to correct some of the adverse effects.

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; dysphonia; hoarseness; vocal cord paralysis; laryngeal palsy; sore throat; recurring aspirations; tracheal, esophageal, or pharyngeal perforation; airway obstruction; warmth or tingling in the extremities; neurologic complications including damage to nerve roots, other nerves or the spinal cord, possibly resulting in weakness, pain or even paralysis; dural tears or leak; cerebrospinal fistula; discitis, arachnoiditis, and other types of inflammation; loss of disc height; loss of anatomic sagittal plane curvature, vertebral listhesis; scarring,

herniation or degeneration of adjacent discs; surrounding soft tissue damage, spinal stenosis; spondylolysis; fistula; vascular damage and/or rupture; and headache.

3. Risks associated with a cervical artificial disc device, including the Mobi-C® Cervical Disc Prosthesis, include: early or late loosening of the components; disassembly; bending or breakage of any or all of the components; implant migration; implant malpositioning; implant subsidence; loss of fixation; sizing issues with components; anatomical or technical difficulties; bone fracture; possible tissue reaction; metallosis, and/or scarring 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; loss of neurological function; decreased strength of extremities; decreased reflexes; cord or nerve root injury; interference with radiographic imaging because of the presence of the implant; and the need for subsequent surgical intervention.

For the specific adverse events that occurred in the clinical study of the Mobi-C® Cervical Disc Prosthesis, please see Section X below.

IX. SUMMARY OF PRECLINICAL STUDIES

A variety of testing was conducted to characterize the performance of the Mobi-C® Cervical Disc Prosthesis, as follows:

A. Laboratory Studies

- Static and Dynamic Axial Compression Testing
- Static and Dynamic Shear Compression Testing
- Creep and Stress Relaxation Testing
- Static Expulsion Testing – Full Device
- Static Expulsion Testing – Mobile Insert Only
- Subsidence Testing
- Subluxation Testing
- Durability and Wear Testing
- Wear Particulate Analysis

B.Animal Studies

None

C. Additional Studies

- Sterilization, Packaging, and Shelf Life Testing
- Biocompatibility
- Instrument Testing

Table 3. Summary of Laboratory Studies

Test Name	Purpose	Method	Acceptance Criteria	Results
Static Axial Compression	To evaluate the performance of the Mobi-C® device under static axial compressive loading.	Six (6) Mobi-C® specimens were tested under static compression in ambient air at a rate of 0.2mm/sec until failure.	Static axial compression testing must demonstrate that the device can withstand the maximum axial load that a cervical intervertebral disc can withstand ($75N^2$).	The mean yield load was 1934.98 ± 108.771 N, and mean yield displacement = 0.44 ± 0.03 mm. These results suggest that the Mobi-C® can withstand compressive loading that exceeds the anticipated physiologic loads on the cervical spine.
Dynamic Axial Compression	To evaluate the performance of the Mobi-C® device under dynamic axial compressive loading.	Six (6) Mobi-C® specimens were tested under dynamic compression in phosphate buffered solution ("PBS") at 37 ± 3° C to 10 million cycles, using a sinusoidal wave form with R=10 at 5Hz and 2 Hz until 10 million cycles or gross deformation/ failure.	Dynamic axial compression testing must demonstrate that the device can withstand the maximum axial load that a cervical intervertebral disc can withstand ($75N^2$).	Specimens demonstrated endurance limit of at least 1125N. These results suggest that the Mobi-C® can withstand dynamic compressive loading that exceeds the anticipated physiologic loads on the cervical spine.
Static Compression-Shear	To evaluate the performance of the Mobi-C® device under static compression-shear.	Six (6) Mobi-C® specimens were tested under static compression-shear (45° angle) in ambient air at a rate of 0.2mm/sec until failure.	Static shear compression testing must demonstrate that that the device can withstand the maximum shear load that a cervical intervertebral disc can withstand ($20N^2$).	The mean 2% yield of the samples tested demonstrated that the device withstood 454.36 (114.6N) at mean displacement of 0.41mm of displacement. These results suggest that the Mobi-C® can withstand compressive shear loading that exceeds the anticipated physiologic loads on the cervical spine.

Dynamic Compression-Shear	To evaluate the performance of the Mobi-C® device under dynamic compressive-shear loading.	Six (6) Mobi-C® specimens were tested under dynamic compression shear in phosphate buffered solution ("PBS") at 37 ± 3° C to 10 million cycles, using a sinusoidal wave form with R=10 at 5Hz and 2 Hz until 10 million cycles or gross deformation/ failure.	Dynamic shear compression testing must demonstrate that that the device can withstand the maximum shear load that a cervical intervertebral disc can withstand ($20N^2$).	The two specimens tested at applied load of 450 N ran out to 10 million cycles with no observed failure. These results suggest that the Mobi-C® can withstand dynamic compressive shear loading that exceeds the anticipated physiologic loads on the cervical spine.
Creep Characterization	To evaluate the creep characteristics of the Mobi-C® device.	Twelve (12) Mobi-C® specimens were tested under static compression in 37 ± 3°C phosphate buffered solution ("PBS"). A maximum load was applied for 24 hours and a minimum load was applied for 24 hours. Creep was evaluated at 3600N, 4800N, 6000N, & 7200N.	Test was performed for characterization only.	Specimens tested at loads in excess of 3x the dynamic axial fatigue limit demonstrated permanent height loss of less than 0.8mm. These results suggests that the height loss of the Mobi-C® occurs at loads far in excess of anticipated *in vivo* loads (and beyond failure load of native anatomy).
Static Expulsion of Full Device	To evaluate the loads required to expulse the Mobi-C® device.	Six (6) Mobi-C® specimens with axial preload of 100N were tested in rigid polyurethane foam blocks to determine the amount of force required to displace the device from simulated bone. Devices loaded at 0.1mm/sec in ambient air. Tests were conducted in displacement control at a rate of 6mm/min	Device must withstand the shear failure load of the cervical intervertebral disc ($20N^2$) without expulsion.	The mean peak expulsion load was 142N ±18N at 0.93mm ±0.64mm of displacement. These results suggest that the Mobi-C® can resist pushout forces that exceed the anticipated physiologic loads on the cervical spine.

Static Expulsion of Device Mobile Core Only	To evaluate the loads required to expulse the Mobi-C® mobile insert from the adjacent endplates.	Six (6) Mobi-C® specimens with axial preload of 100N and tested to determine the amount of force required to displace the core from the endplates by at least 3mm. Devices loaded at 0.1mm/sec in ambient air. Tests were conducted in displacement control at a rate of 6mm/min.	Mobile core must withstand the shear failure load of the cervical intervertebral disc ($20N^2$) without expulsion.	Expulsion force of 496.64 N under the worst-case scenario of a force applied directly to the polyethylene inlay at 3.00 mm displacement exceeded the shear failure load. These results suggest that the Mobi-C® can resist disassembly at loads that exceed anticipated physiologic loads on the cervical spine.
Subsidence	To evaluate the Mobi-C® implant's resistance to subsidence into the vertebral endplate.	Six (6) Mobi-C® specimens were inserted into rigid polyurethane blocks simulating cancellous bone and loaded in compression at a rate of 0.1mm/sec in ambient air until 6mm of displacement was reached.	Subsidence testing must demonstrate that the device can withstand loads greater than maximum axial load that a cervical intervertebral disc can withstand ($75N^2$).	The average displacement at the offset load of 1039N ±25N was 3.12mm ±0.25mm. These results suggest that the Mobi-C® can resist subsidence loads that exceed anticipated physiologic loads on the cervical spine.

Subluxation	To characterize the shear force necessary to cause subluxation of the superior endplate relative to the mobile insert.	48 total Mobi-C® specimens were tested (6 for each test configuration, 3 of each height) in deionized water in neutral, flexion/ extension, and lateral bending configurations. Superior endplates were mounted and attached to a rigid superior fixtures and the inferior endplate was mounted to an actuator that applied shear force at 0.1667 mm/sec. Axial vertical preload of 100N was placed on superior test block. Mobile insert was placed between the endplates.	Peak shear force to produce subluxation was required to exceed the shear load that a natural cervical disc can withstand (20 N^2).	All specimens experienced subluxation of the superior endplate from the polyethylene inlay with no observed failure to the inlay and no deformation or damage observed to the metal endplates (peak shear force applied exceeded load that natural disc can withstand). The worst case configuration experienced subluxation at 22.2±0.28N of shear load. These results suggest that the Mobi-C® can resist subluxation loads that exceed anticipated physiologic loads on the cervical spine.

Wear Testing	To determine the wear and durability characteristics of the Mobi-C® device under complex physiologic conditions.	Six (6) Mobi-C® specimens were tested under the ISO 18192-1 (2011) standard with two (2) loaded soak controls: *Coupled Motion* Combined flexion/extension (± 7.5°), lateral bending (± 6°) and rotation (± 4°) under axial compression (50-150N), for 10 million cycles at a frequency of 1Hz. *Controls* Controls were subjected to the axial compression load only. *Wear Particulate Analysis* Collected wear debris at 500,000 and at each 1 million cycle interval above were analyzed via electron microscopy and low angle laser light scattering under ASTM F1877-05. All specimens were placed in a 37 ± 3°C de-ionized water test medium and bovine serum. Specimens were weighed, measured, and the solution was collected at each cycle check.	The device was required to demonstrate wear data and particulate analysis consistent with what has been for other cervical discs made of the same materials (2.59±0.36mg / million cycles).	*Wear Testing* The mean gravimetric wear rate over the 10 million cycles was 1.546 ±0.075mg/million-cycles. Controls demonstrated negligible wear. There were no mechanical failures or damage to tested components. *Wear Particulate Analysis* Wear particles were polymeric, consistent with wear of the polyethylene component, and free of metal wear particles. Average particle size for all samples was 0.77 µm (SEM) and an aspect ratio of 2.15. *Conclusion* The wear rate and the volume and size,of the of the particulate wear debris are similar to other legally-marketed total disc replacements featuring the same materials and similar surface geometry.

Impingement Wear Testing	To determine the wear and durability characteristics of the Mobi-C® device under conditions simulating device impingement.	Six (6) Mobi-C® specimens were tested with two (2) loaded soak controls. Each Mobi-C® specimen underwent 1 million cycles of ISO 18192-1 wear testing followed by an additional 1 million cycles simulating impingement conditions. Custom test fixtures placed the device in excessive angulation at neutral and specimens were mechanically deformed prior to testing in order to achieve the impingement conditions. Solely flexion/extension motion was applied to maximize impingement.	Test was performed for characterization only.	The 1 million cycles of ISO wear yielded 1.53 ± 0.30mg/million-cycles, similar to the results of the 10 million cycle ISO wear study (1.546 ±0.075mg/million-cycles). The mean gravimetric wear rate over the 1 million cycles of impingement testing was negligible for the polyethylene insert. For the endplates, the wear rate (mg/MC) averaged 0.23 ± 0.20 for the superior endplate and 0.87 ± 1.1 for the inferior endplate. There were no mechanical failures.

[2] White AA, Panjabi MM. Clinical Biomechanics of the Spine. Philadelphia: Lippincott, Williams & Wilkins. 1990. Page 9.

B. Additional Studies

Sterilization, Packaging & Shelf Life Testing

The Mobi-C® device is provided pre-assembled in a sterile package ready for use. All Mobi-C® components are sterilized using gamma radiation at a minimum dose of 25 kGy, at a sterilization assurance level (SAL) of 10^{-6} [6]. Sterilization validation according to ANSI/AAMI/ISO 11137-2: 2006 was conducted to confirm that the sterility assurance level of the device is maintained through a sterile barrier. The device is provided sterile in a double barrier system to allow for easy transfer to the sterile field, with a shelf life of 5 years. The general purpose instruments used to implant the Mobi-C® are provided non-sterile for sterilization by the user. Validation of the recommended sterilization cycle was conducted on the worst case instrument set.

Biocompatibility
The components of the Mobi-C® are constructed of Cobalt, Chromium, Molybdenum (CoCrMo) alloy with Titanium (per ASTM F1580)and hydroxyapatite (per ISO 13779) plasma spray coating and Ultra High Molecular Weight Polyethylene (UHMWPE). The CoCrMo alloy conforms to ISO 5832-12 Alloy. The UHMWPE conforms to ISO 5834-2. All these materials have a long history of use in medical implants with no significant biocompatibility issues, as shown in the literature.

Instrument Testing
Implantation of the Mobi-C® requires a set of instruments suitable for cervical spinal interbody surgery. These instruments are made of materials that have a long history of use in contact with human tissue and fluids. Validation testing was conducted with the instruments, including cleaning, steam sterilization (according to ISO 17665-1:2006), and simulated surgery on cadaveric segments performed by designing surgeons.

X. SUMMARY OF PRIMARY CLINICAL STUDIES

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of reconstruction of the disc with the Mobi-C® Cervical Disc Prosthesis at two contiguous levels from C3-C7 following multi-level discectomy for treatment of intractable radiculopathy (arm pain and/or a neurological deficit) with or without neck pain, or myelopathy due to a multi-level abnormality localized to the level of the disc space and at least one of the following conditions confirmed by radiographic imaging (CT, MRI, X-rays): herniated nucleus pulposus, spondylosis (defined by the presence of osteophytes), and/or visible loss of disc height compared to adjacent levels in skeletally mature patients without prior cervical fusion. The study was performed in the United States under IDE # G050212. This IDE study consisted of one-level and two-level treatment arms conducted simultaneously under the same FDA-approved protocol. The basis for this summary is data from the second arm of the two arm study consisting of treatment with the Mobi-C® Cervical Artificial Disc at two contiguous levels. Data from this two contiguous level clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

Patients were treated between April 2006 and March 2008. The database for this PMA reflected data collected through August 2011 and included 356 patients (339 patients with surgery). There were 24 investigational sites.

The study was a prospective, multi-center, two-arm, randomized (2:1), unmasked, concurrently controlled, non-inferiority clinical study to compare the safety and effectiveness of the Mobi-C® Cervical Disc Prosthesis to the standard of care (a legally marketed alternative with similar indications for use), anterior cervical discectomy and fusion (ACDF) using a semi-constrained, rotational anterior cervical plate (Depuy Spine SLIM-LOC™ Anterior Cervical Plate System; Medtronic Sofamor Danek ATLANTIS™ or ATLANTIS™ VISION Anterior Cervical Plate System) and structural corticocancellous allograft bone

(frozen or freeze-dried, must be obtained from an American Association of Tissue Banks (AATB) accredited bone bank) in treating patients with degenerative disc disease (DDD) with radiculopathy or myeloradiculopathy at two contiguous levels between C3 and C7.

The first subject enrolled at each center was a non-randomized subject (i.e. training case) receiving the Mobi-C® Cervical Disc Prosthesis in order for the staff to become familiar with the implantation procedure for the device. As IDE study consisted of one-level and two-level treatment arms conducted simultaneously under the same FDA-approved protocol, some centers enrolled a one-level subject first and conducted a one-level non-randomized training case (n=15), while other centers enrolled a two-level subject first and conducted a two-level non-randomized training case (n=9). All remaining subjects were randomized by Interactive Voice Randomization System (IVRS). The investigator or study coordinator called the IVRS: 1) after the pre-operative inclusion/exclusion checklist confirmed eligibility and the signature page of the subject informed consent form was signed and dated, and; 2) within 14 days before the scheduled surgery date. Subjects were assigned a treatment, either study or control surgery, according to a stratified randomization schedule (by NDI level) with institution balancing. The treatment-assignment was performed using a 2:1 ratio of investigational recipients to control recipients. After assigning treatment, the investigator was not blinded to the treatment. Subjects remained masked to the treatment group assignment until surgery had been performed to minimize the potential for disproportionate drop-outs in the control group. Because masking after surgery was not guaranteed (i.e., the subject would know based on post-operative requirements or X-ray images), the sponsor did not conceal assignment from the subject after surgery. The applicant is not aware of any randomized patient who was unblinded to their treatment.

Patients were evaluated preoperatively, prior to discharge, and then at 6 weeks, 3 months, 6 months, 12 months, 18 months and 24 months and annually thereafter. The recommended postoperative care was according to the individual investigator's discretion and consisted of a physician-managed individual post-operative rehabilitation program which may have included the optional of use of a cervical collar. Subjects were advised according to the individual physician's discretion to increase daily activity (sitting, standing and walking), shower only in absence of wound drainage, and drive after collar removal. The study excluded subjects with a current history of heavy smoking defined as more than one pack of cigarettes per day. Subjects were requested to discontinue the use of NSAIDs from one week prior to surgery until 3 months following surgery in both treatment groups. Control group subjects were permitted to use bone growth stimulators.

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. Overall success was determined by data collected during the initial 24 months of follow-up. All adverse events were independently adjudicated (for seriousness and relationship to the device) by a Clinical Events Committee (CEC) comprised of three clinicians (2 neurosurgeons and 1 orthopedic surgeon) without any relationship to the study or study investigators. A Data Monitoring Committee (DMC) whose membership included a biostatistician, a bioengineer, and the same three clinicians involved in the CEC reviewed interim data during the enrollment phase.

The study was designed using Frequentist statistical methods as a non-inferiority trial with a margin (delta) of 10%. A closed testing procedure was used to allow for superiority to be tested in the event that non-inferiority was established for the primary effectiveness endpoint.

The protocol specified a sample size of 196 Mobi-C® randomized subjects and 98 control subjects per group based on a projected 60% success rate for control subjects and 65% success rate for Mobi-C® subjects, and 80% power for a one-sided 0.05 significance level. With the addition of the anticipated 10% loss-to-follow up, the total planned randomized sample size was 218 Mobi-C® subjects and 109 ACDF control subjects. The study allowed for 1 nonrandomized training case per site, and resulted in 9 nonrandomized Mobi-C® subjects in the two level study arm.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the two level Mobi-C® study arm was limited to patients who met the following inclusion criteria.

1. Age 18-69 years.
2. Diagnosis of radiculopathy or myeloradiculopathy of the cervical spine, with pain, paresthesias or paralysis in a specific nerve root distribution C3 through C7, including at least one of the following:
    - Neck and/or arm pain (at least 30 mm on the 100 mm visual analogue scale [VAS] scale).
    - Decreased muscle strength of at least one level on the clinical evaluation 0 to 5 scale.
    - Abnormal sensation including hyperesthesia or hypoesthesia; and/or
    - Abnormal reflexes.
3. Symptomatic at two contiguous levels from C3 to C7.
4. Radiographically determined pathology at the level to be treated correlating to primary symptoms including at least one of the following:
    - Decreased disc height on radiography, computed tomography (CT), or magnetic resonance imaging (MRI) in comparison to a normal adjacent disc.
    - Degenerative spondylosis on CT or MRI.
    - Disc herniation on CT or MRI.
5. NDI Score of ≥ 15/50 or ≥ 30%.
6. Unresponsive to non-operative, conservative treatment (rest, heat, electrotherapy, physical therapy, chiropractic care and/or analgesics) for:
    - Approximately six weeks from radiculopathy or myeloradiculopathy symptom onset; or
    - Have the presence of progressive symptoms or signs of nerve root/spinal cord compression despite continued non-operative conservative treatment.
7. Appropriate for treatment using an anterior surgical approach, including having no prior surgery at the operative level and no prior cervical fusion procedure at any level.
8. Reported to be medically cleared for surgery.
9. Reported to be physically and mentally able and willing to comply with the Protocol, including the ability to read and complete required forms and willing and able to adhere to the scheduled follow-up visits and requirements of the Protocol.

10. Written informed consent provided by subject or subject's legally authorized representative.
11. Willingness to discontinue all use of non-steroidal anti-inflammatory drugs (NSAIDs) from one week before surgery until 3 months after surgery.

Patients were <u>not</u> permitted to enroll in the Mobi-C® study if they met any of the following exclusion criteria.

1. Reported to have an active systemic infection or infection at the operative site.
2. Reported to have a history of or anticipated treatment for active systemic infection, including HIV or Hepatitis C.
3. More than one immobile vertebral level between C1 to C7 from any cause including but not limited to congenital abnormalities and osteoarthritic "spontaneous" fusions.
4. Previous trauma to the C3 to C7 levels resulting in significant bony or disco-ligamentous cervical spine injury.
5. Reported to have had any prior spine surgery at the operative level.
6. Reported to have had a prior cervical fusion procedure at any level.
7. Axial neck pain in the absence of other symptoms of radiculopathy or myeloradiculopathy justifying the need for surgical intervention.
8. Disc height less than 3 mm as measured from the center of the disc in a neutral position and disc height less than 20% of the anterior-posterior width of the inferior vertebral body.
9. Radiographic confirmation of severe facet joint disease or degeneration.
10. Reported to have an increased risk of osteoporosis/osteopenia. This was defined as a T-score less than (worse than) -1.5 on a previous or required Hologic Sahara or dual energy X-ray absorptiometry (DEXA) scan. All subjects that met one or more of the following were to undergo a Hologic Sahara or DEXA scan as part of the study enrollment procedures:
    - Females 50 years and older;
    - Females who were post-menopausal or post-hysterectomy with oophorectomy;
    - Subjects taking bisphosphonate medication for the treatment of osteoporosis; and/or
    - Subjects with history of chronic use of high dose steroids. High dose steroid use is defined as part of Exclusion Criterion #22.

    All females less than 50 years of age, and all males, who had not had a Hologic Sahara or DEXA scan within six months of surgery, were screened for osteoporosis using the Simple Calculated Osteoporosis Risk Estimation (SCORE) questionnaire. Subjects whose screening suggests increased risk (SCORE greater than 6) were to undergo a Hologic Sahara or DEXA scan as part of the study enrollment procedures.
11. Reported to have Paget's disease, osteomalacia or any other metabolic bone disease other than osteoporosis, which is addressed above.
12. Reported active malignancy that included a history of any invasive malignancy (except non-melanoma skin cancer), unless the subject had been treated with curative intent and there had been no clinical signs or symptoms of the malignancy for at least five years.
13. Symptomatic DDD or significant cervical spondylosis at more than two levels.
14. Spondylolysis.

15. Marked cervical instability on resting lateral or flexion-extension radiographs demonstrated by:
    - Translation ≥ 3.5 mm, and/or
    - Greater than 11° angular difference to that of either adjacent level.
16. Known allergy to cobalt, chromium, molybdenum or polyethylene.
17. Segmental angulation of greater than 11° at treatment or adjacent levels.
18. Reported pregnancy or nursing at time of enrollment, or with plans to become pregnant within the next three years.
19. Reported to have rheumatoid arthritis, lupus, or other autoimmune disease that affect the musculoskeletal system.
20. Congenital bony and/or spinal cord abnormalities that affect spinal stability.
21. Reported to have diseases or conditions that would preclude accurate clinical evaluation (e.g. neuromuscular disorders).
22. Reported concomitant conditions requiring daily, high-dose oral and/or inhaled steroids. High dose steroid use is defined as:
    - Daily, chronic use of oral steroids of 5 mg/day or greater.
    - Daily, chronic use of inhaled corticosteroids (at least twice per day).
    - Use of short-term (less than 10 days) oral steroids at a daily dose greater than 40 mg within one month of the study procedure.
23. Reported to have current or recent history of substance abuse (alcoholism and/or narcotic addiction) requiring intervention.
24. Clinically Severe Obesity, as defined by National Institutes of Health (NIH) Clinical Guidelines Body Mass Index (BMI) > 40).
25. Reported use of any other investigational drug or medical device within the last 30 days prior to surgery.
26. Evidence of symptomatic moderate to severe facet joint degeneration or disease where the investigator felt this was a major contributor to the subject's pain as diagnosed by injection and imaging.
27. Reported to be taking medications known to potentially interfere with bone/soft tissue healing (e.g., high-dose oral and/or inhaled steroids, immunosuppressant medication, chemotherapeutic agents). High dose steroid use is defined as part of Exclusion Criterion #22.
28. Reported to have pending personal litigation relating to spinal injury (worker's compensation was not an exclusion).
29. Reported to have a current history of heavy smoking (more than one pack of cigarettes per day).
30. Anticipated or potential relocation greater than 50 miles that may interfere with completion of follow-up examinations.
31. Reported to have mental illness or belonged to a vulnerable population, as determined by the investigator (e.g., prisoner or developmentally disabled), that would compromise ability to provide informed consent or compliance with follow-up requirements.
32. Reported to have an uncontrolled seizure disorder.
33. Reported to have taken epidural steroids within 14 days prior to surgery.

