

## SUMMARY OF SAFETY AND EFFECTIVENESS DATA

### I. GENERAL INFORMATION

Device Generic Name:	Total Hip System, Ceramic Articulation
Device Trade Name:	<i>Trilogy AB</i> <sup>®</sup> Acetabular System
Applicant's Name:	Zimmer, Inc. P.O. Box 708 Warsaw, IN 46581-0708
Premarket Approval (PMA) Number:	P040048
Date of Panel Recommendation:	None
Date of Notice of Approval to Applicant:	June 28, 2006

The approval of the *Trilogy AB* Acetabular System is being granted in part due to a licensing agreement with CeramTec, who owns the rights to the PMA for the TRANSCEND Ceramic Articulation System (P010001) and also distributes the ceramic components used in both the *Trilogy AB* Acetabular System and the TRANSCEND System. The *Trilogy AB* Acetabular System uses the same ceramic heads and ceramic liners as the TRANSCEND System while employing Zimmer's own acetabular shells and femoral stems. A component comparison along with preclinical test results were used to demonstrate that the Zimmer *Trilogy AB* Acetabular System performs similarly to the TRANSCEND System. Therefore, the clinical data referenced from the PMA for the TRANSCEND System has been used to predict the clinical outcome of the *Trilogy AB* Acetabular System.

### II. INDICATIONS FOR USE

The *Trilogy AB* Acetabular System is indicated for either cemented or noncemented use in skeletally mature individuals undergoing primary surgery for rehabilitating hips damaged as a result of noninflammatory degenerative joint disease (NIDJD) such as osteoarthritis, avascular necrosis, congenital hip dysplasia, and traumatic arthritis.

### III. CONTRAINDICATIONS

- Skeletal immaturity
- Infection
- Any nerve or muscle disease that may have a negative effect on gait or weight bearing
- Loss of abductor musculature in the affected limb
- Poor bone stock
- Poor skin coverage around the hip joint
- Rapid disease progression as obvious by joint destruction or bone absorption seen on x-ray

### IV. WARNINGS, PRECAUTIONS

Please reference the *Trilogy AB* Acetabular System package insert to find the Warnings and Precautions.

### V. DEVICE DESCRIPTION

The *Trilogy AB* Acetabular System is a ceramic on ceramic acetabular bearing couple. The system consists of aluminum oxide ( $Al_2O_3$ ) ceramic femoral heads and inserts (or liners) manufactured by CeramTec AG. The ceramic components are to be used with Zimmer's commercially available 12/14 taper femoral stems, acetabular shells and bone screws.

#### Acetabular Inserts

The ceramic inserts are available in 28mm and 32mm inside diameter (ID) sizes. The 28mm inserts fit the acetabular shells with outer diameters (OD) ranging from 48-70mm and the 32mm inserts fit the acetabular shells ranging from 56-70mm OD.

#### Acetabular Shells

The shells are made from *Titanium*® Ti-6Al-4V Alloy with a titanium fiber metal mesh coating. The fiber metal shells are also available with *Calcicoat*® Ceramic Coating (HA/TCP). The acetabular shells are available in 12 sizes ranging from 48 to 70mm in 2mm increments. The shell is available in a multi-hole or a cluster-hole design to provide additional fixation.

#### Acetabular Screws

Titanium alloy screws in 4.5 and 6.5 mm diameters with lengths from 15 to 60mm in 5mm increments are available for supplemental fixation.

#### Femoral Heads

The 28mm and 32mm alumina ceramic heads are available with either -3.5mm, 0mmr +3.5mm neck lengths.

### Femoral Stems

The *Trilogy AB* femoral heads can be used with the *VerSys*® Hip System Fiber Metal MidCoat Stems or the *VerSys Heritage*™ Femoral Stems. Both stem families have a 12/14 neck taper to mate with the corresponding alumina ceramic femoral heads of the *Trilogy AB* System.

*VerSys*® Hip System Fiber Metal MidCoat Stems are manufactured from *Tivanium*® Ti-6Al-4V Alloy and feature a proximal porous surface of commercially pure titanium fiber metal. The stems are also available with *Calcicoat*® Ceramic Coating (HA/TCP) and are indicated for cementless use.

*VerSys Heritage*™ Femoral Stems are manufactured from *Zimaloy*® Cobalt-Chromium-Molybdenum Alloy and are indicated for cemented use.

## **VI. ALTERNATIVE PRACTICES AND PROCEDURES**

Depending on individual circumstances, alternative procedures may include the use of other commercially available total hip replacement implants, non-surgical treatment such as reduced activity and/or pain medication, or other surgical treatments that do not involve the use of an implant, such as hip joint fusion. Other bearing surface alternatives used in total hip replacement include: ceramic on polyethylene, metal on metal, and metal on polyethylene bearing articulations.