2. Follow-up Schedule

All patients were scheduled to return for follow-up examinations at 6 weeks (±1 week), 3 months (±30 days), 6 months (±30 days), 12 months (±30 days), 18 months (±30 days), 24 months (±30 days), and annually thereafter (±30 days). The following parameters were measured throughout the study:

Table 4. Clinical Evaluation Schedule

Evaluation	Pre-op	Surgery/ Hospital Discharge	6 wks	3 mo	6 mo	12 mo	18 mo	24 mo & annually
Neck Disability Index	X		X	X	X	X	X	X
Neck and Arm Pain (VAS)	X		X	X	X	X	X	X
Health Status (SF-12)	X				X	X	X	X
Neurological Status/Gait	X		X	X	X	X	X	X
Dysphagia Scale (FOSS)*			X	X	X	X	X	X
Adverse Events**	X	X	X	X	X	X	X	X
Demographic/Baseline Data	X							
Operative Data		X						
Medication Use	X	X	X	X	X	X	X	X
Radiographs								
Neutral (AP & Lateral)	X	X	X	X	X	X	X	X
Dynamic(F/E/ RSB/LSB)§	X		X	X	X	X	X	X
CT and/or MRI	X							
Radiographic Outcomes:								
Fusion status	X				X	X	X	X
Device condition	X	X	X	X	X	X	X	X
Subsidence/ migration	X	X	X	X	X	X	X	X
Range of motion	X	X	X	X	X	X	X	X
Radiolucency	X			X	X	X	X	X
Disc height	X	X	X	X	X	X	X	X
Patient Satisfaction				X	X	X	X	X

* Functional Outcome Swallowing Scale for Dysphagia (FOSS)

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

§ Dynamic radiographs included flexion (F) / extension (E) bending and right side bending (RSB)/ left side bending (LSB) radiographs

3. Clinical Endpoints

The effectiveness of the Mobi-C® was assessed using a composite definition of study success. Effectiveness was further evaluated by monitoring 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 12 questionnaire (SF-12) as well as patient satisfaction compared to the ACDF control group. The same criteria were used to measure success in both groups.

The safety of the Mobi-C® Cervical Disc Prosthesis was assessed by comparison to the ACDF control group with respect to the nature and frequency of adverse events (overall and in terms of seriousness and relationship to the implant), secondary surgical procedures as well as maintenance or improvement in neurological status.

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

According to the IDE protocol, an individual patient in either treatment group was considered a success if the following criteria were met at 24 months:

- Improvement in NDI of at least 15/50 points in subjects with a baseline NDI score of ≥ 30/50 points, or a 50% improvement in subjects with a baseline NDI score of < 30/50 points;
- No study failures due to secondary surgical interventions at the index levels;
- Absence of major complications defined as radiographic failure, neurological failure, or failure by adverse event as adjudicated by the CEC.

A variation of the primary endpoint analysis was prospectively planned to assess subject success when major complications due to radiographic assessment were removed from the analysis. This variation was considered in order to compare the treatment groups after removing the radiographic assessments altogether.

Secondary endpoints, measured in both treatment groups, included neck pain (VAS), arm pain (VAS), muscle strength, sensory deficit, significant neurological deterioration, adjacent segment degeneration, displacement or migration of the device, range of motion, radiolucency, quality of life (SF-12), Dysphagia (FOSS scale), and gait analysis (Nurick classification).

Overall study success criteria were based on a comparison of individual patient success rates, such that the patient success rate for the Mobi-C® investigational group must be non-inferior to that of the ACDF fusion control group. Frequentist statistical methods were used to test for non-inferiority using an exact 95% one-sided confidence bound for the difference between the study and control success rates; if a 10% offset could be ruled out according to the 95% lower bound, then superiority was to be tested. A closed testing procedure was used to allow

for superiority to be tested in the event that non-inferiority was established for the primary effectiveness endpoint.

B. Accountability of PMA Cohort

A total of 339 subjects completed study surgery. This included 234 subjects treated with Mobi-C® (225 randomized, 9 training) and 105 ACDF control subjects. There were an additional 17 subjects who were randomized, but withdrew prior to surgery. At the time of database lock, of the 339 subjects with surgery, complete 24 month primary endpoint data was available for 208 Mobi-C® patients (98.6%), 83 ACDF control patients (93.3%) and 6 non-randomized Mobi-C® patients (75.0%). At this time point, 195 Mobi-C® patients (92.4%), 81 ACDF control patients (91.0%) and 5 non-randomized Mobi-C® patients (62.5%) presented with complete data within the FDA Guidance Window. As the protocol specified follow-up windows were narrower than those specified in FDA guidance documents, accountability according to protocol-specified visits windows has also been provided. A summary of patient accountability data for the 12 month, 24 month, and 36 month follow-up visits is provided in **Table 5**, and a summary of data available at 24 months for each specific evaluation is provided in **Table 6**.

Table 5. Patient Accountability (based on treatment assignment)

Number of Patients	12 Months (±2 Months)			24 Months (±2 Months)			36 Months (±2 Months)		
	Mobi-C®	ACDF	Training	Mobi-C®	ACDF	Training	Mobi-C®	ACDF	Training
w/ Surgery	225	105	9	225	105	9	225	105	9
Theoretical	225	105	9	225	105	9	225	105	9
Deaths	0	0	0	1	0	0	1	0	0
Failures[1]	8	6	0	13	16	1	14	17	1
Not yet overdue	-	-	-	-	-	-	-	-	-
Expected[2]	217	99	9	211	89	8	210	88	8
Actual, efficacy[3] (% Follow-up)	205 (94.5%)	89 (89.9%)	8 (88.9%)	208 (98.6%)	83 (93.3%)	6 (75.0%)	185 (88.1%)	70 (79.5%)	3 (37.5%)
Actual, efficacy in window[4] (% Follow-up)	199 (91.7%)	83 (83.8%)	8 (88.9%)	195 (92.4%)	81 (91.0%)	5 (62.5%)	165 (78.6%)	65 (73.9%)	2 (25.0%)
Actual, any data[5] (% Follow-up)	208 (95.9%)	89 (89.9%)	9 (100.0%)	208 (98.6%)	83 (93.3%)	7 (87.5%)	188 (89.5%)	70 (79.5%)	5 (62.5%)

[1]A failure is any patient who experienced a major complication via the CEC assessment of adverse events or was a study failure due to subsequent surgical intervention. Note that this row is cumulative.

[2]Expected equals theoretical minus cumulative failures.

[3] Refers to any patient having a value for the composite endpoint, i.e, for patient success, if all composite endpoint measures were collected and successes for that particular timepoint, or for patient failure, at least one composite endpoint measure was a failure for that particular timepoint.

[4]Refers to defined follow-up windows from the FDA Guidance Document entitled "Clinical Data Presentations for Orthopedic Device Applications" (2004): 6 wks: 28 ≤ day ≤ 56, 3 mo: 77.25 ≤ day ≤ 105.25, 6 mo: 152.5 ≤ day ≤ 212.5, 12 mo: 305≤ day ≤ 425, 18 mo: 487.5 ≤ day ≤ 607.5, 24 mo: 670 ≤ day≤ 790
[5]Any data refers to patients with any evaluation data available for that visit. That is, the patient appears at the visit.

Table 6. Patient Data Accounting at Month 24

Parameter	Mobi-C®	ACDF	Training
Total Randomized	232	115	9
Total Treated[1]	225	105	N/A
Safety Population[2]	225	105	9
As-treated[3]	214	95	N/A
Composite Effectiveness Endpoint[4]	221 (98.2%)	99 (94.3%)	7 (77.8%)
NDI†	216 (96.0%)	89 (84.8%)	7 (77.8%)
VAS Neck and Arm Pain†	216 (96.0%)	87 (82.9%)	8 (88.9%)
SF-12†	211 (93.8%)	87 (82.9%)	8 (88.9%)
Patient Satisfaction‡	216 (96.0%)	87 (82.9%)	8 (88.9%)
Dysphagia Scale (FOSS) †	216 (96.0%)	89 (84.8%)	8 (88.9%)
Neurological Exam†	216 (96.0%)	89 (84.8%)	8 (88.9%)
Radiologic Assessments†			
Radiographic major complication – Both levels	218 (96.9%)	89 (84.8%)	8 (88.9%)
ROM – Superior level	216 (96.0%)	89 (84.8%)	8 (88.9%)
ROM – Inferior level	214 (95.1%)	88 (83.8%)	8 (88.9%)
Adjacent segment degeneration- Both levels	216 (96.0%)	87 (82.9%)	8 (88.9%)
Migration / Subsidence – Both levels	216 (96.0%)	89 (84.8%)	8 (88.9%)
Radiolucency – Both levels	216 (96.0%)	89 (84.8%)	8 (88.9%)
Change in FSU Height – Superior	215 (95.6%)	89 (84.8%)	8 (88.9%)
Change in FSU Height - Inferior	209 (92.9%)	87 (82.9%)	8 (88.9%)

[1] Refers to all subjects who were randomized and received surgery.
[2] Refers to all treated subjects, randomized and training.
[3] Refers to all subjects who were randomized, received surgery as specified in the protocol, and met all eligibility criteria
[4] All treated subjects for which a composite effectiveness endpoint value (success or failure) was known.
† Accounting is affected by subjects lost to follow up and/or missing

Throughout this summary, the population of all subjects treated with surgery, including randomized Mobi-C® subjects (N=225), randomized ACDF control subjects (N=105), and Mobi-C® non-randomized training subjects (N=9) will be used for safety analyses and will be termed as the **"Safety Population"**. The as-treated population (also termed **"Primary Analysis Population"**) is used for effectiveness analyses (225 randomized Mobi-C® subjects, 105 randomized ACDF control subjects).

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are consistent with demographics reported for prior cervical artificial disc studies conducted in the US. Demographic data showed that the treatment groups were well-balanced and no statistically significant differences were noted in the demographic characteristics, as shown below (**Table 7**).

Table 7. Patient Demographics and Baseline Characteristics – Primary Analysis Population

Demographic Measure	Randomized Mobi-C® (N=225)	Non-Randomized Mobi-C® (N=9)	Randomized ACDF (N=105)	P-value (Randomized groups)
Gender				
Male	113 (50.2%)	6 (66.7%)	45 (42.9%)	0.2375**
Female	112 (49.8%)	3 (33.3%)	60 (57.1%)	
Age (years)	45.3 ±8.10 Range: 27-67	40.0 ±9.45 Range: 23-51	46.2±7.99 Range: 27-66	0.3725***
Ethnicity				
Hispanic or Latino	14 (6.2%)	1 (11.1%)	7 (6.7%)	>0.9999**
Not Hispanic or Latino	211 (93.8%)	8 (88.9%)	98 (93.3%)	
Race				
American Indian Alaska Native	3 (1.3%)	0	1 (1.0%)	
Caucasian	212 (94.2%)	7 (77.8%)	99 (94.3%)	
Asian	4 (1.8%)	0	0	>0.9999**
Black	5 (2.2%)	2 (22.2%)	4 (3.8%)	
Native Hawaiian/other Pacific Islander	0	0	0	
Other	1 (0.4%)	0	1 (1.0%)	
Height (in)	67.86±3.604 Range: 59.0-78.0	68.61±2.497 Range: 65.0-72.5	67.51±3.765 Range: 60.0-76.0	0.4093***
Weight (lbs)	181.71±36.117 Range: 92.0-300.0	172.11±44.363 Range: 105.0-235.0	182.86±34.828 Range: 115.0-280.0	0.7858***
BMI (kg/m^2)	27.625 ±4.4697 Range: 16.83 – 39.54	25.41±4.982 Range: 16.44-31.43	28.102±4.1953 Range: 19.66-39.78	0.3586***
Smoke more than one pack per day (yes)*	0	0	0	>0.9999**
History non-op care (yes):				
Pain Medication[1]	208 (92.4%)	9 (100.0%)	100 (95.2%)	0.7169**
Opioid Use[2]	-	-	-	-
Opium Alkaloid	27 (12.0%)	2 (22.2%)	7 (6.7%)	0.1741**
Semi-Synthetic Opioid Derivative	119 (52.9%)	5 (55.6%)	60 (57.1%)	0.4794**
Synthetic Opioid	18 (8.0%)	0	18 (17.1%)	0.0215**
Physical therapy	110 (48.9%)	4 (44.4%)	49 (46.7%)	0.9290**
Collar	27 (12.0%)	0	15 (14.3%)	0.6324**
Chiropractic	61 (27.1%)	2 (22.2%)	23 (21.9%)	0.5518**
Cervical Traction	45 (20.0%)	3 (33.3%)	21 (20.0%)	0.6021**
Bedrest /Immobilization	110 (48.9%)	3 (33.3%)	49 (46.7%)	0.6397**
Acupuncture	18 (8.0%)	11 (11.1%)	6 (5.7%)	0.4529**
Work Status (Being able to Work)	141 (62.7%)	5 (55.6%)	64 (61.0%)	>0.9999**
Driving Status (Being able to drive)	210 (93.3%)	8 (88.9%)	102 (97.1%)	0.4026**

*Data on amount and length of tobacco use was not captured.

**Using Fisher Exact test to compare frequencies between the treatments.

***Using unpaired t test to compare across treatment group.

[1]Aggregate usage of medications determined to be Pain Medication presented for baseline comparison.

[2]Opioid usage (aggregate) with specific categories is presented separately as a subset of Pain Medication.

Note – 'Injections' were not categorically defined in the Study Protocol, and as such are not presented here.

The mean baseline pre-operative assessments for NDI, VAS neck pain, VAS arm pain, and both component scales of SF-12 were also similar between treatment groups. There were no statistical differences between pre-operative neurological status or range of motion between the groups, as shown in **Table 8.**

Table 8. Preoperative Evaluation of Endpoints

Variable	Randomized Mobi-C® (N=225)	Non-Randomized Mobi-C® (N=9)	Randomized ACDF (N=105)	P-Value (Randomized Groups)
NDI	53.86 ± 15.576	58.5±15.78	55.35±15.321	0.4150**
VAS Neck Pain	71.24 ±20.504	71.63±12.386	74.56±18.937	0.1619**
VAS Left Arm Pain	48.32 ±34.818	51.31±32.212	49.92±33.799	0.6948**
VAS Right Arm Pain	41.91 ±35.265	47.38±36.115	45.64±35.440	0.3726**
SF-12 PCS	33.390 ±6.7184	31.521±6.0942	32.524±7.6635	0.3051**
SF-12 MCS	41.944 ±11.3041	43.588±14.6502	42.019±11.9173	0.9564**
Neurological Status (normal[1])				
Motor	99 (44.0%)	4 (44.4%)	54 (51.4%)	0.2363*
Sensory				
Light Touch	110 (48.9%)	3 (33.3%)	56 (53.3%)	0.4796*
Pin Prick	108 (48.0%)	4 (44.4%)	52 (49.5%)	0.8140*
Reflexes	80 (35.6%)	3 (33.3%)	41 (39.0%)	0.5424*
Other assessments (gait[2])	215 (95.6%)	9 (100.0%)	98 (93.3%)	0.5908*
Baseline ROM Flexion-extension (°)				
Superior Level	9.13±4.849	7.39±3.728	9.33±4.875	0.7355**
Inferior Level	7.44±4.341	6.30±4.382	7.14±3.860	0.5574**
Baseline ROM Lateral bending (mm)				
Superior Level	5.76±3.374	4.38±2.522	5.48±3.041	0.4777**
Inferior Level	4.91±3.265	6.65±5.526	4.77±2.866	0.7227**

*Using Fisher Exact test to compare frequencies between the treatments

** Using unpaired t-test to make comparison across treatments for all Mobi-C® subjects compared to ACDF subjects.

[1] Normal defined as normal status for both left and right sided assessments.

[2] Gait was the only other neurological assessment performed, per the study protocol.

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the Safety Population cohort of 339 total patients with surgery (225 randomized Mobi-C® patients, 9 non-randomized Mobi-C® patients, and 105 ACDF control patients).

Adverse events that occurred in the PMA clinical study:

Summary

A summary of the total number of adverse events is shown in **Table 9**. Adverse events were classified by both the Clinical Events Committee (CEC) and the Investigator for relationship to the device and seriousness of the event. The information is presented in **Table 9**. The overall adverse event rate (defined as the percentage of patients experiencing at least 1 adverse event in each category) was similar for the randomized Mobi-C® group (89.3%), non-randomized Mobi-C® training group (100.0%), and ACDF control group (95.2%).

Table 9. Summary of Adverse Events through Month 24 – Safety Population

	Mobi-C® Non-Randomized (N=9)			Mobi-C® Randomized (N=225)			ACDF with Anterior Cervical Plate (N=105)				
	Events N	Subjects N (%)	Subject-Level CI*	Events N	Subjects N (%)	Subject-Level CI***	Events N	Subjects N (%)	Subject-Level CI***	Event Level P-value*	Subject Level P-value**
All Adverse Events	54	9 (100.0%)	(0.664, 1.000)	1467	201 (89.3%)	(0.845, 0.930)	884	100 (95.2%)	(0.892, 0.984)	0.0202	0.0952
Treatment-Emergent Adverse Events	54	9 (100.0%)	(0.664, 1.000)	1442	200 (88.9%)	(0.840, 0.927)	867	100 (95.2%)	(0.892, 0.984)	0.0209	0.0665
Related Adverse Events (a)	6	4 (44.4%)	(0.137, 0.788)	75	36 (16.0%)	(0.115, 0.215)	78	30 (28.6%)	(0.202, 0.382)	0.0158	0.0116
Definitely Related	0	0		10	9 (4.0%)	(0.018, 0.075)	10	8 (7.6%)	(0.033, 0.145)	0.1804	0.1855
Possibly Related	6	4 (44.4%)	(0.137, 0.788)	65	34 (15.1%)	(0.107, 0.205)	68	26 (24.8%)	(0.169, 0.341)	0.0283	0.0457
Related Adverse Events (b)	5	3 (33.3%)	(0.075, 0.701)	67	36 (16.0%)	(0.115, 0.215)	74	36 (34.3%)	(0.253, 0.442)	0.0060	0.0003
Definitely Related	0	0	-	10	9 (4.0%)	(0.018, 0.075)	5	5 (4.8%)	(0.016, 0.108)	0.9042	0.7730
Possibly Related	5	3 (33.3%)	(0.075, 0.701)	57	34 (15.1%)	(0.107, 0.205)	69	34 (32.4%)	(0.236, 0.422)	0.0045	0.0004
Serious Adverse Events	1	1 (11.1%)	(0.003, 0.482)	103	55 (24.4%)	(0.190, 0.306)	68	34 (32.4%)	(0.236, 0.422)	0.1730	0.1438
Related Serious Adverse Events (c)	0	0	-	10	7 (3.1%)	(0.013, 0.063)	23	13 (12.4%)	(0.068, 0.202)	0.0156	0.0021
Definitely Related	0	0	-	1	1 (0.4%)	(0.000, 0.025)	10	8 (7.6%)	(0.033, 0.145)	0.0105	0.0006
Possibly Related	0	0	-	9	6 (2.7%)	(0.010, 0.057)	13	7 (6.7%)	(0.027, 0.133)	0.1610	0.1244
Related Serious Adverse Events (d)	0	0	-	16	8 (3.6%)	(0.015, 0.069)	22	15 (14.3%)	(0.082, 0.225)	0.0331	0.0008
Definitely Related	0	0	-	3	2 (0.9%)	(0.001, 0.032)	5	5 (4.8%)	(0.016, 0.108)	0.1401	0.0355
Possibly Related	0	0	-	13	7 (3.1%)	(0.013, 0.063)	17	12 (11.4%)	(0.060, 0.191)	0.0736	0.0043
Unanticipated Adverse Device Effects	0	0	-	1	1 (0.4%)	(0.000, 0.025)	1	1 (1.0%)	(0.000, 0.052)	0.6296	0.5358

* The event-level incidences between Mobi-C® Randomized and ACDF treatment groups will be analyzed using an unpaired t-test.
** The subject-level p-value between Mobi-C® Randomized and ACDF treatment groups will be calculated using Fisher Exact test.
*** The subject-level incidences of these outcomes will be analyzed using a 95% two-sided Binomial exact confidence interval.
(a) Adverse events classified by the investigator as possibly or definitely related to study device.
(b) Adverse events classified by CEC members as possibly or definitely related to study device.
(c) Serious adverse events classified by the investigator as possibly or definitely related to study device.
(d) Serious adverse events classified by CEC members as possibly or definitely related to study device.

Adverse Events by Level of Treatment

Table 10a provides summary data on the number of adverse events in each treatment group, including statistical analysis and comparison between the randomized and non-randomized Mobi-C® subjects. **Table 10b** provides data on the number of adverse events in each treatment group stratified by level of treatment. The percentage of subjects with treatment emergent adverse events was equivalent for the Mobi-C® and the ACDF groups across all levels. There was a trend across levels toward fewer device-related AEs, and device-related serious AEs for the Mobi-C® group. Across treatment groups, relatively fewer subjects were treated at C3-4, C4-5 (N=3) compared with treatment at the C4-5, C5-6 (N=84) and C5-6, C6-7 (N=252) levels.

Table 10a. Summary of Adverse Events through Month 24 – Safety Population

	Mobi-C® Non-Randomized (N=9)			Mobi-C® Randomized (N=225)			ACDF with Anterior Cervical Plate (N=105)				
	Events N	Subjects N (%)	Subject-Level CI*	Events N	Subjects N (%)	Subject-Level CI***	Events N	Subjects N (%)	Subject-Level CI***	Event Level P-value*	Subject Level P-value**
All Adverse Events	54	9 (100.0%)	(0.664, 1.000)	1467	201 (89.3%)	(0.845, 0.930)	884	100 (95.2%)	(0.892, 0.984)	0.0202	0.0952
Treatment-Emergent Adverse Events	54	9 (100.0%)	(0.664, 1.000)	1442	200 (88.9%)	(0.840, 0.927)	867	100 (95.2%)	(0.892, 0.984)	0.0209	0.0665

CI = confidence interval

* The event-level incidences between Mobi-C® Randomized and ACDF groups are presented using an unpaired t-test.

** The subject-level p-values between Mobi-C® Randomized and ACDF groups are calculated using Fisher Exact test.

*** The subject-level incidences of these outcomes are analyzed using a 95% two-sided Binomial exact confidence interval.

Table 10b. Total Adverse Events by Level Treated

	Mobi-C® (N=234)*			ACDF (N=105)		
	Events N	Subjects N (%)	Subject-Level CI**	Events N	Subjects N (%)	Subject-Level CI**
Treated Segment: C3-C4, C4-C5	(N=1)			(N=2)		
TEAEs	6	1 (100%)	-	16	2 (100.0%)	-
Treated Segment: C4-C5, C5-C6	(N=61)			(N=23)		
TEAEs	379	53 (86.9%)	(0.758, 0.942)	225	22 (95.7%)	(0.781, 0.999)
Treated Segment: C5-C6, C6-C7	(N=172)			(N=80)		
TEAEs	1111	155 (90.1%)	(0.846, 0.941)	626	76 (95.0%)	(0.877, 0.986)

TEAE = treatment emergent adverse event

* Includes all Mobi-C® study subjects.

**The subject-level incidences of these outcomes are analyzed using a 95% two-sided Binomial exact confidence interval.

All Adverse Events

The adverse events reported in the PMA from all 339 total patients (225 randomized Mobi-C® patients, 105 ACDF control patients, 9 non-randomized Mobi-C® patients) are shown in **Table 11** This table includes adverse events from all patients, randomized and non-randomized, to establish the safety profile of the device for the primary study endpoint (24 months). Adverse events are listed in alphabetical order according to adverse event

categories. Definitions of the adverse event categories are provided in **Table 12**. **Table 13** is presented in a similar fashion as **Table 11** (using the categories as defined in **Table 12**), and includes all known adverse event data at the time of PMA submission, including all available subject AE data through 24 months of follow up. 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.