## **VII. MARKETING HISTORY**

The *Trilogy AB* Acetabular System has been marketed internationally since 1999. The components have been sold in the European Union countries, Australia, Asia, New Zealand, Eastern Europe and Canada and the device has not been withdrawn from marketing for any reason related to safety or effectiveness.

## **VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH**

The *Trilogy AB* Acetabular System is similar to the previously approved TRANSCEND Ceramic Hip System (P010001). Zimmer references the clinical data from P010001, under a licensing agreement, as clinical support for the *Trilogy AB* Acetabular System. The clinical data are relevant because the ceramic femoral heads and acetabular inserts of the *Trilogy AB* Acetabular System have identical articulating surfaces to the ceramic femoral heads and acetabular inserts of the TRANSCEND Ceramic Hip System. A system comparison between the *Trilogy AB* Acetabular System and the TRANSCEND Ceramic Hip System was performed to demonstrate that the systems perform similarly enough on the bench that the clinical data referenced can be used to predict the clinical outcomes for the *Trilogy AB* Acetabular System.

Please refer to Table 3 in Section X (Summary of Clinical Investigations) for a tabulation of reported adverse events that occurred in the referenced study (P010001).

**Potential Adverse Events Associated with Any Total Hip Arthroplasty**

1. Excessive wear of the ceramic components secondary to damage of mating wear surfaces or debris particles;
2. Although rare, metal sensitivity reactions in patients following joint replacement have been reported;
3. Implantation of foreign material in tissues can result in histological reactions involving macrophages and fibroblasts;
4. Possible detachment of the porous coating, which could lead to increased debris particles;
5. Pain;
6. Femoral or acetabular perforation, or bone fracture while seating the device;
7. Damage to blood vessels resulting in hematoma;
8. Temporary or permanent nerve damage resulting in pain or numbness of the affected limb;
9. Undesirable shortening or lengthening of the limb;
10. Traumatic arthrosis of the hip from intraoperative positioning of the extremity;
11. Cardiovascular disorders including venous thrombosis, pulmonary embolism, or myocardial infarction;
12. Temporary or permanent neuropathies;
13. Delayed wound healing;
14. Infection;
15. Migration, loosening, subluxation, or dislocation of the prosthesis;
16. Periarticular calcification or ossification, with or without impediment to joint mobility;
17. Inadequate range of motion due to improper selection or positioning of components, by femoral impingement, and periarticular calcification; and
18. Death.

**Potential Adverse Effects Associated with the *Trilogy AB* Acetabular System**

1. Wear of the ceramic acetabular components has been reported following total hip replacement. Higher rates of wear may be initiated by particles of cement, metal, or other debris that can cause abrasion of the articulating surfaces. Higher rates of wear may shorten the useful life of the prosthesis, and lead to early revision surgery to replace the worn prosthetic components.
2. While rare, fatigue fracture of the prosthetic component can occur as a result of trauma, strenuous activity, improper alignment, or duration of service.
3. Component dissociation.
4. Breakage or chipping of the femoral head or acetabular insert.

## IX. SUMMARY OF PRECLINICAL STUDIES

The results of the preclinical testing listed below demonstrate that the Zimmer *Trilogy AB* Acetabular System performs similarly on the bench to the has been found to be similar on the bench to the CeramTec TRANSCEND Ceramic Hip System (P010001). The *Trilogy AB* Acetabular System uses the same ceramic femoral heads and acetabular inserts as the TRANSCEND system and uses Zimmer's own femoral stems and acetabular shells to comprise the system. The comparability of the *Trilogy AB* Acetabular System and the TRANSCEND System was demonstrated through a side-by-side component comparison and a comparison of preclinical test results.

CeramTec conducted preclinical tests of the material used to manufacture the alumina ceramic components, in addition to testing some of the actual components. The alumina ceramic material conforms to ASTM F603<sup>1</sup> and ISO 6474<sup>2</sup> and has been used successfully for many years as an orthopedic implant material. Zimmer did not perform any additional animal or preclinical testing relative to the biocompatibility, immunological, or toxicological aspects of the alumina ceramic, titanium or cobalt-chromium alloys used for the femoral stems, or commercially pure fiber metal bonded to the shell substrate. Zimmer conducted a series of mechanical tests to support the design of the *Trilogy AB* ceramic articulation. Listed hereafter is a brief description of those tests.

### **Ceramic Insert Testing:**

The purpose of this testing was to evaluate the performance of the *Trilogy AB* ceramic inserts in *Trilogy AB* Acetabular shells. Inserts of "worst-case" geometry (as defined below) were tested for torque strength, lever out force, burst strength, push-out strength, axial fatigue strength and post-fatigue burst and push-out strength. The femoral heads and inserts were tested for anatomic fatigue strength, wear and range of motion.