The most commonly reported categories of adverse events through month 24 were Neck Pain (in 32.1% in Mobi-C® subjects and 46.7% of ACDF subjects), Arm Pain (in 17.1% of all Mobi-C® subjects and 23.8% of ACDF subjects), Back Pain (in 27.4% of all Mobi-C® subjects and 23.8% of ACDF subjects), Neurological – Upper Extremity Sensory (in 29.9% of all Mobi-C® subjects and 44.8% of ACDF subjects), Shoulder Pain (in 22.2% of all Mobi-C® subjects and 31.4% of ACDF subjects), and Other Pain (in 56.0% of all Mobi-C® subjects and 61.0% of ACDF subjects). Notably, the ACDF subjects reported higher rates for dysphagia and dysphonia (22.9%) compared to Mobi-C® subjects (16.7%). The nonunion rate in ACDF subjects based on investigator reporting was 12.4%. The heterotopic ossification rate at the level of surgery was 1.3% in Mobi-C® subjects. One unanticipated adverse device effects was reported in each randomized group (Mobi-C®, 0.4%; ACDF, 1%)

Table 11. All Treatment Emergent Adverse Events through 24 Months in US IDE Study – All Study Subjects

	Surgery to Discharge		Discharge to Week 6		Week 6 to Month 3		Months 3 to 6		Months 6 to 12		Months 12 to 18		Months 18 to 24		Mobi-C®		ACDF	
Complication	M	F	M	F	M	F	M	F	M	F	M	F	M	F	**#Patients (% of 234)**	**Total Events**	**#Patients (% of 105)**	**Total Events**
All Adverse Events[1]	148	53	149	76	137	134	156	96	288	166	232	102	140	84	209 (89.3%)	1496	100 (95.2%)	867
Anatomy/Technical Difficulty	1	0	2	0	1	0	1	1	3	2	0	1	2	1	9 (3.8%)	9	5 (4.8%)	5
Cervical –Study Surgery	1	0	2	0	1	0	1	0	0	1	0	0	1	1	6 (2.6%)	6	2 (1.9%)	2
Cervical – Non Study Surgery	0	0	0	0	0	0	0	1	3	1	0	0	1	0	3 (1.3%)	3	2 (1.9%)	2
Non-Cervical	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1 (1.0%)	1
Cancer	0	0	0	0	0	0	0	0	1	1	1	0	0	0	3 (1.3%)	3	1 (1.0%)	1
Cardiovascular	1	2	2	1	2	1	0	0	8	4	10	1	7	3	21 (9.0%)	29	10 (9.5%)	12
Death	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1 (0.4%)	1	0	0
Dysphagia/Dysphonia	12	6	10	10	6	2	2	1	4	2	2	2	3	2	39 (16.7%)	43	24 (22.9%)	27
Dysphagia	9	6	10	10	6	2	2	1	4	1	1	2	2	1	37 (15.8%)	38	24 (22.9%)	25
Dysphonia	3	0	0	0	0	0	0	0	0	1	1	0	1	1	5 (2.1%)	5	2 (1.9%)	2
Gastrointestinal	26	12	13	3	11	9	5	3	8	2	17	13	16	9	47 (20.1%)	97	32 (30.5%)	52
Heterotopic Ossification	0	0	0	1	0	0	1	0	2	0	2	0	3	0	6 (2.6%)	6	1 (1.0%)	1
Cervical - Index Level	0	0	0	0	0	0	0	0	2	0	1	0	1	0	3 (1.3%)	3	0	0
Cervical - Adjacent Level	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1 (0.4%)	1	0	0
Non Cervical	0	0	0	1	0	0	0	0	0	0	1	0	2	0	2 (0.9%)	2	1 (1.0%)	1
Infection	6	5	16	6	7	11	12	9	16	6	17	6	24	7	56 (23.9 %)	98	30 (28.6%)	50
Superficial Wound – Cervical	4	3	3	1	0	0	0	0	1	0	0	0	0	0	8 (3.4%)	8	4 (3.8%)	4
Deep Wound – Cervical	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Other Wound - Non Study Surgery	0	0	0	0	1	1	0	0	0	1	0	1	0	0	3 (1.3%)	3	3 (2.9%)	3
Systemic	1	0	1	1	1	1	2	0	1	1	3	0	5	2	10 (4.3%)	13	5 (4.8%)	5
Local	1	2	12	4	5	9	10	9	14	4	14	5	19	5	47 (20.1%)	74	23 (21.9%)	38
Malpositioned Implant	0	0	1	0	0	0	1	0	0	0	2	0	0	0	4 (1.7%)	4	0	0
Neck and/or Arm Pain	10	2	27	17	27	19	30	18	34	20	20	22	24	11	102 (43.6%)	167	63 (60.0%)	111
Neck Pain	9	2	14	14	12	12	20	9	16	13	12	10	14	5	75 (32.1%)	95	49 (46.7%)	68
Arm Pain	1	0	10	3	12	6	9	5	14	3	7	10	5	6	40 (17.1%)	55	25 (23.8%)	32

	Surgery to Discharge		Discharge to Week 6		Week 6 to Month 3		Months 3 to 6		Months 6 to 12		Months 12 to 18		Months 18 to 24		Mobi-C®		ACDF	
Complication	M	F	M	F	M	F	M	F	M	F	M	F	M	F	**#Patients (% of 234)**	**Total Events**	**#Patients (% of 105)**	**Total Events**
Neck And Arm Pain	0	0	3	0	3	1	1	4	4	4	1	2	5	0	8 (3.4%)	17	6 (5.7%)	11
Neurological	21	8	69	54	61	49	79	42	70	57	67	40	85	40	124 (53.0%)	426	78 (74.3%)	278
Upper Extremity – Sensory	1	0	45	27	26	21	39	14	41	23	37	20	39	24	70 (29.9%)	218	47 (44.8%)	119
Upper Extremity – Motor	3	1	4	2	4	1	2	2	3	6	3	3	2	3	17 (7.3%)	19	16 (15.2%)	17
Upper Extremity – Reflex	0	0	3	11	19	12	15	15	8	10	7	2	22	4	21 (9.0%)	65	17 (16.2%)	53
Lower Extremity – Sensory	0	0	2	4	0	0	6	0	3	1	3	3	1	1	9 (3.8%)	14	6 (5.7%)	8
Lower Extremity – Motor	1	0	1	1	0	1	1	0	1	1	2	0	2	0	5 (2.1%)	7	4 (3.8%)	4
Lower Extremity – Reflex	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Upper & Lower Extremity – Sensory	0	0	2	0	0	0	0	0	0	0	0	0	0	0	1 (0.4%)	2	0	0
Upper & Lower Extremity - Motor	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1 (0.4%)	1	0	0
Upper & Lower Extremity - Reflex	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Neck	6	1	6	3	3	7	2	5	3	4	4	4	7	2	29 (12.4%)	30	17 (16.2%)	25
Back	0	1	3	0	2	1	2	1	3	2	0	1	3	1	11 (4.7%)	13	7 (6.7%)	8
Spinal Cord Disturbance	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Gait Disturbance	0	0	0	0	0	0	2	1	1	0	1	1	1	0	3 (1.3%)	5	2 (1.9%)	2
Non Specific	0	1	1	0	1	2	0	1	0	2	1	2	0	1	3 (1.3%)	3	6 (5.7%)	9
Other*	9	4	2	6	6	4	10	3	7	8	9	4	8	4	40 (17.1%)	49	26 (24.8%)	33
Non-Union	0	0	0	0	0	0	0	2	0	8	3	7	0	0	1 (0.4%)	3	13 (12.4%)	18
Other**	36	25	26	11	14	10	19	13	26	13	48	21	22	12	99 (42.3%)	189	58 (55.2%)	104
Other Pain	11	0	30	17	34	21	46	19	42	32	68	25	32	19	131 (56.0%)	267	64 (61.0%)	132
Shoulder	4	0	12	7	8	8	9	5	9	7	13	5	6	3	52 (22.2%)	61	33 (31.4%)	36
Back	2	0	4	4	8	3	19	5	10	7	23	5	11	5	64 (27.4%)	80	25 (23.8%)	29
Torso	0	0	0	1	0	1	0	0	0	2	2	1	2	0	4 (1.7%)	4	4 (3.8%)	5
Lower Extremity	2	0	2	2	5	2	8	5	7	9	19	5	9	8	37 (15.8%)	51	21 (20.0%)	29
Headache	3	0	10	2	11	6	8	3	12	5	10	7	4	2	47 (20.1%)	58	20 (19.0%)	25
Other***	0	0	2	1	2	1	2	1	4	2	1	2	0	1	8 (3.4%)	13	8 (7.6%)	8

	Surgery to Discharge		Discharge to Week 6		Week 6 to Month 3		Months 3 to 6		Months 6 to 12		Months 12 to 18		Months 18 to 24		Mobi-C®		ACDF	
Complication	M	F	M	F	M	F	M	F	M	F	M	F	M	F	**#Patients (% of 234)**	**Total Events**	**#Patients (% of 105)**	**Total Events**
Respiratory	4	1	3	1	1	1	1	5	7	1	11	2	4	1	19 (8.1%)	29	11 (10.5)	12
Spinal Disorder	0	1	2	1	1	0	2	3	4	7	5	4	4	4	13 (5.6%)	18	13 (12.4%)	20
Cervical - Study Surgery	0	1	2	0	0	0	1	1	0	0	1	3	0	1	3 (1.3%)	4	6 (5.7%)	6
Cervical - Non Study Surgery	0	0	0	0	0	0	1	0	3	4	3	1	2	2	6 (2.6%)	8	4 (3.8%)	7
Non Cervical	0	0	0	1	1	0	0	2	1	3	1	0	2	1	5 (2.1%)	6	5 (4.8%)	7
Trauma	2	1	4	2	10	2	10	7	27	12	25	3	13	7	52 (22.2%)	89	20 (19.0%)	36
Upper Extremity Nerve Entrapment	1	0	2	0	4	0	3	2	2	3	2	2	2	0	13 (5.6%)	16	6 (5.7%)	7
Urogenital	0	2	3	0	2	2	3	1	3	6	7	3	4	0	15 (6.4%)	23	10 (9.5%)	14
Vascular Intraop	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1 (1.0%)	1
Wound Issue - Non-Infection	2	1	1	2	0	0	0	0	0	0	1	0	0	0	4 (1.7%)	4	3 (2.9%)	3
Hematoma	2	0	1	2	0	0	0	0	0	0	0	0	0	0	3 (1.3%)	3	2 (1.9%)	2
Hematoma Evacuation	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CSF Leakage	0	1	0	0	0	0	0	0	0	0	1	0	0	0	1 (0.4%)	1	1 (1.0%)	1

M= All Mobi-C® Subjects; F = All ACDF Subjects

[1] Sum of all treatment emergent adverse events experienced in the study for each treatment group.

*Neurological Other includes Neurological events not appropriately defined elsewhere in the Neurological category. This includes amnesia, convulsion, facial neurologic events (dysaesthesia, hypoaesthesia), unexplained loss of consciousness, 'other' nerve compression, Parkinson's disease, and stroke.

**Other includes events not appropriately defined elsewhere. This includes adverse drug reactions, allergies, anemia, anxiety, arthritis, attention deficit disorder, benign neoplasm, blood & lymphatic system disorders, complications from other medical procedures, congenital defects, dehydration, dermatitis, diabetes, dizziness, ear/eye disorders, endocrine disorders, fatigue, feeling hot, fever, gout, high/low cholesterol, immune system disorders, injury/poisoning, lupus, menopause, miscarriage, muscle atrophy, nutritional disorders, obesity, osteoarthritis, osteoporosis, other inflammation, other medical procedures, plantar fasciitis, polyps, pregnancy, psychiatric disorders, rotator cuff syndrome, skin disorders, sinus infection, social issues, sleep disorders, swelling, tendonitis, thyroid conditions, vascular disorders, and weight gain/loss.

***Other Pain Other includes events not appropriately defined elsewhere. This includes facial pain, fibromyalgia, muscle soreness, chronic pain, nerve pain and arthritis.

Table 12. Adverse Event Categories and Subcategories

AE Category or Subcategory	Definition
Anatomy/Technical Difficulty	Includes surgical procedure related events, such as technical issues with the device or with the anatomy during surgery or post-operative. Where events are more accurately described in another category (such as 'Malpositioned Implant') they will be placed into the more accurate category.
Cervical – Study Surgery	Stratified by cervical study surgery related to illustrate clinical relevance to the study. Study Surgery is intended to mean the index level, or other events directly attributed to the study surgery or device. Includes technical issues with the device or with anatomy during surgery or post-operative.
Cervical – Non Study Surgery	Stratified by cervical non-study surgery related to illustrate clinical relevance to the study. This AE subcategory is unrelated (lacks clinical relevance) to the index level and is unrelated to study surgery.
Non Cervical	Non Cervical captures non-study related events, such as technical difficulty with an unrelated procedure.
Cancer	All reported AEs of cancer (malignancy or malignant tumor/neoplasm).
Cardiovascular	All reported AEs of the cardiovascular system.
Death	All reports of death.
Dysphagia/Dysphonia	
Dysphagia	All reported AEs of Dysphagia and other terms consistent with "difficulty swallowing".
Dysphonia	All reported AEs of Dysphonia and other terms consistent with "voice change and/or disruption".
Gastrointestinal	All reported AEs of the gastrointestinal system, except those more appropriately categorized elsewhere.
Heterotopic Ossification	
Cervical – Index Level	All reported AEs of Heterotopic Ossification, stratified by cervical events at the index level.
Cervical – Adjacent Level	All reported AEs of Heterotopic Ossification, stratified by cervical events at the adjacent levels.
Non Cervical	Events that occur outside of the cervical spine, or non-specific event reports, are displayed separately in this category.
Infection	
Superficial Wound - Cervical	Superficial Wound – superficial surgical incision or surgical wound related infections (includes only study surgery events).
Deep Wound - Cervical	Deep Wound – deep surgical incision or surgical wound related infections (includes only study surgery events).
Other Wound – Non Study Surgery	Other Wound – superficial and/or deep wound related events from non-study surgery.
Systemic	Systemic infections include infections such as Hepatitis and Influenza.
Local	Local infections include infections isolated to a specific region or organ.
Malpositioned Implant	All AE reports of Malpositioned Implant, such as 'misplaced screw' and 'subsidence'. The term Malpositioned indicates an implant or component that is reported in a sub optimal or undesired position, regardless of causality. This is not mutually exclusive to surgeon error or sub-optimal placement of the original implant configuration.
Neck and/or Arm Pain	All AE reports of pain (and related pain terms) specific to neck, arm, or neck and arm.

AE Category or Subcategory	Definition
Neck Pain	All AE reports of pain (and related pain terms) specific to neck. Neck includes the anatomy consistent with the cervical spine (spinal disorders are recorded elsewhere).
Arm Pain	All AE reports of pain (and related pain terms) specific to arm.
Neck and Arm Pain	All AE reports of pain (and related pain terms) specific to neck and arm. Neck includes the anatomy consistent with the cervical spine (spinal disorders are recorded elsewhere).
Neurological	All neurological AEs defined further as follows.
Upper Extremity – Sensory	Upper Extremity - shoulder, arm and hand neurologic AEs stratified by sensory changes.
Upper Extremity – Motor	Upper Extremity - shoulder, arm and hand neurologic AEs stratified by motor changes.
Upper Extremity - Reflex	Upper Extremity - shoulder, arm and hand neurologic AEs stratified by reflex changes.
Lower Extremity – Sensory	Lower Extremity - hip, leg, buttocks, and foot neurologic AEs stratified by sensory changes.
Lower Extremity – Motor	Lower Extremity - hip, leg, buttocks, and foot neurologic AEs stratified by motor changes.
Lower Extremity - Reflex	Lower Extremity - hip, leg, buttocks, and foot neurologic AEs stratified by reflex changes.
Upper & Lower Extremity – Sensory	Upper & Lower Extremity – both, stratified by sensory changes.
Upper & Lower Extremity – Motor	Upper & Lower Extremity – both, stratified by motor changes.
Upper & Lower Extremity - Reflex	Upper & Lower Extremity – both, stratified by reflex changes.
Neck	Neck – includes neurologic AEs reported in the neck (including the cervical spine region) that were clearly identified as neurologic in nature according to the AE term reported by the investigator. This includes events such as, burning and/or tingling sensation, muscle spasms and muscle stiffness and/or weakness in the neck. These events differ from "Neck Pain" because the primary reported term is neurological in nature as opposed to pain-related in nature.
Back	Back – includes neurologic AEs reported in the back (including thoracic and lumbar regions) that were clearly identified as neurologic in nature according to the AE term reported by the investigator. This includes events such as numbness and/or tingling sensation, muscle spasms, and muscle stiffness and/or weakness in the back. These events differ from "Back Pain" because the primary reported term is neurological in nature as opposed to pain-related in nature.
Spinal Cord Disturbance	Includes AEs reported as resulting in spinal cord disturbance.
Gait Disturbance	Includes AEs reported as resulting in gait disturbance.
Non Specific	Non-Specific - includes general neurological AEs such as 'tingling' or 'numbness' and neurological AEs of unspecified origin.
Other	Other - neurological events not otherwise defined above, such as 'facial neuralgia' and neurological diseases like Parkinson's.
Non-Union	All reported AEs of non-union, including cervical fusion failure, pseudarthrosis, and pending non-unions as reported. This category is limited to study surgery related events of non-union.

AE Category or Subcategory	Definition
Other	Includes AEs not otherwise more appropriately defined by the remaining categories. Other included events classified as disorders of: Blood & Lymphatic System, Congenital/Genetic, Ear & Labyrinth, Endocrine, Eye, Immune System, Metabolism/Nutrition, Musculoskeletal & Connective Tissue, Benign Neoplasm, Nervous System, Psychiatric, Reproductive System, Skin, and Vascular System as well as events including Poisoning, Pregnancy, Social Circumstances, and Surgical/Medical procedures not defined elsewhere.
Other Pain	Includes AEs reported as pain specific to an anatomic region. This group is stratified as follows:
Shoulder	Shoulder –includes pain reported in the shoulder joint, scapula, clavicle, AC joint, and other reports of 'shoulder pain'.
Back	Back - includes pain reported in the thoracic, lumbar, and sacral spine, as well as other reports of back pain, such as low back pain.
Torso	Torso – includes pain reported in the torso region, including rib & abdominal region, and chest pains.
Lower Extremity	Lower Extremity – includes pain reported in the hip, buttock, thigh, knee, lower leg, ankle, foot, and other reports of 'lower extremity or leg pain'.
Headache	Headaches – includes all AE reports of headaches and pain from headache (including migraine).
Other	Other –includes all other Pain AE reports not categorized elsewhere.
Respiratory	All reported AEs of the respiratory system, except those more appropriately categorized elsewhere.
Spinal Disorder	Spinal Disorder consists of events reported as a spinal diagnosis/disorder, such as degenerative disc disease, disc herniation, stenosis, adjacent level degeneration, etc. As reported, these AEs are categorized as cervical and non-cervical and will be categorized on relatedness to study surgery.
Cervical – Study Surgery	AEs are categorized as cervical and will be categorized on relatedness to study surgery.
Cervical – Non Study Surgery	AEs are categorized as cervical and will be categorized on relatedness to study surgery.
Non Cervical	Non-cervical includes events not related to the study surgery.
Trauma	Includes all AEs of trauma or similar terms, as reported. This includes falls, motor vehicle accidents, assault, injury, etc. This category includes both cervical and non-cervical AEs of Trauma.
Upper Extremity Nerve Entrapment	All reported AEs of Carpal Tunnel Syndrome and Cubital Tunnel Syndrome, including AEs directly attributed to Carpal Tunnel Syndrome or Cubital Tunnel Syndrome, as well as Carpal Tunnel surgery.
Urogenital	All reported AEs of the urogenital anatomy, except those more appropriately categorized elsewhere.
Vascular Intraop	Includes all vascular AEs from surgery or during surgery – such as excessive bleeding.
Wound Issue – Non Infection	
Hematoma	Hematoma categories will be populated according to the medical definition for these events and will only capture Study Surgery events.
Hematoma Evacuation	Hematoma categories will be populated according to the medical definition for these events and will only capture Study Surgery events.
CSF Leakage	CSF categories will be populated according to the medical definition for these events and will only capture Study Surgery events.

Table 13. All Treatment Emergent Adverse Events through 60 Months in US IDE Study – Safety Population

Complication	Mobi-C®			ACDF		
	#Patients (% of 234)	Total Events	Subject-Level CI*	#Patients (% of 105)	Total Events	Subject-Level CI*
Anatomy/Technical Difficulty	11 (4.7%)	11	(2.4, 8.3)	5 (4.8%)	5	(1.6, 10.8)
Cervical – Non Study Surgery	4 (1.7%)	4	(0.5, 4.3)	2 (1.9%)	2	(0.2, 6.7)
Cervical –Study Surgery	6 (2.6%)	6	(0.9, 5.5)	2 (1.9%)	2	(0.2, 6.7)
Non-Cervical	1 (0.4%)	1	(0.0, 2.4)	1 (1.0%)	1	(0.0, 5.2)
Cancer	4 (1.7%)	4	(0.7, 3.3)	1 (1.0%)	1	(0.1, 3.4)
Cardiovascular	32 (13.7%)	42	(10.7, 17.1)	20 (19.0%)	24	(14.0, 25.0)
Death	1 (0.4%)	1	(0.1, 1.5)	1 (1.0%)	1	(0.1, 3.4)
Dysphagia/Dysphonia	37 (15.8%)	41	(11.4, 21.1)	22 (21.0%)	26	(13.6, 30.0)
Dysphagia	34 (14.5%)	35	(10.3, 19.7)	22 (21.0%)	24	(13.6, 30.0)
Dysphonia	6 (2.6%)	6	(0.9, 5.5)	2 (1.9%)	2	(0.2, 6.7)
Gastrointestinal	53 (22.6%)	115	(18.9, 26.7)	33 (31.4%)	62	(25.2, 38.2)
Heterotopic Ossification	13 (5.6%)	13	(3.0, 9.3)	4 (3.8%)	4	(1.0, 9.5)
Cervical - Adjacent Level	2 (0.9%)	2	(0.1, 3.1)	3 (2.9%)	3	(0.6, 8.1)
Cervical - Index Level	7 (3.0%)	7	(1.2, 6.1)	0	0	N/A
Non Cervical	4 (1.7%)	4	(0.5, 4.3)	1 (1.0%)	1	(0.0, 5.2)
Infection	61 (26.1 %)	109	(20.6, 32.2)	33 (31.4%)	62	(22.7, 41.2)
Local	50 (21.4%)	83	(16.3, 27.2)	25 (23.8%)	48	(16.0, 33.1)
Other Wound - Non Study Surgery	1 (0.4%)	1	(0.0, 2.4)	3 (2.9%)	3	(0.6, 8.1)
Superficial Wound – Cervical	8 (3.4%)	8	(1.5, 6.6)	4 (3.8%)	4	(1.0, 9.5)
Systemic	13 (5.6%)	17	(3.0, 9.3)	7 (6.7%)	7	(2.7, 13.3)
Malpositioned Implant	4 (1.7%)	4	(0.7, 3.3)	0	0	N/A
Neck and/or Arm Pain	112 (47.9%)	201	(41.3, 54.5)	66 (62.9%)	124	(52.9, 72.1)
Arm Pain	46 (19.7%)	67	(14.8, 25.3)	29 (27.6%)	38	(19.3, 37.2)
Neck And Arm Pain	11 (4.7%)	21	(2.4, 8.3)	7 (6.7%)	12	(2.7, 13.3)
Neck Pain	81 (34.6%)	113	(28.5, 41.1)	52 (49.5%)	74	(39.6, 59.5)
Neurological	139 (59.4%)	556	(52.8, 65.8)	81 (77.1%)	374	(67.9, 84.8)
Back	13 (5.6%)	15	(3.0, 9.3)	10(9.5%)	11	(4.7, 16.8)
Gait Disturbance	4 (1.7%)	6	(0.5, 4.3)	3 (2.9%)	3	(0.6, 8.1)
Lower Extremity – Motor	7 (3.0%)	9	(1.2, 6.1)	4 (3.8%)	5	(1.0, 9.5)
Lower Extremity – Sensory	14 (6.0%)	19	(3.3, 9.8)	8 (7.6%)	10	(3.3, 14.5)
Neck	37 (15.8%)	41	(11.4, 21.1)	18 (17.1%)	28	(10.5, 25.7)
Non Specific	5 (2.1%)	5	(0.7, 4.9)	6 (5.7%)	9	(2.1, 12.0)
Other**	45 (19.2%)	57	(14.4, 24.9)	28 (26.7%)	37	(18.5, 36.2)
Upper & Lower Extremity - Motor	1 (0.4%)	1	(0.0, 2.4)	0	0	N/A
Upper & Lower Extremity - Sensory	1 (0.4%)	2	(0.0, 2.4)	0	0	N/A
Upper Extremity – Motor	20 (8.5%)	24	(5.3, 12.9)	18 (17.1%)	24	(10.5, 25.7)
Upper Extremity – Reflex	25 (10.7%)	78	(7.0, 15.4)	18 (17.1%)	65	(10.5, 25.7)
Upper Extremity – Sensory	81 (34.6%)	299	(28.5, 41.1)	53 (50.5%)	182	(40.5, 60.4)
Non-Union	1 (0.4%)	3	(0.2, 2.2)	14 (13.3%)	18	(9.0, 18.7)
Other* **	110 (47.0%)	238	(42.4, 51.6)	62 (59.0%)	128	(52.1, 65.8)

Complication	Mobi-C®			ACDF		
	#Patients (% of 234)	Total Events	Subject-Level CI*	#Patients (% of 105)	Total Events	Subject-Level CI*
Other Pain	142 (60.7%)	320	(54.1, 67.0)	73 (69.5%)	170	(59.8, 78.1)
Back	70 (29.9%)	96	(24.1, 36.2)	28 (26.7%)	35	(18.5, 36.2)
Headache	49 (20.9%)	63	(15.9, 26.7)	23 (21.9%)	34	(14.4, 31.0)
Lower Extremity	48 (20.5%)	69	(15.5, 26.3)	25 (23.8%)	38	(16.0, 33.1)
Other****	9 (3.8%)	13	(1.8, 7.2)	9 (8.6%)	10	(4.0, 15.6)
Shoulder	58 (24.8%)	70	(19.4, 30.8)	39 (37.1%)	44	(27.9, 47.1)
Torso	7 (3.0%)	9	(1.2, 6.1)	8 (7.6%)	9	(3.3, 14.5)
Respiratory	21 (9.0%)	36	(6.5, 11.9)	11 (10.5)	14	(6.7, 15.4)
Spinal Disorder	20 (8.5%)	28	(5.3, 12.9)	20 (19.0%)	29	(12.0, 27.9)
Cervical - Non Study Surgery	9 (3.8%)	12	(1.8, 7.2)	9 (8.6%)	12	(4.0, 15.6)
Cervical - Study Surgery	3 (1.3%)	4	(0.3, 3.7)	8 (7.6%)	8	(3.3, 14.5)
Non Cervical	8 (3.4%)	12	(1.5, 6.6)	7 (6.7%)	9	(2.7, 13.3)
Trauma	60 (25.6%)	116	(21.7, 29.9)	28 (26.7%)	54	(20.8, 33.2)
Upper Extremity Nerve Entrapment	14 (6.0%)	18	(4.0, 8.5)	6 (5.7%)	8	(3.0, 9.8)
Urogenital	19 (8.1%)	26	(5.8, 11.0)	13 (12.4%)	20	(8.2, 17.6)
Vascular Intraop	0	0	N/A	1 (1.0%)	1	(0.1, 3.4)
Wound Issue – Non-Infection	4 (1.7%)	4	(0.5, 4.3)	3 (2.9%)	3	(0.6, 8.1)
CSF Leakage	1 (0.4%)	1	(0.0, 2.4)	1 (1.0%)	1	(0.0, 5.2)
Hematoma	3 (1.3%)	3	(0.3, 3.7)	2 (1.9%)	2	(0.2, 6.7)

*The subject-level incidences of these outcomes are analyzed using a 95% two-sided Binomial exact confidence interval.

**Neurological Other includes Neurological events not appropriately defined elsewhere in the Neurological category. This includes amnesia, convulsion, facial neurologic events (dysaesthesia, hypoaesthesia), unexplained loss of consciousness, 'other' nerve compression, Parkinson's disease, and stroke.

***Other includes events not appropriately defined elsewhere. This includes adverse drug reactions, allergies, anemia, anxiety, arthritis, attention deficit disorder, benign neoplasm, blood & lymphatic system disorders, complications from other medical procedures, congenital defects, dehydration, dermatitis, diabetes, dizziness, ear/eye disorders, endocrine disorders, fatigue, feeling hot, fever, gout, high/low cholesterol, immune system disorders, injury/poisoning, lupus, menopause, miscarriage, muscle atrophy, nutritional disorders, obesity, osteoarthritis, osteoporosis, other inflammation, other medical procedures, plantar fasciitis, polyps, pregnancy, psychiatric disorders, rotator cuff syndrome, skin disorders, sinus infection, social issues, sleep disorders, swelling, tendonitis, thyroid conditions, vascular disorders, and weight gain/loss.

****Other Pain Other includes events not appropriately defined elsewhere. This includes facial pain, fibromyalgia, muscle soreness, chronic pain, nerve pain and arthritis.

Adverse Events Resulting in Secondary Surgical Interventions

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, qualify as study failures and are reported in **Table 14**, with details provided in **Table 15**. There were fewer secondary surgeries at the index level in the Mobi-C® group compared to the ACDF control group. With respect to subsequent surgical interventions, in total only 7 (3.1%) randomized Mobi-C® subjects and 12 (11.4%) control subjects reported subsequent surgical interventions

qualifying as study failures (i.e. at the index level) through 24 months, with no non-randomized Mobi-C® subjects reporting subsequent surgical interventions qualifying as study failures.

Table 14. Secondary Surgical Interventions at the Index Level by Time- Safety Population

Type of Procedure	Intra-operative		6 Weeks		3 Months		6 Months		12 Months		18 Months		24 Months		≥24 Months		Total Patients (%)	
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M (N=234)	F (N=105)
Revision	0	0	1	0	0	0	0	0	0	0	0	2	0	0	0	2	1 (0.4%)	4 (3.8%)
Reoperation	0	0	0	0	0	0	0	0	1	1	0	1	1	0	1	0	3 (1.3%)	2 (1.9%)
Removal	0	0	0	0	1	0	0	0	0	2	2	1	1	2	0	1	4 (1.7%)	6 (5.7%)
Supplemental Fixation	0	0	0	0	0	0	0	0	0	1	0	0	0	2	1	0	1 (0.4%)	3 (2.9%)
Total	0	0	1	0	1	0	0	0	1	4	2	4	2	4	2	3	9 (3.8%)	15 (14.3%)

M= All Mobi-C® Subjects; F = All ACDF Subjects
Note – interval captures interventions between the two study time points.

Table 15. Secondary Surgical Interventions at the Index Level - Procedure Details

Group	Associated AE(s)	Secondary Surgical Intervention Detail	Months Post-Op*
M	Hematoma	Revision - Repositioning of the device at the inferior index level during hematoma evacuation	0.25
M	Device migration	Removal of Mobi-C® at the inferior index level and conversion to ACDF; the superior index level was left intact	2
M	Ongoing bilateral arm pain	Reoperation - cervical posterior foraminotomy of the inferior index level and the adjacent level below	8
M	Sub optimal bony fixation	Removal of Mobi-C® at both index levels and conversion to ACDF	13
M	Neck and shoulder pain	Removal of Mobi-C® at both index levels and conversion to ACDF	17
M	Facet spondylosis	Reoperation – posterior bilateral facet decortication at both index levels and posterior fusion hardware	22
M	Neck and arm pain	Removal of Mobi-C® at the inferior index level and conversion to ACDF; the superior index level was left intact	23
M	Radiculopathy	Supplemental fixation in the form of posterior fusion instrumentation at the inferior index level and adjacent level below	40
M	Stenosis	Removal of Mobi-C® at inferior index level and conversion to ACDF; the superior level was left intact	52
F	Pseudarthrosis at both index levels	Reoperation – posterior hemilaminotomy at both index levels	8
F	Pseudarthrosis at both index levels	Supplemental Fixation in the form of posterior fusion instrumentation at both index levels	9

Group	Associated AE(s)	Secondary Surgical Intervention Detail	Months Post-Op*
F	Failure of fusion	Removal of ACDF hardware and repeat ACDF at the index levels and addition of ACDF at the adjacent level above	9
F	Pseudarthrosis at inferior index level	Removal of ACDF hardware and repeat ACDF at the inferior index level	10
F	Cervical spondylosis and arthrosis at superior index level	Removal of ACDF hardware and repeat ACDF at the superior index level	13
F	Fusion failure	Revision – posterior cervical facet fusion at inferior index level	14
F	Pseudarthrosis at both index levels	Revision – posterior cervical fusion at both index levels	15
F	Radiculopathy	Reoperation - hemilaminotomy and posterior decompression at both index levels	16
F	Pseudarthrosis at inferior index level	Supplemental fixation in the form of posterior fusion instrumentation at the inferior index level	19
F	Pseudarthrosis at both index levels	Supplemental fixation in the form of posterior fusion instrumentation at both index levels and the inferior adjacent level	20
F	Herniated Disc at superior adjacent level	Removal of ACDF hardware and extension of fusion with ACDF to superior adjacent level	20
F	Degeneration at adjacent level	Removal of ACDF hardware and adjacent level anterior discectomy and arthroplasty	22
F	Cervical facet syndrome and spondylosis	Removal of ACDF hardware and repeat fusion at inferior index level and extension of fusion at inferior adjacent segment	33
F	Spinal stenosis	Revision – removal of ACDF hardware and extension of fusion to inferior adjacent level	35
F	Motor vehicle accident	Revision – posterior decompression at both index levels	40

M=Mobi-C® Group; F= ACDF Control Group
*The number of months between the study surgery and the second surgery

Device - Related Adverse Events

The relationship between adverse events and the implant (using a 4-tier classification of definitely device-related, possibly device-related, probably not device-related, or unrelated) was assessed separately by both Investigators and the Clinical Events Committee (CEC) from data coded according to Preferred Terms (PT) of the MedRA (Medical Dictionary for Regulatory Activities) Classification. The independent CEC reviewed all adverse events reported in the study and was included in the database for analysis.

Throughout the study, AEs were collected during the course of subject follow up visits by the Investigators, and relationship was recorded. The AE data were then sent periodically to CEC members using CEC adjudication forms. These adjudication forms provided the adverse event term (verbatim), the date of study surgery, the date of event onset, the date of resolution, the event status, and the investigator's determination of relatedness. In addition, CEC members received narratives for all serious adverse events (SAEs) captured in the safety database. These materials were sent separately and concurrently to all three CEC members for adjudication. Each CEC member performed the adjudication independent from the other members. CEC members were also permitted to request additional information,

including complete case report forms (CRFs) and radiographs, for individual subjects. The prevailing assessment among the three CEC members was entered in the database. The CEC used their expert medical judgment (including knowledge and experience as cervical spine surgeons) in conjunction with guidance from the study protocol to determine device relatedness to events.

According to both investigator and CEC assessment, the device-related adverse event profile is lower for the Mobi-C® group compared to the ACDF control group. Events classified as definitely device-related or possibly device-related were grouped together and analyzed as "device-related events". Through the primary endpoint (24 months), a larger percentage of ACDF subjects (28.6%) compared to randomized (16.0%) Mobi-C® subjects reported device-related adverse events as determined by investigators. During this period, device-related adverse events as determined by investigators were reported in 44.4% of non-randomized Mobi-C® subjects. Similarly, as determined by the CEC, 34.3% of ACDF, 16.0% of randomized Mobi-C®, and 33.3% of non-randomized Mobi-C® subjects experienced device-related adverse events. Device-related adverse events which occurred in greater than 5% of subjects in either treatment group (using the CEC determination) were neurological neck (Mobi-C®, 0.9% ; ACDF , 5.7%), dysphagia (Mobi-C®, 3.4% ; ACDF, 7.6%), neck pain (Mobi-C® 6.0%, ACDF 12.4%), and non-union[1] (Mobi-C® 0.4%, ACDF 8.6%).

Table 16 provides additional and complete detail on device related adverse events and the determination of relationship by the investigator.

[1] One Mobi-C© patient had 3 non-union events that occurred after the index level Mobi-C© implants were removed and converted to a two level ACDF. The 3 events were associated with the subsequent ACDF procedure.

Table 16. Device-Related Adverse Events According to Investigator – Safety Population

	Mobi-C® (N=234)*		ACDF (N=105)	
Device Relationship of Adverse Event Determined by Investigator	**Events N**	**Patients N (%)**	**Events N**	**Patients N (%)**
Anatomy/Technical Difficulty	2	2 (0.9%)	2	2 (1.9%)
Cervical - Non Study Surgery	1	1 (0.4%)	1	1 (1.0%)
Cervical - Study Surgery	1	1 (0.4%)	1	1 (1.0%)
Dysphagia/Dysphonia	10	9 (3.8%)	9	8 (7.6%)
Dysphagia	9	9 (3.8%)	8	8 (7.6%)
Dysphonia	1	1 (0.4%)	1	1 (1.0%)
Gastrointestinal	1	1 (0.4%)	0	0
Heterotopic Ossification	3	3 (1.3%)	0	0
Cervical - Index Level	2	2 (0.9%)	0	0
Cervical - Adjacent Level	1	1 (0.4%)	0	0
Malpositioned Implant	4	4 (1.7%)	0	0
Neck and/or Arm Pain	23	19 (8.1%)	23	16 (15.2%)
Neck Pain	16	14 (6.0%)	13	11 (10.5%)
Arm Pain	6	5 (2.2%)	5	5 (4.8%)
Neck and Arm Pain	1	1 (0.4%)	5	2 (1.9%)
Neurological	20	12 (5.1%)	25	10 (9.5%)
Upper Extremity - Sensory	10	7 (3.0%)	14	5 (4.8%)
Neck	4	3 (1.3%)	3	2 (1.9%)
Upper Extremity - Reflex	4	1 (0.4%)	0	0
Upper Extremity - Motor	1	1 (0.4%)	3	3 (2.9%)
Other	0	0	2	2 (1.9%)
Lower Extremity – Sensory	0	0	1	1 (1.0%)
Back	1	1 (0.4%)	1	1 (1.0%)
Non Specific	0	0	1	1 (1.0%)
Non-Union	0	0	9	8 (7.6%)
Other	1	1 (0.4%)	2	2 (1.9%)
Other Pain	11	10 (4.3%)	3	2 (1.9%)
Headache	6	5 (2.1%)	2	2 (1.9%)
Shoulder	4	4 (1.7%)	1	1 (1.0%)
Back	1	1 (0.4%)	0	0
Respiratory	1	1 (0.4%)	0	0
Spinal Disorder	4	3 (1.3%)	5	5 (4.8%)
Cervical - Study Surgery	4	3 (1.3%)	5	5 (4.8%)
Trauma	1	1 (0.4%)	0	0

*Includes all Mobi-C® subjects, including randomized and training subjects.

Serious Adverse Events

In this study, a serious adverse event (SAE) was defined as an event meeting one or more of the following criteria: 1) resulted in death; 2) was life-threatening (immediate risk of death); 3) required inpatient hospitalization or prolonged hospitalization; 4) resulted in persistent or significant disability or incapacity; 5) necessitated medical or surgical intervention to

preclude permanent impairment of a body function or permanent damage to a body structure; or 6) was a congenital anomaly or birth defect.

The percentage of subjects experiencing an SAE was lower for Mobi-C® subjects compared to the ACDF control group subjects. Through 24 months, 32.4% of ACDF control subjects reported at least one SAE compared to 23.9% (56/234) of all Mobi-C® subjects (11.1% non-randomized Mobi-C®, 24.4% randomized Mobi-C®).

Table 17. Summary of Serious Adverse Events (SAE) through Month 24 - Safety Population

	Mobi-C® (N=234)*		ACDF (N=105)	
System Organ Class/Preferred Term	**Events N**	**Subjects N (%)**	**Events N**	**Subjects N (%)**
Anatomy/Technical Difficulty	1	1 (0.4%)	1	1 (1.0%)
Cervical - Study Surgery	1	1 (0.4%)	1	1 (1.0%)
Cancer	1	1 (0.4%)	0	0
Cardiovascular	9	7 (3.0%)	1	1 (1.0%)
Death	1	1 (0.4%)	0	0
Dysphagia/Dysphonia	2	2 (0.9%)	2	2 (1.9%)
Dysphagia	2	2 (0.9%)	2	2 (1.9%)
Gastrointestinal	3	3 (1.3%)	2	2 (1.9%)
Infection	9	6 (2.6%)	4	3 (2.9%)
Systemic	4	3 (1.3%)	1	1 (1.0%)
Local	5	5 (2.1%)	3	2 (1.9%)
Malpositioned Implant	1	1 (0.4%)	0	0
Migration of Implant	1	1 (0.4%)	0	0
Neck And/Or Arm Pain	15	10 (4.3%)	8	6 (5.7%)
Neck And Arm Pain	5	3 (1.3%)	3	1 (1.0%)
Arm Pain	2	2 (0.9%)	1	1 (1.0%)
Neck Pain	8	7 (3.0%)	4	4 (3.8%)
Neurological	5	5 (2.1%)	5	5 (4.8%)
Upper Extremity – Sensory	0	0	1	1 (1.0%)
Neck	1	1 (0.4%)	3	3 (2.9%)
Back	1	1 (0.4%)	0	0
Other	3	3 (1.3%)	1	1 (1.0%)
Non-Union	3	1 (0.4%)	14	11 (10.5%)
Other	14	12 (5.1%)	13	9 (8.6%)
Other Pain	15	10 (4.3%)	3	3 (2.9%)
Shoulder	5	4 (1.7%)	0	0
Back	4	4 (1.7%)	0	0
Torso	1	1 (0.4%)	0	0
Lower Extremity	1	1 (0.4%)	3	3 (2.9%)
Headache	3	3 (1.3%)	0	0
Other	1	1 (0.4%)	0	0
Respiratory	3	3 (1.3%)	0	0
Spinal Disorder	4	4 (1.7%)	8	7 (6.7%)
Cervical - Study Surgery	1	1 (0.4%)	5	5 (4.8%)
Cervical - Non Study Surgery	2	2 (0.9%)	2	1 (1.0%)
Non Cervical	1	1 (0.4%)	1	1 (1.0%)

	Mobi-C® (N=234)*		ACDF (N=105)	
System Organ Class/Preferred Term	**Events N**	**Subjects N (%)**	**Events N**	**Subjects N (%)**
Trauma	10	7 (3.0%)	3	2 (1.9%)
Upper Extremity Nerve Entrapment	5	4 (1.7%)	0	0
Urogenital	1	1 (0.4%)	1	1 (1.0%)
Wound Issue – Non-Infection	2	2 (0.9%)	3	3 (2.9%)
Hematoma	2	2 (0.9%)	2	2 (1.9%)
CSF Leakage	0	0	1	1 (1.0%)

*Includes all Mobi-C® subjects, including randomized and training subjects.

Device-Related Serious Adverse Events

Serious adverse events classified as "device-related" were defined as serious events which were rated as "definitely device-related" or "possibly device-related". The percentage of subjects experiencing device-related serious adverse events was lower for Mobi-C® subjects compared to ACDF control group subjects. Based on classification by investigators, device-related serious adverse events were noted in 3.0% of all Mobi-C® subjects compared to 12.4% of ACDF subjects (**Table 18**). In Mobi-C® subjects device-related serious adverse events were noted in 7 randomized Mobi-C® subjects (3.1%) and 0 non-randomized Mobi-C® subjects.

Table 18. Device Related Serious Adverse Events

Group	Event Term(s)	Investigator Relationship to device*
M	1. Migration of Implant	1. Definitely
M	1. Neck pain	1. Possibly
M	1. Pain in Extremity	1. Possibly
M	1. Dysphagia 2. Neck Pain	1. Possibly 2. Possibly
M	1. Neck Pain 2. Pain in Extremity	1. Possibly 2. Possibly
M	1. Neck Pain 2. Shoulder Pain	1. Possibly 2. Possibly
M	1. Cervical spinal stenosis	1. Possibly
7 Total w/ Related SAE	**10 Serious Adverse Events**	**10 Total Related SAE**
F	1. Neuralgia 2. No therapeutic response	1. Possibly 2. Definitely
F	1. Radiculopathy 2. No therapeutic response	1. Possibly 2. Possibly
F	1. Intervertebral disc protrusion	1. Possibly
F	1.Spinal osteoarthritis** 2. No therapeutic response	1. Possibly** 2. Definitely
F	1. Shoulder pain 2. Hypoesthesia 3. No therapeutic response 4. Pain in extremity 5. Neck pain	1. Possibly 2. Possibly 3. Possibly 4. Possibly 5. Possibly
F	1. No therapeutic response	1. Definitely
F	1. Intervertebral disc degeneration	1. Definitely
F	1. Pain in Extremity	1. Possibly
F	1. No therapeutic response 2. Intervertebral disc protrusion 3. Neck pain	1. Definitely 2. Possibly 3. Possibly
F	1. Neck pain	1. Definitely
F	1. Dysphagia	1. Possibly
F	1. No therapeutic response 2. Radiculopathy	1. Definitely 2. Definitely
F	1. No therapeutic response 2. Spinal disorder	1. Definitely 2. Definitely
13 Total w/ Related SAE	**24 Serious Adverse Events**	**24 Total Related SAE**

M = Mobi-C® Group; F= ACDF Control Group

Note - Device Related SAEs were classified by the investigator as possibly or definitely related to study device.

*Relationship between an AE and the implant: this was assessed on the basis of the following definitions:

• Definitely device-related - there was a definitive causal and/or temporal connection between the AE and the device.

• Possibly device-related - there was a reasonable possibility that the AE may have been primarily caused by the device.

• Probably not device-related - there was no reasonable possibility that the AE may have been caused by the device.

• Unrelated - there was no causal connection between the AE and the device

**Indicates a post-month 24 SAE which was in the clinical database at the time of the PMA

Neurological Status

The neurologic status is summarized in **Table 19**. Diminished neurological status resulted in study failure, and was assessed using a neurological status scale, based on five types of measurement parameters (motor, sensory-light touch, sensory-pin prick, reflexes, and gait assessment) at 24 months relative to pre-operative baseline.

The protocol-specified analysis defined neurologic deterioration as a decrease of two points in any of the treated level motor or reflex assessments or a decrease of one point for any of the treated level sensory tests. A secondary analysis using an FDA definition of change in neurologic status defined as any neurologic deterioration compared to baseline status was also performed. The randomized Mobi-C® subjects demonstrated numerically similar percentages of patients with stable/improved neurologic status as the control ACDF group at each time point and this finding was consistent for both the protocol-specified and FDA-specified definitions for neurologic deterioration. No deterioration in spinal cord function was observed in any study subjects. Gait disturbance was noted in 3 (1.3%) randomized Mobi-C® subjects and 2 (1.9%) control ACDF subjects.

Table 19. Neurological Status

Visit (months)	Status	Randomized Mobi-C® (N=225) Protocol Definition[1]	Non-Randomized Mobi-C® (N=9) Protocol Definition[1]	Randomized ACDF (N=105) Protocol Definition[1]	p-value*
6	No Deterioration Deterioration	207/216 (95.8%) 9/216 (4.2%)	8/8 (100.0%) 0/8	92/97 (94.8%) 5/97 (5.2%)	p=0.7690
12	No Deterioration Deterioration	204/213 (95.8%) 9/213 (4.2%)	8/9 (88.9%) 1/9 (11.1%)	83/92 (90.2%) 9/92 (9.8%)	p=0.0676
18	No Deterioration Deterioration	197/209 (94.3%) 12/209 (5.7%)	7/7 (100.0%) 0/7	82/85 (96.5%) 3/85 (3.5%)	p=0.5662
24	No Deterioration Deterioration	204/216 (94.4%) 12/216 (5.6%)	7/8 (87.5%) 1/8 (12.5%)	83/89 (93.3%) 6/89 (6.7%)	p=0.7897
Visit (months)	**Status**	**Randomized Mobi-C® (N=225) FDA Definition[2]**	**Non-Randomized Mobi-C® (N=9) FDA Definition[2]**	**Randomized ACDF (N=105) FDA Definition[2]**	**p-value***
6	No Deterioration Deterioration	197/216 (91.2%) 19/216 (8.8%)	8/8 (100.0%) 0/8	89/98 (90.8%) 9/98 (9.2%)	p=1.0000
12	No Deterioration Deterioration	194/213 (91.1%) 19/213 (8.9%)	8/9 (88.9%) 1/9 (11.1%)	76/92 (82.6%) 16/92 (17.4%)	p=0.0486
18	No Deterioration Deterioration	183/209 (87.6) 26/209 (12.4%)	7/7 (100.0%) 0/7	78/85 (91.8%) 7/85 (8.2%)	p=0.4150
24	No Deterioration Deterioration	193/216 (89.4%) 23/216 (10.6%)	7/8 (87.5%) 1/8 (12.5%)	78/89 (87.6%) 11/89 (12.4%)	p=0.6908

*Using Fisher Exact test to compare frequencies between the treatments

[1] Study protocol definition of neurologic failure defined as a decrease of two points in any of the treated level motor or reflex assessments or a decrease of one point for any of the treated level sensory tests.

[2] FDA definition of neurologic failure defined as any neurologic deterioration compared to baseline status.

Adjacent Level Symptoms and Treatments

Data regarding radiographic changes resulting from adjacent segment radiographic degeneration was reported as a secondary radiographic endpoint. Serious adverse events (SAEs) were closely tracked and data which is known regarding adjacent level SAEs is discussed here. Regarding SAEs occurring at an adjacent level during the primary analysis study period (through 24 months), fewer Mobi-C® subjects (0.9%, 2/234) reported such events compared to ACDF control subjects (3.8%, 4/105). Following 24 month follow-up, six subjects have experienced or reported new adjacent level SAEs including 3 subjects in the ACDF group and 3 subjects in the Mobi-C® group bringing the combined total known adjacent level SAE rate to (2.1%, 5/234) in the Mobi-C® group and (6.7%, 7/105) in the ACDF group. Secondary surgeries reported at adjacent levels were also documented, and reported in **Table 20.** This table reports all known adjacent level surgeries, including those reported beyond the primary analysis endpoint. Fewer Mobi-C® subjects (2.1%, 5/234) reported such events compared to ACDF control subjects (6.7%, 7/105).

Table 20. Secondary Surgical Interventions at Level Adjacent to Index Level

Group	Treated Levels	Event Term(s)	Time to Adjacent Level Surgery	Description of Subsequent Adjacent Level Surgery
M	C5-6 C6-7	C4-5 Herniated nucleus pulposus	1 year, 4 months	Index levels implants intact, adjacent level anterior discectomy and fusion at C4-5
M	C5-6 C6-7	Severe neck pain	1 year, 8 months	Index levels implants intact, rhizomtomy at adjacent superior level and at above adjacent
M	C5-6 C6-7	C4-5 Herniated nucleus pulposus	3 years	Index levels implants intact, adjacent level anterior discectomy and fusion at C4-5
M	C4-5 C5-6	C6-7 Radiculopathy	3 years, 5 months	Index levels implants intact, adjacent level anterior discectomy and fusion at C6-7
M	C5-6 C6-7	C7-8 Radiculopathy	3 years, 6 months	Index levels implants intact, adjacent level foraminotomy at C7-T1
F	C4-5 C5-6	Neck pain	9 months	Removal of implants at index levels and repeat ACDF including the adjacent level above at C3-4
F	C5-6 C6-7	C4-5 Herniated nucleus pulposus	1 year, 8 months	Removal of implants at index levels and adjacent level anterior discectomy and fusion at C4-5
F	C3-4 C4-5	C5-6 Adjacent level degeneration	1 year 10 months	Removal of implants at index levels and adjacent level arthroplasty at C5-6
F	C5-6 C6-7	C7-T1 Herniated nucleus pulposus	2 years, 3 months	Index levels implants intact, adjacent level fusion at C7-T1
F	C5-6 C6-7	C4-5 Herniated nucleus pulposus	2 years, 9 months	Index levels implants intact, adjacent level fusion at C4-5 level
F	C5-6 C6-7	C7-T1 cervical facet syndrome and spondylosis	2 years, 9 months	Removal of implants at index levels and adjacent level anterior discectomy and fusion at C7-T1
F	C4-5 C5-6	C6-7 Adjacent level degeneration	1 year, 9 months	Removal of implants at index levels and repeat ACDF at inferior index level and inferior adjacent level. Additional posterior fusion with posterior hardware at both original index levels and inferior adjacent level.

M = Mobi-C® Group; F= ACDF Control Group

Surgery and Hospitalization Data

Surgical data is provided in **Table 21.** The most common treated surgical levels were C5-C6 and C6-C7. Mean surgery time was 20.22 minutes longer for the Mobi-C® randomized group than for the control ACDF randomized group. Mean blood loss was similar for both groups.

Mean return to work time was 20.9 days shorter for the Mobi-C® randomized group than the ACDF randomized group, though no statistical difference was found between the mean return to work time for all Mobi-C® subjects as compared to control subjects. Data regarding the amount/type of decompression and handling of the posterior longitudinal ligament for each procedure was not systematically collected. A total of 234 Mobi-C® devices were implanted during the study. The design, footprint and height of the Mobi-C® devices used are presented in **Table 22**.

Table 21. Surgical Data

Measure	Non-Randomized Mobi-C® (N=9)	Randomized Mobi-C® (N=225)	Randomized ACDF (N=105)	P Value **	P Value ***
Treated Level				-	-
C3-C4, C4-C5 (%)	0	1 (0.4%)	2 (1.9%)		
C4-C5, C5-C6 (%)	1(11.1%)	60 (26.7%)	23 (21.9%)		
C5-C6, C6-C7 (%)	8 (88.9%)	164 (72.9%)	80 (76.2%)		
Surgery Time (hours)	2.740±0.6846	2.135±0.7680	1.798±0.8598	0.0291	0.0002
Blood Loss (mls)	75.0±57.10	67.0±90.87	70.3±78.78	0.8306	0.7803
Hospitalization (days)	2.3±0.5	2.2±0.5	2.4±2.07	0.4160	0.2306
Return to Work Time (days)	38.0±23.25	45.9±102.31	66.8±113.70	0.5735	0.1923

Mean ± standard deviation

* Duration of hospitalization is defined as [Date of Discharge - Date of Surgery + 1].

**Using unpaired t-test to make comparison across randomized and non-randomized Mobi-C subjects

*** Using unpaired t-test to make comparison across treatments for all Mobi-C® subjects compared to ACDF subjects.

Table 22. All Mobi-C® Devices Implanted by Size and Level

	C3-C4, C4-C5	C4-C5, C5-C6	C5-C6, C6-C7	Total
13×15 H5	0	60	123	**183**
13×15 H6	1	6	13	**20**
13×15 H7	0	0	1	**1**
13×17 H5	0	11	36	**47**
13×17 H6	0	3	14	**17**
13×17 H7	0	0	2	**2**
15×17 H5	1	23	101	**125**
15×17 H6	0	15	30	**45**
15×17 H7	0	1	2	**3**
15x20 H5	0	2	12	**14**
15x20 H6	0	1	8	**9**
15x20 H7	0	0	0	**0**
Total	**2**	**122**	**342**	**466**

2. Effectiveness Results

Primary Effectiveness Analysis

The analysis of effectiveness was based on the Primary Analysis Population of 330 total patients with surgery (225 randomized Mobi-C® patients, and 105 ACDF patients). The hypothesis for the study was that the Mobi-C® study device would be non-inferior to conventional ACDF, using allograft corticocancellous bone followed by placement of a semi-constrained, rotational anterior cervical plate, with respect to the rate of individual subject success. The analysis goal was to establish non-inferiority using a composite success measure. The primary endpoint of the study was individual patient success defined as: 1) improvement in NDI at 24 months as compared to baseline (date of surgery), 2) absence of protocol defined Subsequent Surgical Intervention (i.e. index level Removal, Revision, Reoperation, or Supplemental Fixation), and 3) absence of major complications. There were three specific types of major complications defined as failures: 1) neurologic deterioration, 2) radiologic failure (bridging bone and lack of motion at the index level for Mobi-C® subjects; failure of fusion for ACDF subjects), and 3) adverse events determined to be major complications and related to the study device (as determined by the independent CEC oversight committee). Fusion success in ACDF control subjects was defined as evidence of bridging trabecular bone and < 2° total angular motion (from flexion to extension) and < 50% radiolucency along the graft/endplate interface. For Mobi-C® subjects radiologic failure was defined as evidence of continuous bridging bone and < 2° total angular motion (from flexion to extension). An alternative primary endpoint analysis was prospectively planned to assess subject success when major complications due to radiographic assessment were removed from the analysis. Non-inferiority was tested using an exact 95% one-sided confidence bound for the difference between the study and control success rates; if a 10% offset could be ruled out according to the 95% lower bound, then superiority was to be tested. A closed testing procedure was used to allow for superiority to be tested in the event that non-inferiority was established for the primary effectiveness endpoint. A similar approach was used for the secondary effectiveness endpoints.

The individual patient success rate was defined in the original IDE protocol as the number of patients classified as success divided by the number of patients evaluated at 24 months. The overall success rates at 24 months postoperative and the success rates for each of the individual success components is provided in **Table 23**. The composite success rate seen for randomized Mobi-C® subjects was 69.7% at the 24-month visit, 32.3% higher than the 37.4% success rate observed in the ACDF subjects. The protocol specified that the trial would successfully demonstrate non-inferiority if the exact 95% one-sided confidence bound for the difference between the Mobi-C® and control success rate ruled out a 10% offset. Therefore, the results of the primary composite endpoint analysis demonstrated non-inferiority of Mobi-C® compared to control. **Table 24** shows the alternative primary endpoint analysis (Variation 1) which confirms the primary analysis results (Overall Success: Mobi-C® randomized subjects, 72.4%; ACDF control subjects, 49.5%). **Table 25a** provides summary data on the time course of overall success for each treatment group. **Table 25b** includes data for the protocol specified primary endpoint, the protocol specified variation 1 of the primary

endpoint, the FDA requested primary endpoint, and the FDA requested variation 1 of the primary endpoint.

Table 23. Overall Success (Protocol -Specified) at 24 Months

Component	Non-Randomized Mobi-C® (N=9)	Randomized Mobi-C® (N=225)	Randomized ACDF (N=105)	p-value
NDI Improvement	5/7 (71.4%)	169/216 (78.2%)	55/89 (61.8%)	p=0.0042***
No failure due to Subsequent Surgery	9/9 (100%)	218/225 (96.9%)	93/105 (88.6%)	p<0.0001**
No Major Complications	7/9 (77.8%)	197/225 (87.6%)	76/105 (72.4%)	p<0.0001***
Overall Success	4/7 (57.1%)	154/221 (69.7%)	37/99 (37.4%)	p<0.0001**

* Patients 101-041 (ACDF), 102-011 (ACDF), 102-014 (ACDF), 102-026 (Mobi-C®), 104-004 (Mobi-C®), 104-007 (ACDF), 105-043 (ACDF), 105-068 (ACDF), 106-006 (Mobi-C®), 111-002 (ACDF), 114-015 (Mobi-C®), 114-047 (Mobi-C®), 121-013 (ACDF), 130-020 (ACDF), and 121-055 (ACDF) have had their data censored after a revision, removal, or supplemental fixation surgery

** Using Farrington-Manning test to compare between the treatments

***Using Fisher Exact test to compare frequencies between the treatments

Table 24. Overall Success (Alternative Primary Endpoint Variation 1) at 24 Months

Component	Non-Randomized Mobi-C® (N=9)	Randomized Mobi-C® (N=225)	ACDF (N=105)	p-value
NDI Improvement	5/7 (71.4%)	169/216 (78.2%)	55/89 (61.8%)	p=0.0042***
No failure due to Subsequent Surgery	9/9 (100%)	218/225 (96.9%)	93/105 (88.6%)	p<0.0001**
No Major Complications	7/9 (77.8%)	205/225 (91.1%)	92/105 (87.6%)	p=0.3301***
Overall Success	4/7 (57.1%)	160/221 (72.4%)	49/99 (49.5%)	p<0.0001**

* Patients 101-041 (ACDF), 102-011 (ACDF), 102-014 (ACDF), 102-026 (Mobi-C®), 104-004 (Mobi-C®), 104-007 (ACDF), 105-043 (ACDF), 105-068 (ACDF), 106-006 (Mobi-C®), 111-002 (ACDF), 114-015 (Mobi-C®), 114-047 (Mobi-C®), 121-013 (ACDF), 130-020 (ACDF), and 121-055 (ACDF) have had their data censored after a revision, removal, or supplemental fixation surgery

** Using Farrington-Manning test to compare between the treatments

***Using Fisher Exact test to compare frequencies between the treatments

Variation 1 definition utilizes the composite endpoint with the radiographic component of major complication being removed from consideration.

Table 25a. Summary - Timecourse of Overall Success

Visit	Success in Mobi-C® Group: n/N' (proportion: pm) (N=225)	Success in ACDF with Anterior Cervical Plate: n/N' (proportion: pc) (N=105)	Difference/ Lower Bound* for pm-pc	p-value**	p-value***
Month 6	156/216 (0.7222)	24/97 (0.2474)	0.4748 / 0.3870	<0.0001	<0.0001
Month 12	148/213 (0.6948)	32/95 (0.3368)	0.3580 / 0.2628	<0.0001	<0.0001
Month 18	142/212 (0.6698)	36/92 (0.3913)	0.2785 / 0.1794	<0.0001	<0.0001
Month 24	154/221 (0.6968)	37/99 (0.3737)	0.3231 / 0.2283	<0.0001	<0.0001

* The 95% one-sided confidence bound is presented for testing non-inferiority of Mobi-C® using two

proportion test with a 10% non-inferiority margin.
**Using Farrington-Manning test to compare between the treatments, to confirm non-inferiority.
***Using Fisher Exact test to compare the frequencies between the treatments to establish superiority.
Note: No radiographic assessments of major complications were performed before Month 6, so the primary effectiveness success rate is not calculated for earlier visits.
Note: Percentages are based on the number of available observations.

Table 25b. Detail - Timecourse of Overall Success

		6 mo	12 mo	24 mo	36 mo
Protocol – Specified Definition	**NR Mobi-C® (N=9)**	4/7 (57.1%)	2/8 (25.0%)	4/7 (57.1%)	1/4 (25.0%)
	R Mobi-C® (N=225)	156/216 (72.2%)	148/213 (69.5%)	154/221 (69.7%)	133/199 (66.8%)
	R ACDF (N=105)	24/97 (24.7%)	32/95 (33.7%)	37/99 (37.4%)	36/87 (41.4%)
Protocol – Specified Definition (Variation 1)	**NR Mobi-C® (N=9)**	4/7 (57.1%)	2/8 (25.0%)	4/7 (57.1%)	2/5 (40.0%)
	R Mobi-C® (N=225)	157/216 (72.7%)	151/213 (70.9%)	160/221 (72.4%)	143/201 (71.1%)
	R ACDF (N=105)	49/96 (51.0%)	44/95 (46.3%)	49/99 (49.5%)	40/87 (46.0%)
FDA Defined Alternative Definition *	**NR Mobi-C® (N=9)**	4/7 (57.1%)	2/8 (25.0%)	4/7 (57.1%)	1/4 (25.0%)
	R Mobi-C® (N=225)	146/216 (67.6%)	138/213 (64.8%)	143/221 (64.7%)	128/200 (64.0%)
	R ACDF (N=105)	20/98 (20.4%)	25/95 (26.3%)	32/99 (32.3%)	29/87 (33.3%)
FDA Defined Alternative Definition* (Variation 1)	**NR Mobi-C® (N=9)**	4/7 (57.1%)	2/8 (25.0%)	4/7 (57.1%)	2/5 (40.0%)
	R Mobi-C® (N=225)	147/216 (68.1%)	141/213 (66.2%)	148/221 (67.0%)	136/201 (67.7%)
	R ACDF (N=105)	40/97 (41.2%)	34/95 (35.8%)	42/99 (42.4%)	32/87 (36.8%

NR Mobi-C®=Non-randomized Mobi-C®; R Mobi-C®=Randomized Mobi-C®; R ACDF=Control
Protocol specified definition utilizes a two point reduction in any motor or reflex assessment or one point reduction in sensory assessment at the treated level as the definition of neurologic deterioration.
Variation 1 definition utilizes the composite endpoint with the radiographic component of major complication being removed from consideration.
FDA Alternative definition counts any subject with any neurological deterioration compared to baseline status at the treated level as a failure due to a neurological major complication at that timepoint.
**FDA Defined Alternative Definition (Variation 1)* includes both the FDA Alternative definitions of neurological major complication (counts any subject with any neurological deterioration compared to baseline status at the treated level as a failure due to neurological major complication at that timepoint) and Variation 1 (the composite endpoint with the radiographic component of major complication being removed from consideration).
Note: Percentages are based on the number of available observations.

Table 26 provides data on overall success in each treatment group stratified by level treated. There were no statistical differences in overall success between the randomized groups at C3-4, C4-5, C5-6 and C6-7 according to the protocol-specified definition.

Table 26. Primary Effectiveness Analyses by Level Treated at 24 Months

	Success in Mobi-C® Non-Randomized Group: n/N' – (proportion: pm) (N=9)	Success in Mobi-C® Randomized Group: n/N' – (proportion: pm) (N=225)	Success in ACDF Randomized Group: n/N' (proportion: pc) (N=105)	Difference/Lower Bound* for pm-pc (ITT)
PROTOCOL-SPECIFIED				
Treated Segment: C3-C4, C4-C5	(N=0)	(N=1)	(N=2)	
Month 24	0	1/ 1 (1.0000)	0/2	1.000 / 1.000
Treated Segment: C4-C5, C5-C6	(N=1)	(N=60)	(N=23)	
Month 24	1/ 1 (1.0000)	36/59 (0.6102)	6/23 (0.2609)	0.3493 / 0.1660
Treated Segment: C5-C6, C6-C7	(N=8)	(N=164)	(N=80)	
Month 24	3/6 (0.5000)	117/161 (0.7267)	31/74 (0.4189)	0.3078 / 0.1972
VARIATION 1				
Treated Segment: C3-C4, C4-C5	(N=0)	(N=1)	(N=2)	
Month 24	0	1/ 1 (1.0000)	0/2	1.000 / 1.000
Treated Segment: C4-C5, C5-C6	(N=1)	(N=60)	(N=23)	
Month 24	1/ 1 (1.0000)	37/59 (0.6271)	8/23 (0.3478)	0.2793 / 0.0859
Treated Segment: C5-C6, C6-C7	(N=8)	(N=164)	(N=80)	
Month 24	3/6 (0.5000)	122/161 (0.7578)	41/74 (0.5541)	0.2037 / 0.0936

* The 95% one-sided confidence bound is presented for testing non-inferiority of Mobi-C® using two proportion test with a 10% non-inferiority margin.
Note: Proportions are based on the number of available observations.
Note: Primary effectiveness analysis variation 1 is the composite endpoint with the radiographic component of major complication being removed from consideration.

Sensitivity Analyses

Various pre-defined sensitivity analyses were conducted to assess the robustness of the study conclusions. Specifically, the following three additional analyses were provided to address the effect of study withdrawals and missing data on the primary endpoint for the Primary Analysis population:

• Technique 1: A nested analysis of the subset of subjects who achieved a 24 Month Visit within the ±30 day window was performed. This analysis was continued by adding subjects in the following order: subjects who had a 24 Month Visit out of the ±30 day window, subjects missing the 24 Month Visit but having post-Month 24 data, subjects having any post-baseline data.

• Technique 2: All missing outcomes were considered failures.

• Technique 3: All missing outcomes were considered failures for Mobi-C® subjects, but successes for ACDF subjects (worst case scenario).

Non-inferiority was established for all three scenarios for the Primary Analysis population. Due to the relatively small numbers of non-Caucasians treated in the IDE (5.8% of subjects were non-Caucasian), limited data is available to assess potential variability in outcomes based on race. Covariate analysis considering race as a baseline variable did not show any interaction with treatment which was predictive of outcome.

Poolability Analysis

Analyses were also conducted to assess poolability of data across sites for both the Primary Analysis population and Safety populations using the Breslow-Day test for the analysis. All tests were non-significant, indicating that there is no particular evidence of a differential treatment effect among sites. These outcomes provide confidence in pooling the data across investigational sites.

Comparison of Randomized and Non-Randomized Mobi-C® Outcomes

A statistical comparison of the primary endpoint and components, secondary endpoints, and adverse events for the randomized (n=225) and non-randomized (n=9) Mobi-C® groups is provided in **Table 27**. For both the protocol-specified and FDA-defined primary endpoints (including the variation 1 analyses), there were no statistical differences between the two groups. However, there were some significant differences when analyzing the components of the primary outcome, as well as secondary outcomes. In addition, as shown above (**Table 21)**, surgery time was longer for the non-randomized Mobi-C® group while hospitalization and length of stay were similar for the non-randomized group compared to the randomized group. However, the small sample size of the non-randomized (n=9) Mobi-C® group compared to the randomized group (n=225) should be noted when interpreting any differences shown between the two groups.

Table 27. Comparison of Randomized and Non-Randomized Patient Outcomes at 24 Months

Outcome Measure	Randomized Mobi-C® (N=225)	Non-Randomized Mobi-C® (N=9)	Difference/95% Lower Bound for pm(R)-pc(NR)
Protocol-Specified Primary Endpoint:	154/221 (69.7%)	4/7 (57.1%)	0.1254/-0.1864
NDI improvement	169/216 (78.2%)	5/7 (71.4%)	0.0681/-0.2165
No failure due to Subsequent Surgery	218/225 (78.2%)	9/9 (100%)	-0.0311/-0.0501
No Major Complications	197/225 (87.6%)	7/9 (77.8%)	0.0978/-0.3286
Protocol-Specified Primary Endpoint (Variation 1):	160/221 (72.4%)	4/7 (57.1%)	0.1526/-0.1591
NDI improvement	169/216 (78.2%)	5/7 (71.4%)	0.0681/-0.2165
No failure due to Subsequent Surgery	218/225 (96.9%)	9/9 (100.0%)	-0.0311/-0.0501
No Major Complications	205/225 (91.1%)	7/9 (77.8%)	0.1333/-0.3634
FDA-Defined Primary Endpoint:	143/221 (64.7%)	4/7 (57.1%)	0.0756/-0.2365
NDI improvement	169/216 (78.2%)	5/7 (71.4%)	0.0681/-0.2165
No failure due to Subsequent Surgery	218/225 (96.9%)	9/9 (100.0%)	-0.0311/-0.0501
No Major Complications	181/225 (80.4%)	7/9 (77.8%)	0.0267/-0.2587
FDA-Defined Primary Endpoint (Variation 1):	148/221 (67.0%)	4/7 (57.1%)	0.0983/-0.2138
NDI improvement	169/216 (78.2%)	5/7 (71.4%)	0.0681/-0.2165
No failure due to Subsequent Surgery	218/225 (96.9%)	9/9 (100.0%)	-0.0311/-0.0501
No Major Complications	187/225 (83.1%)	7/9 (77.8%)	0.0533/-0.2849
Secondary Endpoints:			
NDI (Mean ± SD)	16.5±16.91	19.6±15.82	-3.1523/-13.1899
Neck Pain VAS (Mean ± SD)	16.59±24.146	18.25±26.858	-1.6574/-16.0708
Left Arm Pain VAS (Mean ± SD)	10.38±19.364	21.88 ±28.623	-11.5000/-23.2288
Right Arm Pain VAS (Mean ± SD)	9.81±17.884	10.88±16.873	-1.0648/-11.6819
Patients with any AE	201 (89.3%)	9 (100.0%)	-0.1067/-0.1405
Patients with any Device Related AE (investigator)	36 (16.0%)	4 (44.4%)	-0.2844/-0.5598
Patients with any Device Related AE (CEC)	36 (16.0%)	3 (33.3%)	-0.1733/-0.4349

Secondary Effectiveness Analysis

In addition to the components of the primary endpoint presented above, secondary effectiveness variables were also assessed for the Primary Analysis population. Thirteen secondary endpoints were measured at the 24 Month Visit compared to baseline:

- Neck pain
- Arm pain
- Muscle strength
- Sensory deficit
- Significant neurological deterioration
- Adjacent segment degeneration
- Displacement or migration of the device, graft, or plate
- Range of motion
- Absence of radiolucency
- Patient satisfaction.
- Qualify of life (SF-12)
- Dysphagia - Functional outcome swallowing scale (FOSS)
- Observational gait analysis using the Nurick classification of cervical spondylotic myelopathy (CSM).

Pre-defined sequential testing was outlined for five secondary endpoints using the following pre-defined sequential testing order: Neck Disability Index, dysphagia (FOSS), SF-12(PCS), subject satisfaction, and VAS neck pain. Non-inferiority was tested first before superiority was tested with the exception of dysphagia where only superiority was tested. Endpoints were tested in the stated order until significance was no longer achieved and the testing was stopped at that point. The following secondary endpoint success definitions were specified:

- Neck disability index: 10%, 24 Months
- Dysphagia (graded Stage 0 – Stage V): Overall/6 weeks/3 months/6 months
- SF-12 PCS: 5 units, 24 Months
- Patient Satisfaction (1 question answered on a 4 point scale): 0.4 units, 24 Months
- VAS neck pain: 10 mm, 24 Months

Neck Disability Index

Subjects in both treatment groups showed improvement in NDI after study surgery. The Mobi-C® group showed a greater improvement in mean NDI score compared to the ACDF group at 24 months; this difference was statistically significant (p=0.0032). Using the sensitivity analysis, all three techniques indicated the lower bound for NDI improvement remained above the pre-specified non-inferiority margin of -10%. The number and percentage of subjects at each postoperative time point who showed improvement (by amount), maintenance, or deterioration (by amount) in NDI from the preoperative level are presented in **Table 28**. An improvement of 15 points out of 100 total possible points (or 7.5/50) is widely accepted as a minimum clinically important difference (MCID) for NDI[3]. Deterioration of any amount (defined as a decrease of >8/100 from baseline NDI score) was not reported by more than 5 Mobi-C® randomized subjects or 5 ACDF control subjects at any single time point.

Table 28. Timecourse of Improvement in NDI- Safety Population

Category	6 Weeks			3 Months			6 Months			12 Months			24 Months		
	NR Mobi-C® (N=8)	R Mobi-C® (N=219)	R ACDF (N=102)	NR Mobi-C® (N=8)	R Mobi-C® (N=219)	R ACDF (N=102)	NR Mobi-C® (N=7)	R Mobi-C® (N=219)	R ACDF (N=98)	NR Mobi-C® (N=8)	R Mobi-C® (N=216)	R ACDF (N=95)	NR Mobi-C® (N=7)	R Mobi-C® (N=221)	R ACDF (N=99)
Improvement[1]	5 (62.5%)	159 (72.6%)	67 (65.7%)	7 (87.5%)	185 (84.5%)	75 (73.5%)	6 (85.7%)	192 (87.7%)	75 (76.5%)	5 (62.5%)	184 (85.2%)	69 (72.6%)	7 (100.0%)	191 (86.4%)	67 (67.7%)
Maintained[2]	3 (37.5%)	50 (22.8%)	28 (27.5%)	1 (12.5%)	28 (12.8%)	21 (20.6%)	1 (14.3%)	20 (9.1%)	19 (19.4%)	3 (37.5%)	25 (11.6%)	19 (20.0%)	0	22 (10.0%)	21 (21.2%)
Deteriorated[3]	0	5 (2.3%)	4 (3.9%)	0	3(1.4%)	5 (4.9%)	0	3 (1.4%)	2 (2.0%)	0	3 (1.4%)	3 (3.2%)	0	2 (0.9%)	1 (1.0%)

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

[1] Clinically significant improvement of ≥ 15 point improvement from baseline (*see* Carreon LY, Glassman SD, Campbell MJ, Anderson PA (2010). Neck Disability Index, Short Form-36 Physical Component Summary, and Pain Scales for Neck and Arm Pain: The Minimum Clinically Important Difference and Substantial Clinical Benefit After Cervical Spine Fusion. Spine J 10(6):469-74).

[2] Maintained indicates change in NDI of -8 to 14 points as compared to baseline.

[3] Deteriorated indicates worsening NDI score of > 9 points as compared to baseline.

Dysphagia

Dysphagia was measured using a staged functional outcome swallowing scale from Stage 0 to Stage 5. Results were comparable between both treatment groups through 24 months.

Table 29. Dysphagia Assessment- Primary Analysis Population

	Mobi-C® (N=225)						ACDF (N=105)					
	Stage 0	**Stage 1**	**Stage 2**	**Stage 3**	**Stage 4**	**Stage 5**	**Stage 0**	**Stage 1**	**Stage 2**	**Stage 3**	**Stage 4**	**Stage 5**
Week 6	165 (75.7%)	50 (22.9%)	2 (0.9%)	1 (0.5%)	0	0	67 (65.7%)	35 (34.3%)	0	0	0	0
Month 3	191 (88.0%)	26 (12.0%)	0	0	0	0	85 (84.2%)	15 (14.9%)	1 (1.0%)	0	0	0
Month 6	200 (92.2%)	17 (7.8%)	0	0	0	0	86 (87.8%)	12 (12.2%)	0	0	0	0
Month 12	204 (95.3%)	10 (4.7%)	0	0	0	0	84 (91.3%)	8 (8.7%)	0	0	0	0
Month 18	198 (95.2%)	10 (4.8%)	0	0	0	0	78 (91.8%)	7 (8.2%)	0	0	0	0
Month 24	208 (96.3%)	8 (3.7%)	0	0	0	0	84 (94.4%)	5 (5.6%)	0	0	0	0

Stage 0 = normal function and asymptomatic; S**tage I** = normal function but with episodic or daily symptoms of dysphagia; **Stage II** = compensated abnormal function manifested by significant dietary modifications or prolonged mealtime (without weight loss or aspiration); **Stage III** = decompensated abnormal function with weight loss of 10% or less of body weight over 6 months due to dysphagia, or daily cough, gagging, or aspiration during meals; **Stage IV** = severely decompensated abnormal function with weight loss of more than 10% of body weight over 6 months due to dysphagia, or severe aspiration with bronchopulmonary complications, non-oral feeding recommended for most of nutrition, and **Stage V** = non-oral feeding for all nutrition.**(From [4]Salassa JR Dig Dis 1999;17(4):230-4)**

Other Secondary Endpoints

The remaining secondary endpoints were not tested for non-inferiority according to the closed test procedure and are reported descriptively since the Mobi-C® group did not demonstrate superiority to ACDF patients with respect to dysphagia.

SF-12(MCS)

Quality of life, which was measured using the Medical Outcomes Study 12-item Short Form Health Survey (SF-12). Mobi-C® and ACDF patients showed similar improvement in the SF-12 MCS score at 24 months after surgery.

SF-12(PCS)

Quality of life, which was measured using the Medical Outcomes Study 12-item Short Form Health Survey (SF-12). Mobi-C® and ACDF patients showed similar improvement in the SF-12 PCS score at 24 months after surgery.

Table 30. Summary of Quality of Life (SF-12 MCS and SF-12 PCS) Safety Population

	6 mo			12 mo			24 mo		
	T	**M**	**F**	**T**	**M**	**F**	**T**	**M**	**F**
SF-12 MCS	**N=7**	**N=195**	**N=93**	**N=8**	**N=194**	**N=84**	**N=7**	**N=203**	**N=83**
Improved	3 (42.9%)	101 (51.8%)	50 (53.8%)	2/8 (25.0%)	108 (55.7%)	42 (50.0%)	4 (57.1%)	113 (55.7%)	43 (51.8%)
Maintained	0	49 (25.1%)	17 (18.3%)	1/8 (12.5%)	41 (21.1%)	20 (23.8%)	0	41 (20.2%)	21 (25.3%)
Deteriorated	4 (57.1%)	45 (23.0%)	26 (28.0%)	5/8 (62.5%)	45 (23.2%)	22 (26.2%)	3 (42.9%)	49 (24.1%)	19 (22.9%)
SF-12 PCS	**N=7**	**N=195**	**N=93**	**N=8**	**N=194**	**N=84**	**N=7**	**N=203**	**N=83**
Improved	4 (57.1%)	151 (77.4%)	57 (61.3%)	5/8 (62.5%)	144 (74.2%)	56 (66.7%)	4 (57.1%)	157 (77.3%)	52 (62.7%)
Maintained	1 (14.3%)	22 (11.3%)	14 (15.1%)	1/8 (12.5%)	25 (12.9%)	7 (8.3%)	1 (14.3%)	24 (11.8%)	15 (18.1%)
Deteriorated	2 (28.6%)	22 (11.3%)	22 (23.7%)	2/8 (25.0%)	25 (12.9%)	21 (25.0%)	2 (28.6%)	22 (10.8%)	16 (19.3%)

T =Non-randomized Mobi-C®; M=Randomized Mobi-C®; F=Control Randomized

Improved ≥15% change from baseline

Maintained ≥0% change from baseline, and <15% change from baseline

Deteriorated <0% change from baseline

* Patients 101-041 (ACDF), 102-011 (ACDF), 102-014 (ACDF), 102-026 (Mobi-C®), 104-004 (Mobi-C®), 104-007 (ACDF), 105-043 (ACDF), 105-068 (ACDF), 106-006 (Mobi-C®), 111-002 (ACDF), 114-015 (Mobi-C®), 114-047 (Mobi-C®), 121-013 (ACDF), 130-020 (ACDF), and 121-055 (ACDF) have had their data censored after a revision, removal, or supplemental fixation surgery

VAS Neck Pain and Arm Pain

Both randomized groups demonstrated similar postoperative improvement in neck pain according to VAS. Mean scores were similar between the randomized Mobi-C® group and ACDF group at most visits, with differing changes from baseline attributed to imbalances present at baseline. The majority of subjects in both treatment groups showed maintained or improved VAS as compared to baseline levels at each time point. In the data presentations below (**Table 31**), the improved group was defined by a greater than 20mm increase in VAS score compared to baseline and the maintained group was defined by a change in VAS of -6 to 20 mm as compared to baseline.

Table 31. Timecourse of VAS Neck and Arm Pain Improvement

Neck	6 Weeks			3 Months			6 Months			12 Months			24 Months		
	T (N=8)	M (N=219)	F (N=102)	T (N=8)	M (N=219)	F (N=102)	T (N=7)	M (N=219)	F (N=98)	T (N=8)	M (N=216)	F (N=95)	T (N=7)	M (N=221)	F (N=99)
Impoved[1]	7 (87.5%)	177 (80.8%)	75 (73.5 %)	8 (100.0%)	179 (81.7%)	76 (74.5%)	6 (85.7%	185 (84.5%)	71 (72.4%)	7 (87.5%)	173 (80.1%)	67 (70.5%)	5 (71.4%)	179 (81.0%)	73 (73.7%)
Maintained[2]	1 (12.5%)	35 (16.0%)	19 (18.6%)	0	34 (15.5%)	23 (22.5%)	1 (14.3%)	27 (12.3%)	19 (19.4%)	1 (12.5%)	32 (14.8%)	22 (23.2%)	2 (28.6%)	30 (13.6%)	13 (13.1%)
Deteriorated[3]	0	2 (0.9%)	5 (4.9%)	0	3 (1.4%)	2 (2.0%)	0	3 (1.4%)	5 (5.1%)	0	7 (3.2%)	3 (3.2%)	0	7 (3.2%)	1 (1.0%)
Right Arm	**6 Weeks**			**3 Months**			**6 Months**			**12 Months**			**24 Months**		
	T (N=8)	M (N=219)	F (N=102)	T (N=8)	M (N=219)	F (N=102)	T (N=7)	M (N=219)	F (N=98)	T (N=8)	M (N=216)	F (N=95)	T (N=7)	M (N=221)	F (N=99)
Improved[1]	4 (50.0%)	110 (50.2%)	52 (51.0%)	4 (50.0%)	114 (52.1%)	49 (48.0%)	4 (57.1%)	112 (51.1%)	46 (46.9%)	3 (37.5%)	111 (51.4%)	38 (40.0%)	4 (57.1%)	116 (52.5%)	44 (44.4%)
Maintained[2]	4 (50.0%)	89 (40.6%)	41 (40.2%)	4 (50.0%)	93 (42.5%)	39 (38.2%)	1 (14.3%)	92 (42.0%)	41 (71.8%)	4 (50.0%)	86 (39.8%)	39 (41.1%)	3 (42.8%)	88 (39.8%)	34 (34.3%)
Deteriorated[3]	0	13 (5.9%)	5 (4.9%)	0	8 (3.7%)	11 (10.8%)	2 (28.6%)	11 (5.0%)	8 (8.2%)	1 (12.5%)	15 (6.9%)	15 (15.8%)	0	12 (5.4%)	9 (9.1%)
Left Arm	**6 Weeks**			**3 Months**			**6 Months**			**12 Months**			**24 Months**		
	T (N=8)	M (N=219)	F (N=102)	T (N=8)	M (N=219)	F (N=102)	T (N=7)	M (N=219)	F (N=98)	T (N=8)	M (N=216)	F (N=95)	T (N=7)	M (N=221)	F (N=99)
Improved[1]	4 (50.0%)	126 (57.5%)	61 (59.8%)	4 (50.0%)	125 (57.1%)	57 (55.9%)	4 (57.1%)	127 (58.0%)	53 (54.1%)	4 (50.0%)	124 (57.4%)	53 (55.8%)	3 (42.9%)	130 (58.8%)	55 (55.6%)
Maintained[2]	3 (37.5%)	71 (32.4%)	31 (30.4%)	2 (25.0%)	78 (35.6%)	37 (36.3%)	2 (28.6%)	80 (36.5%)	34 (34.7%)	1 (12.5%)	79 (36.6%)	30 (31.6%)	3 (42.9%)	77 (34.8%)	26 (26.3%)
Deteriorated[3]	1 (12.5%)	16 (7.3%)	6 (5.9%)	2 (25.0%)	11 (5.0%)	5 (4.9%)	1 (14.3%)	7 (3.2%)	8 (8.2%)	3 (37.5%)	7 (3.2%)	9 (9.5%)	1 (14.3%)	8 (3.6%)	6 (6.1%)

T = Non-randomized Mobi-C®; M = Randomized Mobi-C®; F = ACDF Control Randomized

[1] Improvement defined as > 20 mm improvement in VAS from baseline.

[2] Maintained indicates change in VAS of -6 to 20 mm as compared to baseline.

[3] Deteriorated indicates worsening VAS score of > 6 mm as compared to baseline.

Subject Satisfaction

Patient satisfaction was assessed by questionnaire which included the following queries:
▪ Question 1: How satisfied are you with the surgical treatment you received? (Possible answers included: very satisfied, somewhat satisfied, somewhat dissatisfied, very dissatisfied)
▪ Question 2: Would you recommend the same treatment to a friend with the same condition? (Possible answers included: definitely yes, probably yes, probably no, definitely no)

At Month 24 follow-up, Question #1 responses of "very satisfied" (randomized Mobi-C®, 85.6%, ACDF, 78.2%) and Question #2 responses of "definitely yes" (randomized Mobi-C®, 85.6%, ACDF, 72.4%) showed a greater percentage of "very satisfied" and "definitely yes" responses in the Mobi-C® group.

Table 32. Patient Satisfaction

	Non-randomized Mobi-C® (N=9)	Randomized Mobi-C® (N=225)	ACDF (N=105)
Question 1: Satisfaction "Very Satisfied"			
12 months	7 (77.8%)	187 (88.2%)	69 (75.8%)
24 months	7 (87.5%)	185 (85.6%)	68 (78.2%)
Question 2: Recommendation "Definitely Yes"			
12 months	8 (88.9%)	179 (84.4%)	64 (70.3%)
24 months	8 (100.0%)	185 (85.6%)	63 (72.4%)

Radiographic Assessments

Range of Motion

Radiographic evaluation of mean ranges of motion for flexion/extension bending and left/right lateral bending for the treated levels at the preoperative, 12 month, and 24 month time point are shown in **Table 33** for all subjects. Anticipated differences between ACDF and Mobi-C® were noted in view of differing modes of action (fusion vs. motion preservation). At the 24 Month Visit, Mobi-C® mean range of motion values of superior and inferior levels respectively were 10.10 ° (±5.938°), 8.30 ° (±5.277°) for flexion/extension bending and 5.45° (±3.260°), 5.35° (±3.296°) for left/right lateral bending. ACDF superior and inferior mean range of motion values respectively were 0.50° (±0.717°), 1.17° (±1.699°) for flexion/extension bending and 0.74° (±1.024°), 0.82° (±0.938°) for left/right lateral bending.

Table 33. Radiographic Range of Motion

Component		Preoperative			12 months			24 months		
		T (N=8)	M (N=222)	F (N=100)	T (N=8)	M (N=213)	F (N=91)	T (N=8)	M (N=216)	F (N=89)
Range of Motion (°) Flexion-Extension	Superior Level	7.39± 3.728	9.13± 4.849	9.33± 4.875	11.46± 5.248	10.07± 5.635	0.83± 1.116	10.84± 6.404	10.10± 5.938	0.50± 0.717
	Inferior Level	T (N=8)	M (N=209)	F (N=98)	T (N=8)	M (N=209)	F (N=89)	T (N=8)	M (N=214)	F (N=88)
		6.30± 4.382	7.44± 4.341	7.14± 3.860	9.16± 4.453	8.30± 4.860	1.44± 1.485	7.80± 4.938	8.30± 5.277	1.17± 1.699
Component		**Preoperative**			**12 months**			**24 months**		
		T (N=6)	**M (N=206)**	**F (N=96)**	**T (N=8)**	**M (N=212)**	**F (N=90)**	**T (N=7)**	**M (N=216)**	**F (N=89)**
Range of Motion (°) Lateral Bending	Superior Level	4.38± 2.522	5.76± 3.374	5.48± 3.041	5.83± 1.180	5.64± 3.191	0.92± 0.945	5.19± 2.236	5.45± 3.260	0.74± 1.024
	Inferior Level	T (N=6)	M (N=206)	F (N=96)	T (N=8)	M (N=212)	F (N=90)	T (N=7)	M (N=216)	F (N=89)
		6.65± 5.526	4.91± 3.265	4.77± 2.866	4.35± 1.978	5.36± 3.097	1.08± 1.058	3.97± 2.591	5.35± 3.296	0.82± 0.938

T = Non-randomized Mobi-C®; M = Randomized Mobi-C®; F = ACDF Control Randomized

Figure 3a. Mobi-C® Time Course of Mean Flexion/Extension Range of Motion at Superior Index Level

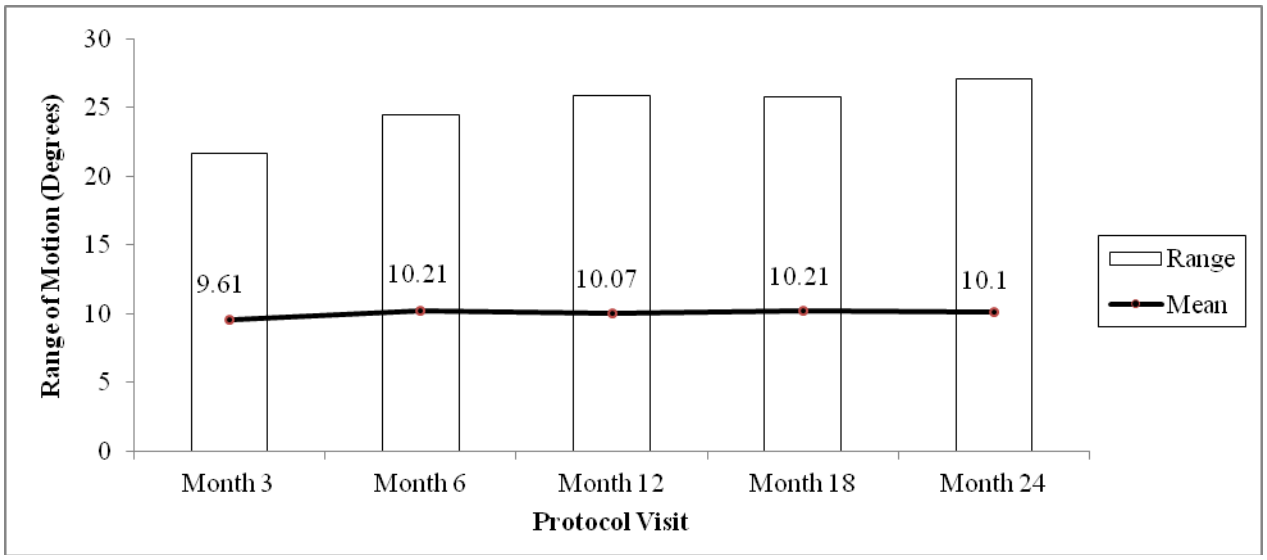
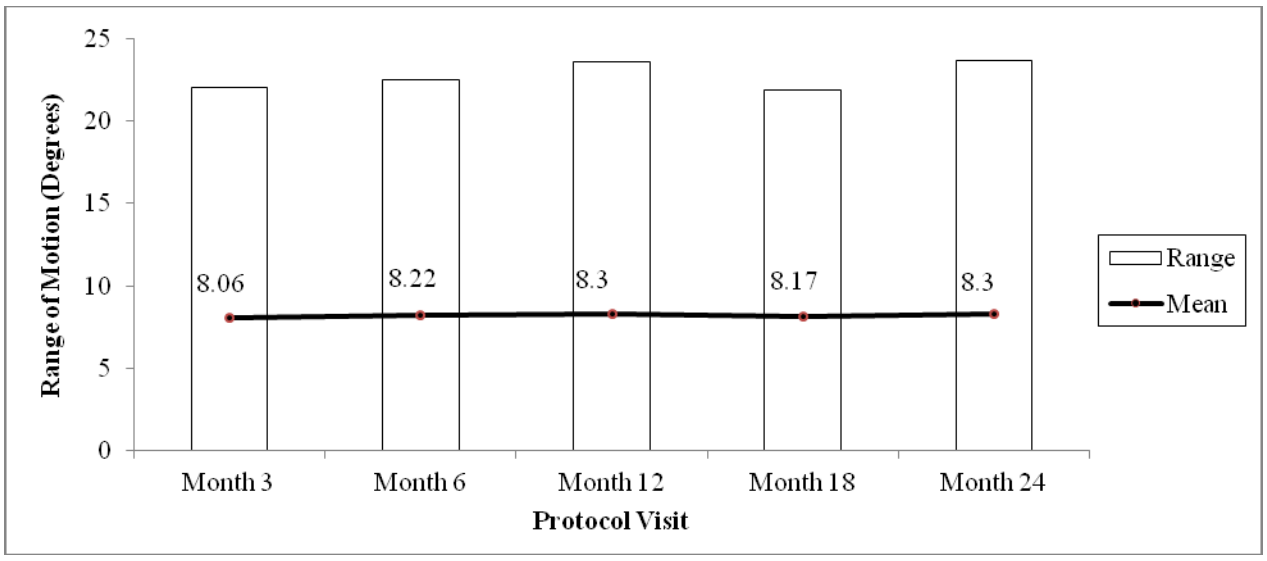


Figure 3b. Mobi-C® Time Course of Mean Flexion/Extension Range of Motion at Inferior Index Level



The protocol-specified range of motion (ROM) success criteria for Mobi-C® subjects required ROM greater than or equal to 2° in flexion-extension and lack of bridging bone at the index level. The criteria for fusion in the ACDF group required development of bridging bone and < 2 ° of angular motion. In the Primary Analysis population, 98.6% (211/214) randomized Mobi-C® subjects achieved ROM success according to the protocol specified criteria (≥ 2° ROM with no bridging bone) while 1.4% (3/214) of Mobi-C® subjects were ROM failures (< 2° ROM with bridging bone). FDA requested a secondary analysis using the ROM success criteria of ≥4 ° flexion-extension combined superior and inferior index

level motion which demonstrated that 95.8% (205/214) Mobi-C® subjects achieved ROM success while 4.2% (9/214) of randomized Mobi-C® subjects were ROM failures (≤ 4° ROM).

Table 34 presents data on change in range of motion from preoperative baseline to Month 24 for the primary analysis endpoint. In total, 67/229 (29.3%) experienced a decrease in ROM of greater than 2 degrees, though many of these subjects did not experience bridging bone and were therefore not ROM failures by protocol definition.

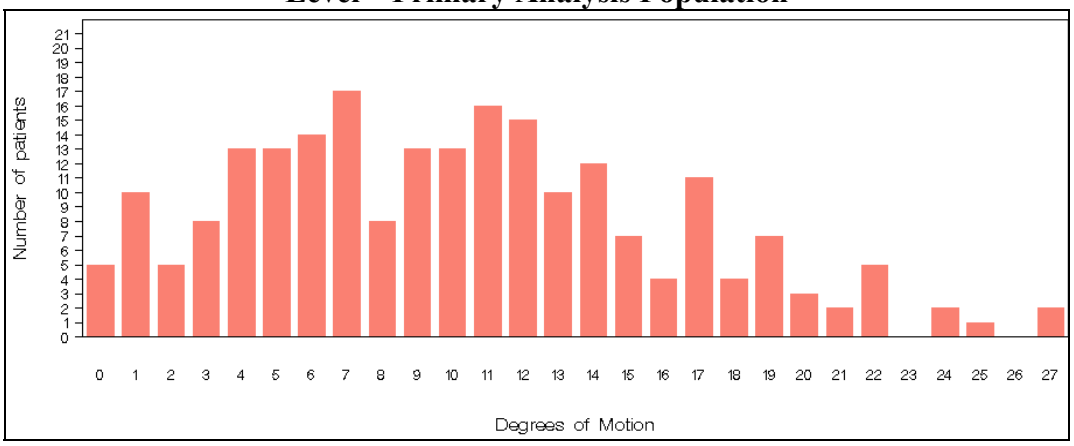
Table 34. Radiographic Change in Range of Motion for Mobi-C®

			24 Month
NR Mobi-C® N=8	Superior Level	Increased (≥2°)	4(50.0%)
		No change (≥-2 to <2)	1 (12.5%)
		Decreased (<-2)	2 (25.0%)
	Inferior Level	Increased (≥2°)	3(37.5%)
		No change (≥-2 to <2)	1 (12.5%)
		Decreased (<-2)	3 (37.5%)
	Combined	Increased (≥2°)	4 (50.0%)
		No change (≥-2 to <2)	0
		Decreased (<-2)	3 (37.5%)
R Mobi-C® N=221	Superior Level	Increased (≥2°)	93 (42.1%)
		No change (≥-2 to <2)	63 (28.5%)
		Decreased (<-2)	57 (25.8%)
	Inferior Level	Increased (≥2°)	89 (40.3%)
		No change (≥-2 to <2)	57 (25.8%)
		Decreased (<-2)	55 (24.9%)
	Combined	Increased (≥2°)	106 (48.0%)
		No change (≥-2 to <2)	31 (14.0%)
		Decreased (<-2)	64 (29.0%)
All Mobi-C® N=229	Superior Level	Increased (≥2°)	97 (42.4%)
		No change (≥-2 to <2)	64 (27.9%)
		Decreased (<-2)	59 (25.8)
	Inferior Level	Increased (≥2°)	92 (40.2%)
		No change (≥-2 to <2)	58 (25.3%)
		Decreased (<-2)	58 (25.3%)
	Combined	Increased (≥2°)	110 (48.0%)
		No change (≥-2 to <2)	31 (13.5%)
		Decreased (<-2)	67 (29.3%)

Note: Patients 101007, 101041, 102011, 102014, 102026, 104004, 104007, 105016, 105043, 105068, 106006, 110017, 111002, 114015, 114047,121013, 121055, 130020, 130030, and 123004 have had their data censored after a revision, removal, or supplemental fixation surgery.

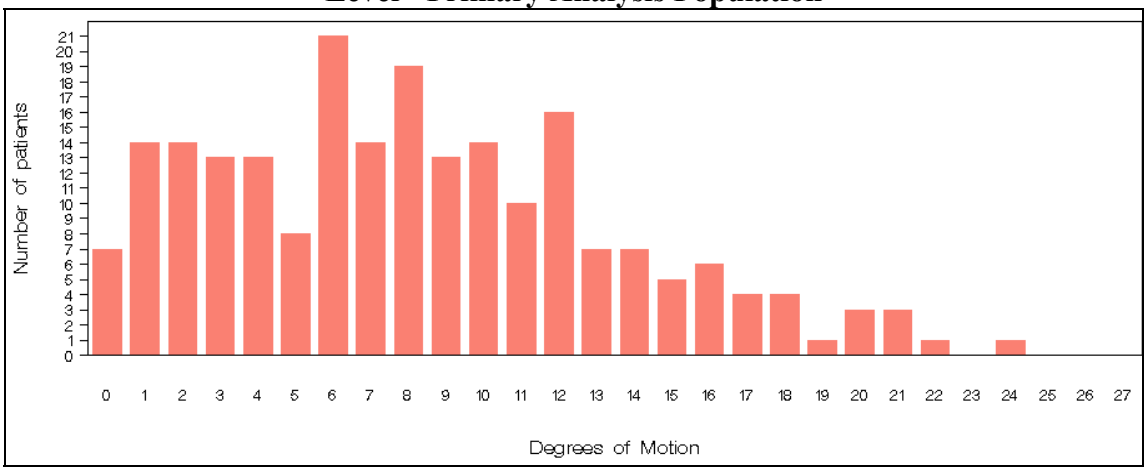
A histogram of angular range of motion on flexion/extension radiographs at 24 months for all patients treated with Mobi-C® is provided in **Figure 4a** and **Figure 4b** below. This histogram uses values obtained by rounding recorded range of motion for each subject to the nearest integer.

Figure 4a. Histogram of Mobi-C® Angular Range of Motion at Month 24, Superior Treated Level – Primary Analysis Population



Note: Degrees of motion have been rounded to the nearest integer. The range of motion values are measured from flexion/extension radiographs at 24 months.

Figure 4b. Histogram of Mobi-C® Angular Range of Motion at Month 24, Inferior Treated Level - Primary Analysis Population



Note: Degrees of motion have been rounded to the nearest integer. The range of motion values are measured from flexion/extension radiographs at 24 months

The data was evaluated to demonstrate the correlation between range of motion (absolute and change from baseline) and overall success (primary endpoint and alternate primary endpoint), NDI and VAS pain scores by evaluating the percentage of patients successful on each outcome stratified by range of flexion-extension motion. Patients who achieved success in the primary endpoint demonstrated a larger mean change from mean baseline motion (flexion-extension) compared to patients who were primary endpoint failures.

Fusion

For control subjects, failure of fusion at either of the treated levels was defined as ≥ 2° of segmental movement on lateral flexion-extension X-rays, radiolucent lines at greater than 50% of the graft-vertebral interfaces or lack of evidence of bridging trabecular bone. This assessment was determined by independent qualitative radiographic analysis of the 24 month radiographs, in accordance with the MMI protocol. The ACDF subjects were required to demonstrate fusion status at both treated segments. Fusion status of the control ACDF group at the 6 month, 12 month and 24 month time points is provided in **Table 35**.

Table 35. Radiographic Fusion Failure for Control ACDF	**6 mo**	**12 mo**	**24 mo**
Fusion failure	52/94 (55.3%)	33/94 (35.1%)	20/99 (20.2%)

The data in Table 35 shows that at 6 and 12 months, 94 subjects had radiographs available for analysis, 52 subjects showed radiographic fusion failure at 6 months and 33 showed radiographic fusion failure at 12 months. At 24 months 99 subjects had radiographs available with 20 radiographic fusion failures. Table 35 is based upon the radiographic definition of non-fusion per the study protocol, also referred to as radiographic major complication. In contrast, the Non-Union data presented in Table 11 (Adverse Events) are derived from investigator reports of adverse events and were dependent upon investigator interpretation. Therefore, the fusion failure rates and non-union adverse events are different values.

Radiolucency

Radiolucency was evaluated using a qualitative scale as defined in the study protocol as: none, mild (< 25%), moderate (25-50%), or severe (>50%). Radiolucency was assessed in 2 Mobi-C® subjects at the 24 Month Visit (1.3%), and in 2 ACDF subjects at the 24 Month Visit (2.9%), and in all cases was reported as mild in severity (≤ 25% coverage of radiolucent lines along the device/endplate interface) in both treatment groups.

Subsidence or Migration of the Device, Graft or Cage

Subsidence was defined in the study protocol as ≥ 3 mm cranial or caudal motion of the device (or device component) perpendicular to the vertebral endplates. Migration was defined in the study protocol as ≥ 3 mm anterior or posterior motion of the device (or device component) parallel to the vertebral endplates. The radiographic assessments revealed one case of migration and no cases of subsidence according to this definition in either treatment group.

Functional Spinal Unit (FSU) Height Change

Radiographic disc height was assessed by an independent radiographic core laboratory.

Mean change from baseline in FSU height at the superior level ranged from -0.26 mm (6 weeks post-op) to -0.43 mm (24 months post op) in the randomized Mobi-C® subjects, compared with -0.50 mm (6 weeks post-op) to -0.70 mm (24 months post op) in the ACDF group.

Mean change from baseline in FSU height at the inferior level ranged from -0.24 mm (6 weeks post-op) to -0.35 mm (24 months post op) in the randomized Mobi-C® subjects, compared with -0.73 mm (6 weeks post-op) to -0.81 mm (24 months post op) in the ACDF group.

Table 36a. Radiographic FSU Height Superior Level – Safety Population

	Pre-Operative			Post-Operative			6 weeks		
	T (N=6)	M (N=221)	F (N=101)	T (N=7)	M (N=219)	F (N=89)	T (N=7)	M (N=214)	F (N=99)
FSU Height & (SD) mm	27.68 (3.149)	28.96 (2.614)	28.47 (2.668)	29.54 (2.682)	31.14 (2.624)	30.33 (2.484)	29.29 (2.605)	30.87 (2.464)	29.55 (2.586)
FSU Change* & (SD) mm	-	-	-	-	-	-	-0.23 (0.095)	-0.26 (0.3337)	-0.50 (0.483)
	6 Months			12 Months			24 Months		
	T (N=7)	M (N=212)	F (N=98)	T (N=7)	M (N=213)	F (N=91)	T (N=8)	M (N=215)	F (N=89)
FSU Height & (SD) mm	29.17 (2.715)	30.78 (2.447)	29.26 (2.591)	29.11 (2.840)	30.75 (2.458)	29.50 (2.553)	29.03 (2.618)	30.70 (2.508)	29.21 (2.601)
FSU Change* & (SD) mm	-0.36 (0.215)	-0.33 (0.376)	-0.64 (0.664)	-0.41 (0.329)	-0.36 (0.387)	-0.68 (0.608)	-0.54 (0.336)	-0.43 (0.398)	-0.70 (0.675)

T = Non-randomized Mobi-C®; M = Randomized Mobi-C®; F = ACDF Control Randomized

* - Change calculated as difference between Post-Operative FSU Height and FSU Height at timepoints. All available radiographs used in the analysis.

Table 36b. Radiographic FSU Height Inferior Level – Safety Population

	Pre-Operative			Post-Operative			6 weeks		
	T (N=6)	M (N=215)	F (N=99)	T (N=7)	M (N=208)	F (N=85)	T (N=7)	M (N=209)	F (N=98)
FSU Height & (SD) mm	28.72 (2.117)	29.71 (2.604)	29.22 (2.537)	30.47 (1.767)	31.73 (2.385)	30.73 (2.438)	30.14 (1.603)	31.59 (2.410)	29.87 (2.611)
FSU Change* & (SD) mm	-	-	-	-	-	-	-0.34 (0.264)	-0.24 (0.316)	-0.73 (0.657)
	6 Months			12 Months			24 Months		
	T (N=7)	M (N=205)	F (N=96)	T (N=7)	M (N=206)	F (N=89)	T (N=8)	M (N=209)	F (N=87)
FSU Height & (SD) mm	30.03 (1.738)	31.50 (2.396)	29.56 (2.541)	30.03 (1.729)	31.47 (2.365)	29.80 (2.485)	30.21 (1.758)	31.50 (2.393)	29.61 (2.577)
FSU Change* & (SD) mm	-0.46 (0.288)	-0.32 (0.339)	-0.86 (0.826)	-0.44 (0.282)	-0.35 (0.356)	-0.88 (0.844)	-0.46 (0.294)	-0.35 (0.385)	-0.81 (0.866)

T = Non-randomized Mobi-C®; M = Randomized Mobi-C®; F = ACDF Control Randomized

* - Change calculated as difference between Post-Operative FSU Height and FSU Height at timepoint. All available radiographs used in the analysis.

Table 37. Summary of Disc FSU Height Change at 24 Months for ITT Population – Radiographic Measurements

Component	Randomized Mobi-C®	Randomized ACDF	P-Value
Superior Disc Height Change	-0.43 ± 0.398	-0.70 ± 0.675	0.0006
Inferior Disc Height Change	-0.35 ± 0.385	-0.81 ± 0.866	<0.0001

Source Table 7.2.13.1

* Using unpaired t-test to compare the change from baseline value between the treatments.

Note: Patients 101007, 101041, 102011, 102014, 102026, 104004, 104007, 105016, 105043, 105068, 106006, 110017, 111002, 114015, 114047,121013, 121055, 130020, 130030, and 123004 have had their data censored after a revision, removal, or supplemental fixation surgery.

Heterotopic Ossification

Available radiographs for all treated Mobi-C® patients at the 6, 12, 24 month and later time points were assessed for heterotopic ossification (HO) by two independent radiologists and a third radiologist to adjudicate in instances of disagreement using a classification system (**Table 38**) adapted from [5]McAfee and [6]Mehren.

Table 38. Heterotopic Ossification Classification System

Assessment	Definition
0 - Class 0	No evidence of osteophyte formation or heterotopic ossification.
1 - Class I	HO is detectable in the front or sides or the vertebral body, or as islands of bone in the adjacent soft tissue, but is not in the intervertebral disc space. Bone is not present between the planes formed by the two vertebral endplates.
2 - Class II	HO is growing into the disc space. Bone is present between the planes formed by the two adjacent endplates but is not significantly blocking or articulating between adjacent vertebral endplates or osteophytes.
3 - Class III	The range of motion of the vertebral endplates is blocked by the formation of HO and/or postoperative osteophytes on flexion-extension radiographs, but some movement of the prosthesis still remains.
4 - Class IV (Bridging Bone)	HO is causing bony ankylosis. An apparent continuous connection of bridging bone exists between the adjacent vertebral endplates with little or no motion occurring across the treated segment.
5 - Indeterminate	A reliable determination cannot be made from the available imaging due to technical factors, sub-optimal image quality, obscured anatomy, obstructed view due to parallax effects or other imaging artifacts. The cause will be documented.
6 - Unable to Assess	The relevant images are missing or unavailable for review, or the relevant anatomy is not visible in the field of view.

[5] McAfee PC, et al. Classification of heterotopic ossification (HO) in artificial disc replacement. *J Spinal Disorders & Techniques* 2003; 16(4):384-389.

[6] Mehren C, Suchomel P, Grochulla F, Barsa P, Sourkova P, Hradil J, Korge A, Mayer H. Heterotopic Ossification in Total Cervical Artificial Disc Replacement. Spine 31(24):2802-2806, 2006.

Radiographs were assessed to determine the HO grade (**Table 39**) as well as to determine the number of patients with stable or progressing HO (progressing by at least one grade) from visit to visit. Grade 0, I, or II HO was defined as not being clinically-relevant while grade III or IV HO was defined as clinically relevant. The majority of Mobi-C® subjects (randomized and non-randomized) were assessed as having HO defined as not being clinically relevant (Grade 0, I, or II). The HO grade was unchanged or changed by 1 grade only through 36 months across both Mobi-C® groups in the majority of subjects. Note that 1 of 179 subjects (randomized) and 0 subjects (non-randomized) with determinate radiographs at both 12 and 36 months experienced an increase in HO of two grades and no subjects experienced an increase in more than two grades. At 36 months 12 Mobi-C® randomized subjects and 0 Mobi-C® non-randomized subject were assessed as having Grade IV HO.

Table 39a. Heterotopic Ossification for All Mobi-C® Subjects by Visit – Superior Level

Time Period/ Grade	Non-Randomized Mobi-C®	Randomized Mobi-C®	ALL Mobi-C®
12 months	N=8	N=213	N=221
Grade 0	2 (25.0%)	34 (15.7%)	36 (16.3%)
Grade I	0	22 (10.2%)	22 (10.0%)
Grade II	6 (75.0%)	153 (70.8%)	159 (71.9%)
Grade III	0	2 (0.9%)	2 (0.9%)
Grade IV	0	1 (0.6%)	1 (0.5%)
Indeterminate	0	1 (0.5%)	1 (0.5%)
24 months	N=7	N=218	N=225
Grade 0	2 (28.6%)	21 (9.6%)	23 (10.2%)
Grade I	0	15 (6.9%)	15 (6.7%)
Grade II	5 (71.4%)	156 (71.6%)	161 (71.6%)
Grade III	0	17 (7.8%)	17 (7.6%)
Grade IV	0	8 (3.7%)	8 (3.6%)
Indeterminate	0	1 (0.5%)	1 (0.4%)
Stable*	6 (100.0%)	165 (79.0%)	171 (79.5%)
Worsening**	0	44 (21.1%)	44 (20.5%)
36 months	N=6	N=197	N=203
Grade 0	0	12 (6.1%)	12 (5.9%)
Grade I	0	7 (3.6%)	7 (3.4%)
Grade II	4 (66.7%)	146 (74.1%)	150 (73.9%)
Grade III	2 (33.3%)	19 (9.6%)	21 (10.3%)
Grade IV	0	12 (6.1%)	12 (5.9%)
Indeterminate	0	1 (0.5%)	1 (0.5%)
Stable*	2 (50.0%)	169 (87.6%)	171 (86.8%)
Worsening**	2 (50%)	24 (12.44%)	26 (13.2%)

*Stable = No change in grade from previous visit.

**Worsening = Increase in grade from previous visit.

Table 39b. Heterotopic Ossification for All Mobi-C® Subjects by Visit – Inferior Level

Time Period/ Grade	Non-Randomized Mobi-C®	Randomized Mobi-C®	ALL Mobi-C®
12 months	N=8	N=216	N=224
Grade 0	2 (25.0%)	35 (16.2%)	37 (16.5%)
Grade I	0	28 (13.0%)	28 (12.5%)
Grade II	6 (75.0%)	139 (64.4%)	145 (64.7%)
Grade III	0	3 (1.4%)	3 (1.3%)
Grade IV	0	2 (0.9%)	2 (0.9%)
Indeterminate	0	9 (4.2%)	9 (4.0%)
24 months	N=7	N=218	N=225
Grade 0	1 (14.3%)	19 (8.7%)	20 (8.9%)
Grade I	0	7 (3.2%)	7 (3.1%)
Grade II	5 (71.4%)	157 (72.0%)	162 (72.0%)
Grade III	1 (14.3%)	16 (7.3%)	17 (7.6%)
Grade IV	0	6 (2.8%)	6 (2.7%)
Indeterminate	0	13 (6.0%)	13 (5.8%)
Stable*	5 (83.3%)	139 (70.6%)	144 (70.9%)
Worsening**	1 (16.7%)	58 (29.4%)	59 (29.1%)
36 months	N=6	N=197	N=203
Grade 0	0	11 (5.6%)	11 (5.4%)
Grade I	0	6 (3.1%)	6 (3.0%)
Grade II	5 (83.3%)	135 (68.5%)	140 (69.0%)
Grade III	1 (16.7%)	22 (11.2%)	23 (11.3%)
Grade IV	0	9 (4.6%)	9 (4.4%)
Indeterminate	0	14 (7.11%)	14 (6.9%)
Stable*	4 (100.0%)	156 (87.6%)	160 (87.9%)
Worsening**	0	22 (12.4%)	22 (12.1%)

*Stable = No change in grade from previous visit.
**Worsening = Increase in grade from previous visit.

Demographic and baseline characteristics and clinical outcomes were evaluated for potential correlation with the presence of HO. The only statistically significant correlation observed between demographic and baseline characteristics and the presence of HO was male gender. There was no correlation found between presence of HO and clinical outcomes, including NDI, VAS neck and VAS arm pain. Although use of NSAIDs was not part of the post-operative regimen, 25.8% of randomized Mobi-C® subjects reported use of NSAIDS between discharge to week 6 and 23.1% between week 6 and month 3. Based on independent assessment of HO, there was a small negative correlation between post-operative NSAID use and HO at month 24 that approaches but does not reach significance.

HO will be studied further as part of a seven year Postapproval Study (PAS) and ten year Enhanced Surveillance Postmarket Study that will be conducted by the applicant.

Adjacent Segment Degeneration

Adjacent segment degeneration following Mobi-C® and ACDF was assessed at the spinal segment immediately above and below the treated levels based on analysis of radiographs by an independent core lab following the study protocol. Adjacent segment degeneration was determined by assessment of disc space degeneration using a five point scale ([7]Kellgren-Lawrence classification). Facet degeneration was not considered in the assessment of adjacent segment degeneration post-surgery as subjects with evidence of severe facet joint disease or degeneration were excluded from the study. Data is reported as stable ((improvement or no change) and progressing (negative change from prior visit).

At the **above treated level**, the number of subjects reporting no negative changes from baseline in adjacent segment deterioration at the 24 Month visit was higher for the Mobi-C® randomized group (86.9%) than for the ACDF group (66.7%) (**Table 40**).

At the **below treated level**, the number of subjects reporting no negative changes from baseline in adjacent segment deterioration at the 24 Month visit was higher for the Mobi-C® randomized group (97.1%) than the ACDF group (81.9%) (**Table 41**).

Table 40. Adjacent Segment Degeneration - Above Level- All Mobi-C® Subjects by Visit

Time Period/ Grade	Non-Randomized Mobi-C®	Randomized Mobi-C®	All Mobi-C®	ACDF
12 months	N=8	N=214	N=222	N=91
Grade 0	6 (75.0%)	146 (68.2%)	152 (68.5%)	53 (58.2%)
Grade I	2 (25.0%)	39 (18.2%)	41 (18.5%)	19 (20.9%)
Grade II	0	17 (7.9%)	17 (7.7%)	14 (15.4%)
Grade III	0	8 (3.7%)	8 (3.6%)	4 (4.4%)
Grade IV	0	4 (1.9%)	4 (1.8%)	1 (1.1%)
Indeterminate	0	0	0	0
24 months	N=8	N=216	N=224	N=87
Grade 0	6 (75.0%)	135 (62.5%)	141 (62.9%)	40 (46.0%)
Grade I	2 (25.0%)	43 (19.9%)	45 (20.1%)	21 (24.1%)
Grade II	0	23 (10.6%)	23 (10.3%)	15 (17.2%)
Grade III	0	8 (3.7%)	8 (3.6%)	7 (8.0%)
Grade IV	0	6 (2.8%)	6 (2.7%)	4 (4.6%)
Indeterminate	0	1 (0.5%)	1 (0.4%)	0
Stable	7 (100.0%)	185 (86.9%)	192 (87.3%)	56 (66.7%)
Progressing	0	28 (13.2%)	28 (12.7%)	28 (33.3%)
36 months	N=6	N=194	N=200	N=75
Grade 0	3 (50.0%)	110 (56.7%)	113 (56.5%)	22 (29.3%)
Grade I	3 (50.0%)	35 (18.0%)	38 (19.0%)	13 (17.3%)
Grade II	0	31 (16.0%)	31 (15.5%)	27 (36.0%)
Grade III	0	13 (6.7%)	13 (6.5%)	9 (12.0%)
Grade IV	0	4 (2.1%)	4 (2.0%)	3 (4.0%)
Indeterminate	0	1 (0.5%)	1 (0.5%)	1 (1.3%)
Stable	4 (80.0%)	140 (73.3%)	144 (73.5%)	29 (40.8%)
Progressing	1 (20.0)%)	51 (26.7%)	52 (26.5%)	42 (59.2%)

Kellgren-Lawrence Scale - Absence of degeneration in the disc [0]; Minimal anterior osteophytosis [1]; Definite anterior osteophytosis with possible narrowing of the disc space and some sclerosis of the vertebral endplates [2]; Moderate narrowing of the disc space with definite sclerosis of the vertebral endplates and osteophytosis [3]; Severe narrowing of the disc space with sclerosis of the vertebral endplates and multiple large osteophytes [4] Kellgren J, Lawrence J. Osteo-arthrosis and disk degeneration in an urban population. British Medical Journal 1958;17:388.

Table 41. Adjacent Segment Degeneration - Below Level- for All Mobi-C® Subjects by Visit

Time Period/ Grade	Non-Randomized Mobi-C®	Randomized Mobi-C®	All Mobi-C®	ACDF
12 months	N=8	N=214	N=222	N=91
Grade 0	5 (62.5%)	192 (89.7%)	197 (88.7%)	72 (79.1%)
Grade I	1 (12.5%)	11 (5.1%)	12 (5.4%)	11 (12.1%)
Grade II	2 (25.0%)	4 (1.9%)	6 (2.7%)	5 (5.5%)
Grade III	0	2 (0.9%)	2 (0.9%)	2 (2.2%)
Grade IV	0	1 (0.5%)	1 (0.5%)	1 (1.1%)
Indeterminate	0	4 (1.9%)	4 (1.8%)	0
24 months	N=8	N=216	N=224	N=87
Grade 0	5 (62.5%)	190 (88.0%)	195 (87.1%)	65 (74.7%)
Grade I	1 (12.5%)	12 (5.6%)	13 (5.8%)	8 (9.2%)
Grade II	1 (12.5%)	3 (1.4%)	4 (1.8%)	7 (8.0%)
Grade III	1 (12.5%)	3 (1.4%)	4 (1.8%)	5 (5.7%)
Grade IV	0	0	0	1 (1.1%)
Indeterminate	0	8 (3.7%)	8 (3.6%)	1 (1.1%)
Stable	6 (85.7%)	198 (97.1%)	204 (96.7%)	68 (81.9%)
Progressing	1 (14.3%)	6 (2.9%)	7 (3.3%)	15 (18.1%)
36 months	N=6	N=194	N=200	N=75
Grade 0	2 (33.3%)	131 (67.5%)	133 (66.5%)	34 (45.3%)
Grade I	0	18 (9.3%)	18 (9.0%)	7 (9.3%)
Grade II	1 (16.7%)	10 (5.2%)	11 (5.5%)	13 (17.3%)
Grade III	2 (33.3%)	1 (0.5%)	3 (1.5%)	6 (8.0%)
Grade IV	0	1 (0.5%)	1 (0.5%)	5 (6.7%)
Indeterminate	1 (16.7%)	33 (17.0%)	34 (17.0%)	10 (13.3%)
Stable	1 (25.0%)	134 (84.8%)	135 (83.3%)	33 (53.2%)
Progressing	3 (75.0%)	24 (15.2%)	27 (16.7%)	29 (46.8%)

Kellgren-Lawrence Scale - Absence of degeneration in the disc [0]; Minimal anterior osteophytosis [1]; Definite anterior osteophytosis with possible narrowing of the disc space and some sclerosis of the vertebral endplates [2]; Moderate narrowing of the disc space with definite sclerosis of the vertebral endplates and osteophytosis [3]; Severe narrowing of the disc space with sclerosis of the vertebral endplates and multiple large osteophytes [4] Kellgren J, Lawrence J. Osteo-arthrosis and disk degeneration in an urban population. British Medical Journal 1958;17:388.

Pain Medication Use

Pain medication use at baseline preoperative and 24 months postoperative is reported for each group in **Table 42**. The rate of pain medication use was similar for all groups at each time point.

Table 42. Pain Medication Use at Baseline Preoperative and 24 month Postoperative

Procedure	Non-Randomized Mobi-C® (N=9)	Randomized Mobi-C® (N=225)	Randomized ACDF (N=105)
Baseline Preoperative			
ACETIC ACID DERIVATIVES	0	10 (4.4%)	3 (2.9%)
ANILINE ANALGESICS	0	10 (4.4%)	5 (4.8%)
ANILINE ANALGESICS, SALICYLATE	0	3 (1.3%)	2 (1.9%)
ANTIEPILEPTIC	0	14 (6.2%)	12 (11.4%)
ANTISPASMODICS	5 (55.6%)	87 (38.7%)	37 (35.2%)
BARBITURATE	0	2 (0.9%)	1 (1.0%)
BENZODIAZEPINE	2 (22.2%)	33 (14.7%)	15 (14.3%)
COX, LOX INHIBITOR	0	0	0
COX-2 INHIBITOR	2 (22.2%)	9 (4.0%)	3 (2.9%)
ENOLIC ACID	0	4 (8.1%)	5 (4.8%)
OPIUM ALKALOID	2 (22.2%)	27 (12.0%)	7 (6.7%)
PROPIONIC ACID	2 (22.2%)	67 (29.8%)	39 (37.1%)
SALICYLATE	0	25 (11.1%)	11 (10.5%)
SEMI-SYNTHETIC OPIOID DERIVATIVE	5 (55.6%)	119 (52.9%)	60 (57.1%)
SYNTHETIC OPIOID	0	18 (8.0%)	18 (17.1%)
24 months Postoperative			
ACETIC ACID DERIVATIVES	0	10 (4.5%)	3 (3.0%)
ANILINE ANALGESICS	1 (12.5%)	12 (5.4%)	9 (9.1%)
ANILINE ANALGESICS, SALICYLATE	0	4 (1.8%)	2 (2.0%)
ANTIEPILEPTIC	1 (12.5%)	21 (9.5%)	15 (15.2%)
ANTISPASMODICS	3 (37.5%)	68 (30.8%)	31 (31.3%)
BARBITURATE	0	3 (1.4%)	1 (1.0%)
BENZODIAZEPINE	1 (12.5%)	30 (13.6%)	16 (16.2%)
COX, LOX INHIBITOR	0	0	0
COX-2 INHIBITOR	1 (12.5%)	15 (6.8%)	8 (8.1%)
ENOLIC ACID	0	7 (3.2%)	4 (4.0%)
OPIUM ALKALOID	0	40 (18.1%)	12 (12.1%)
PROPIONIC ACID	4 (50.0%)	69 (31.2%)	26 (26.3%)
SALICYLATE	0	32 (14.5%)	9 (9.1%)
SEMI-SYNTHETIC OPIOID DERIVATIVE	3 (37.5%)	68 (30.8%)	39 (39.4%)
SYNTHETIC OPIOID	0	14 (6.3%)	8 (8.1%)

3. Subgroup Analyses

The following preoperative characteristics were evaluated for potential association with outcomes: age, race and gender. The effect of these characteristics on the primary endpoint success rate and its NDI success component by subgroup were conducted, and the results for the 24 Month Visit are summarized in **Table 43**. The Mobi-C® primary endpoint success rates were higher than the control group in every age, race, and gender subgroup.

Table 43. Primary Effectiveness Subgroup Analyses at Month 24 - Primary Analysis Population

Subgroup	Success in Randomized Mobi-C® (N=225)	Success in Randomized ACDF (N=105)	Difference for pm-pc
Age			
<40 years	35/54 (0.6481)	6/20 (0.3000)	0.3481
40 - <50 years	72/101 (0.7129)	17/46 (0.3696)	0.3433
>=50 years	47/66 (0.7121)	14/33 (0.4242)	0.2879
Race			
Caucasian	147/208 (0.7067)	35/93 (0.3763)	0.3304
Black or African American	2/5 (0.4000)	1/4 (0.2500)	0.1500
Other***	5/8 (0.6250)	1/2 (0.5000)	0.1250
Gender			
Male	69/100 (0.6273)	20/41 (0.4878)	0.1395
Female	85/111 (0.7658)	17/58 (0.2931)	0.4727

*Using Farrington-Manning test to compare between the treatments.
**Fisher Exact test to compare the frequencies between the treatments.
***Other consists of the following classifications: American Indian or Alaska Native, Asian, Native Hawaiian/other Pacific Islander, or Other.
Note: Percentages are based on the number of available observations.

Financial Disclosure Analysis:

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 26 principal investigators of which none were full-time or part-time employees of the sponsor and 11 principal investigators had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: 0 investigators
- Significant payment of other sorts: 6 investigators

- Proprietary interest in the product tested held by the investigator: 3 investigators
- Significant equity interest held by investigator in sponsor of covered study: 8 investigators

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Statistical analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. The information provided does not raise any questions about the reliability of the data.

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

Data have been published regarding clinical experience with the Mobi-C® device in France, Italy, Korea, and a European postmarket study. This information is not a factor in the decision regarding this applicant's device.

XII. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

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

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

The valid scientific evidence presented in the preceding sections provides reasonable assurance that the Mobi-C® Cervical Disc Prosthesis is a safe and effective disc replacement for C3-C4 to C6-C7 in skeletally mature patients for reconstruction of the disc at two contiguous levels from C3-C7 following discectomy for treatment of intractable radiculopathy (arm pain and/or a neurological deficit) with or without neck pain, or myelopathy due to abnormality localized to the level of the disc space and at least one of the following conditions confirmed by radiographic imaging (CT, MRI, X-rays): herniated nucleus pulposus, spondylosis (defined by the presence of osteophytes), and/or visible loss of disc height compared to adjacent levels.

A. Effectiveness Conclusions

In the clinical study conducted to support PMA approval, 356 patients were enrolled and a total of 339 subjects completed study surgery, all had reached the 24 month post-operative visit, and 297 (87.6%) had data available for analysis at the completion of the study. Statistical analysis demonstrated that the results from all sites were poolable to determine safety and

effectiveness. Analysis of patient demographic and baseline data showed no statistically significant differences between the treatment groups. Mean surgery time was 21.48 min longer for the randomized investigational Mobi-C® group than for the control ACDF group.

Overall success was defined in the study protocol as improvement in pain and disability using the Neck Disability Index, freedom from subsequent surgery at the index level, and no major complications defined as: 1) radiologic failure, 2) neurologic deterioration, and 3) CEC adjudicated adverse event major complications. The composite success rate for the protocol-specified primary endpoint for Mobi-C® subjects was 69.7% at the 24-month visit, 32.3% higher than the 37.4% success rate observed in the ACDF subjects, and demonstrated non-inferiority of Mobi-C® compared to control. An alternative primary endpoint analysis was prospectively planned to assess subject success when major complications due to radiographic assessment were removed from the analysis. Additional analyses requested by FDA included modified criteria for NDI success and neurological deterioration. The results of overall success, using both sets of success criteria, demonstrate non-inferiority for the Mobi-C® artificial disc compared to the control ACDF group. In addition, the pre-planned statistical analysis plan successfully demonstrated superiority of the Mobi-C® compared to the control group for the primary endpoint analysis.

To assess the impact of patients with unknown outcomes at 24 months or other potential biases, various sensitivity analyses were conducted. The results of all sensitivity analyses indicate that the Mobi-C® device is non-inferior to ACDF. In addition, all components of overall success of the Mobi-C® group are non-inferior to the control group, while subsequent surgery and adverse events rates (including treatment-emergent adverse events, related adverse events, serious adverse events, related serious adverse events) are lower for the Mobi-C® device compared to the control group rates.

Range of motion success for the Mobi-C® group was defined according to study protocol as ≥2° of flexion-extension combined superior and inferior index level ROM and absence of bridging bone. At 24 months, 211/214 (98.6%) of randomized Mobi-C® patients (Primary Analysis population) met range of motion success criteria. Of the 211/214 (98.6%) Mobi-C® patients who were considered range of motion successes at 24 months, 205/214 (95.8%) achieved ≥4° of flexion-extension combined superior and inferior index level ROM.

In conclusion, the study data indicate that, at 24 months postoperatively, the Mobi-C® device implanted at two contiguous levels from C3-C7 is at least as effective as the control treatment (ACDF), for the patient population and indications studied in this investigation, in terms of the overall success according to the protocol-specified composite primary endpoint and alternative primary endpoint definitions analyzed. The study data further conclude that the Mobi-C® device is statistically superior to the control treatment in terms of overall success based on the protocol-specified definition and the FDA modified definitions analyzed.

B. <u>Safety Conclusions</u>

The risks of the Mobi-C® Cervical Disc Prosthesis are based on nonclinical laboratory studies as well as data collected in the clinical study conducted to support PMA approval as described above.

Preclinical testing performed on the device demonstrated that the Mobi-C® Cervical Disc Prosthesis should withstand the expected physiologic loads in the cervical spine.

In the clinical study conducted to support PMA approval, the investigational Mobi-C® device implanted at two contiguous levels from C3-C7 was found to have a reasonable assurance of safety and to be at least as safe as the control treatment. Specifically, the rate of investigational patients having at least one adverse event (Mobi-C® randomized group: 89.3%; ACDF control group: 95.2%), an event classified by the Clinical Events Committee (CEC) or investigator as a serious adverse event (randomized Mobi-C® group: 24.4%; ACDF control group: 32.4%), or an event classified by the CEC or investigator as a serious and device-related adverse event (Mobi-C® randomized group: 3.1% as rated by investigator; 3.6% as rated by CEC; ACDF control group: 12.4% as rated by investigator; 14.3% as rated by CEC) was numerically lower than the ACDF control group rate. The rate of secondary surgery through the most current data lock for Mobi-C® group was lower than the control group with 9 subjects (3.8%) requiring subsequent surgical interventions at the treated level compared to 15 (14.3%) control subjects. The neurological success rate for the investigational group was statistically non-inferior to that of the control group. There were no Mobi-C® device failures.

In conclusion, the safety profile of the Mobi-C® device implanted at two contiguous levels from C3-C7 demonstrates that the device has a reasonable assurance of safety and is at least as safe as the control in regards to adverse event rates and neurologic status, and in terms of the need for secondary surgery.

C. Benefit-Risk Conclusions

The probable benefits of the Mobi-C® Cervical Disc Prosthesis are based on data collected in the clinical study conducted to support PMA approval as described above.

The clinical study demonstrated several benefits of the Mobi-C® Cervical Disc Prosthesis implanted at two contiguous levels from C3-C7 over the 24 month time period studied.

▪The benefit of the Mobi-C® Cervical Disc Prosthesis in terms of clinically meaningful improvement in function (as measured by an improvement in NDI of at least 15/50 points in subjects with a baseline Neck Disability Index (NDI) score of ≥ 30/50 points, or a 50% improvement in subjects with a baseline NDI score of < 30/50 points) at 24 months postoperatively was comparable to the standard of care, ACDF, in that the majority of patients in both treatment groups in the clinical study experienced this benefit (86.4% of randomized Mobi-C® patients and 67.7% of ACDF patients). Additionally, the pre-planned statistical analysis

methods indicate that the Mobi-C® device implanted at two contiguous levels is statistically superior to the control group in terms of overall success.

▪The benefit of the Mobi-C® Cervical Disc Prosthesis in terms of maintenance or improvement in neurologic status (as measured during the neurological examination done by the investigator) at 24 months postoperatively was similar for the Mobi-C® Cervical Disc Prosthesis compared to the standard of care, ACDF, in that the majority of patients in both treatment groups in the clinical study experienced this benefit (94.4% of randomized Mobi-C® patients and 93.3% of ACDF patients per protocol definition of neurologic status; 89.4% of randomized Mobi-C® patients and 87.6% of ACDF patients per FDA definition of neurologic status).

▪ In terms of improvement in neck pain (as measured by a 20mm improvement in pain on a Visual Analog Scale as compared to baseline), at 24 months postoperatively, the benefit of the Mobi-C® was at least comparable to the standard of care, ACDF (81.0% of randomized Mobi-C® patients and 73.7% of ACDF patients with neck pain improvement at 24 months). Similar percentages of patients in both treatment groups in the clinical study experienced the benefit of improvement in arm pain (52.5% of randomized Mobi-C® patients and 44.4% of ACDF patients with right arm pain improvement at 24 months; and 58.8% of randomized Mobi-C® patients and 55.6% of ACDF patients with left arm pain improvement at 24 months).

In addition, although the sponsor did not formally collect data regarding patient tolerance for risk and patient perception of benefit, the patients' perception of their benefit and risk was indirectly measured through a questionnaire. At 24 months following the index procedure, a higher number of Mobi- C® subjects compared to ACDF control subjects reported being "very satisfied" with the surgical treatment received (randomized Mobi-C®, 85.6%, ACDF, 78.2%). At 24 months following the index procedure, a higher number of Mobi-C® subjects compared to ACDF control subjects responded "definitely yes" when asked whether they would recommend the same treatment to a friend with the same condition (randomized Mobi-C®, 85.6%, ACDF, 72.4%).

In addition, there were fewer secondary surgeries at the index level in the Mobi-C® group compared to the ACDF control group. With respect to subsequent surgical interventions, in total, only 7 (3.1%) randomized Mobi-C® subjects and 12 (11.4%) control subjects reported subsequent surgical interventions qualifying as study failures (i.e. at the index level) through 24 months, with no non-randomized Mobi-C® subjects reporting subsequent surgical interventions qualifying as study failures.

Several additional factors were considered in determining the probable benefits and risks for the Mobi-C® device. Limitations of the clinical study design, including the inability to mask patients to their treatment assignment, reliance on subjective endpoints, concerns about potential placebo effect, and subjectivity in adverse event classification, were considered. In

addition, the impact of missing data and the robustness of the sensitivity analyses provided to address the missing data as well as the generalizability of the study results were also considered. Finally, alternative available treatments and risk mitigation strategies were considered as was the fact that the only available indicator of patient tolerance for risk and perspective on benefit was patient satisfaction data.

Note that other theoretical benefits of total disc replacement devices, such as the Mobi-C®, include preservation of range of motion and decreased risk of adjacent segment degeneration; however, the clinical study conducted to support PMA approval of the Mobi-C® was not specifically designed or powered to study these potential benefits as primary endpoints, and any potential benefit in terms of clinically significant reduction in adjacent level degeneration would not necessarily be expected in the two year time period of the clinical study.

In conclusion, given the available information above, the data support that for reconstruction of the disc at two contiguous levels from C3-C7 following discectomy for intractable radiculopathy (arm pain and/or a neurological deficit) with or without neck pain, or myelopathy due to an abnormality localized to the level of the disc space and specific radiographic findings as outlined above in the Indications for Use, the probable benefits of the Mobi-C® Cervical Disc Prosthesis outweigh the probable risks through two years follow-up.

D. Overall Conclusions

The preclinical and clinical data in this application support the reasonable assurance of safety and effectiveness of the Mobi-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 Mobi-C® device in terms of improvement in pain and disability, and the potential for motion preservation, outweigh the risks, both in terms of the risks associated with the Mobi-C® device and surgical procedure when used in the indicated population in accordance with the directions for use, and as compared to the ACDF control treatment in the same indicated population. The statistical superiority of the primary effectiveness outcomes at 24 months further support the overall conclusion.

XIV. CDRH DECISION

CDRH issued an approval order on August 23, 2013. The final conditions of approval cited in the approval order are described below.

The sponsor has agreed to provide the following data as part of the annual report:

The sponsor must attempt to retrieve all explanted Mobi-C® devices (including but not limited to those retrieved from patients in the PAS and ESS) for analysis. All retrievals will be analyzed and reported per the agreed Explant Analysis protocol.

In addition to the Annual Report requirements, the sponsor must provide the following data in post-approval study reports (PAS).

1. *Extended Follow-up of Premarket Cohort:* The sponsor must perform a 7-year post-approval study (PAS) to evaluate the longer term safety and effectiveness of the Mobi-C® Cervical Disc Prosthesis as compared to ACDF by following the 330 subjects from the pivotal investigational device exemption (IDE) study (225 Mobi-C® subjects, and 105 ACDF subjects) annually through 7 years. At each annual (±4 month) visit, the sponsor will collect the following data: Neck Disability Index, neck and right/left arm pain Visual Analog Scale (VAS), health status survey (SF-12), patient satisfaction, neurological status, radiographic information, medication usage and postoperative treatment for pain management, work status, and all adverse events regardless of cause. Radiographic information collected will include: range of motion on flexion/extension films (angulation and translation as well as the correlation of range of motion with outcomes), disc height, radiolucency, device displacement, subsidence and migration, spinal fusion (control arm only), and heterotopic ossification (including grade, stability over time, and correlation with patient characteristics and postoperative outcomes). The sponsor will also collect radiographic and clinical data on adjacent level degeneration/disease including both surgical and non-surgical adjacent level treatments as well as adjacent level diagnoses, adjacent level range of motion and radiographic changes at adjacent levels.

The primary objective of the study is to evaluate the overall success rate, using Overall Success defined as:

- Pain/Disability Improvement of at least 25% in the Neck Disability Index (NDI) at 5 years and 7 years compared with the score at baseline;
- No device failures (at the index level) requiring revision, re-operation, removal or supplemental fixation;
- Absence of major complications defined as 1) neurological deterioration, 2) radiologic failure (bridging bone and lack of motion at the index level for Mobi-C® subjects; failure of fusion for ACDF subjects), and 3) adverse events determined to be major complications and related to the study device (as determined by the independent CEC oversight committee).
- Fusion in ACDF control subjects as defined as evidence of bridging trabecular bone and < 2° total angular motion (from flexion to extension) and < 50% radiolucency along the graft/endplate interface and for Mobi-C® subjects radiologic failure as defined as evidence of continuous bridging bone and < 2° total angular motion (from flexion to extension).

The sponsor also has agreed to conduct an additional analysis evaluating Overall Success Definition 2, defined as follows:

- Pain/Disability Improvement of at least 15 points in the Neck Disability Index (NDI) at 5 years and 7 years compared with the score at baseline;

- No secondary surgery at the index level, including revision, removal, reoperation and supplemental fixation

- No potentially device-related adverse events
- Maintenance or improvement in all components of neurologic status
- No Mobi-C® intraoperative changes in treatment

Success rates between the randomized investigational and control groups will be compared and assessed for non-inferiority based on a ten percent non-inferiority margin for both overall success analyses. Patients who were non-recoverable non-responders prior to 24 months will carry forward as failures for each subsequent annual visit. Several sensitivity analyses will also be done.

FDA will expect at least 85% follow-up at the 7-year time point to provide sufficient data to evaluate safety and effectiveness.

2. Enhanced Surveillance System: The sponsor must perform a 10-year Enhanced Surveillance Study (ESS) of the Mobi-C® Cervical Disc Prosthesis to fully characterize adverse events when the device is used in the intended patient population under general conditions of use in the United States and in the rest of the world. The sponsor will collect, analyze, and submit all adverse event data including subsequent surgeries, heterotopic ossification, device malfunction, device removal, or other serious device-related complications.. Information will be actively collected from annual surgeon surveys and on the company website. Information will also be collected passively through complaints and MDRs, explant analysis, and literature reviews.

All of the surgeons who have been trained on the use of Mobi-C® Cervical Disc Prosthesis the U.S. will be surveyed annually and the number of surveys issued and received will be reported. If a survey response includes any information related to an adverse event, the sponsor will collect additional data as specifically outlined in the ESS protocol and report that data to FDA.

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

XV. APPROVAL SPECIFICATIONS

Directions for Use: See device labeling

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

Post-approval Requirements and Restrictions: See approval order.

XVI. REFERENCES

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