### **Insert Interface Torque**

In the *Trilogy AB* Acetabular System, the insert is intended to lock itself into the shell with a modest impact load. The worst case size could be the larger diameter shell sizes, which have more locking surface area, but less effective hoop stress. However, a smaller diameter shell would have less interface area, but more effective hoop stress. Therefore, three 37mm OD inserts were tested in 48mm shells and three 52mm OD inserts were tested in 70mm shells.

This test was performed with a repeatable 2 kN push in force to set the insert into the shell. The torsional force of the 37mm insert in the 48mm shell was 14.2Nm and the torsional force of the 52mm insert in the 70mm shell was 21.2 Nm.

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<sup>1</sup> ASTM F603 – "Standard Specification for High-Purity Dense Aluminum Oxide for Medical Application"

<sup>2</sup> ISO 6474 – "Implants for Surgery – Ceramic materials based on high purity alumina"

The acceptance criterion was defined as an average torsional force greater than 4Nm. This acceptance criterion was established based on the fact that the torque due to friction at the ball-liner interface is approximately 2.4Nm and the locking mechanism of the liner in the shell should exceed this by a factor of safety. The results of both sets of liners and shells exceeded the acceptance criterion.

#### Insert Lever Out

In this self-locking tapered insert system, impingement of the neck of the femoral stem on the internal edge of the ceramic insert could cause forces tending to push the insert out of the shell. In this test, the insert with the smallest interface diameter and, consequently, the smallest taper interface area was the worst case for testing, this is the 28mm ID, 37mm OD insert.

Three inserts were tested and the resulting lever out force was 79.9 Nm. This lever out force is comparable to the lever out force of other commercially available ceramic on ceramic systems.

#### Insert Burst

The inserts will be subjected to modest impact loads during (intraoperative) implantation and peak loads that occur with patient events such as stumbling or missing a step. These events will place higher loads on the insert that the system must be capable of resisting without failure.

The smallest size insert was selected as the worst case because it has the minimum thickness. Fifteen of the smallest inserts (28/37) were tested. Ten were tested in the smallest diameter shell that they would be used in, and five were tested in a slightly thicker shell to determine if shell stiffness could have an effect. In addition, five of the smallest 32/44 inserts were also tested as the worst case of the larger diameter components.

The FDA *Draft Guidance Document for the Preparation of Premarket Notifications for Ceramic Ball Hip Systems* (January 10, 1995) places a requirement of 46 kN average and no single failure less than 20 kN on ceramic femoral heads. The inserts are loaded by a ceramic head, therefore they should meet at least the same requirement as the ceramic head.

All of the samples met the 46kN ceramic burst strength requirement and none approached 20 kN.

#### Insert Push Out

The self locking tapered insert under physiological pressures could exert forces tending to disassociate the tapered insert from the shell. The resistance of the insert to push out from the shell is a measure of the self-locking capability of the system.

The selection of worst case is difficult because larger diameter shell sizes have more locking surface area, but less effective hoop stress. A smaller diameter shell would have less interface area, but more effective hoop stress. In addition, the presence and distribution of screw holes in the shell surface could possibly change the locking capability of the insert shell assembly. Six samples of 28mm and six samples of 32mm diameter alumina ceramic acetabular inserts were tested in a variety of multi-hole and cluster hole *Trilogy AB* shell sizes ranging from 48 to 70mm diameter.

A repeatable 2kN force was used to push the insert into the shell. The average push-out resistance was 0.83 kN, or 41% of the original force used to push the inserts into the shell. This push out strength is comparable to the push out strength of approved and marketed modular acetabular components.

#### Axial Insert Fatigue

Clinically the insert and shell acetabular system will transfer physiological loads between the leg and the upper torso. These loads are dynamic and repeatable in nature and could cause fatigue fractures in either the shell or the insert.

The factors affecting worst-case selection for axial insert fatigue testing are the same as for insert push out testing. Twenty-five inserts and shells of various sizes were tested to cover all possible cases.

The FDA *Draft Guidance Document for the Preparation of Premarket Notifications for Ceramic Ball Hip Systems* (January 10, 1995) has a fatigue test requirement of 14 kN for 10 million cycles for ceramic femoral heads. The ceramic inserts are loaded by a ceramic head; therefore the inserts must meet at least the same requirements as the ceramic head.

The test samples were fatigue tested at 30 Hz in air. One 48 mm shell test sample was removed from the test because of machine instability. All of the remaining 24 assemblies passed a minimum of 10 million cycles at 14 kN peak load.

#### Post Fatigue Burst

Since these systems are intended for long term clinical use, the measurement of the residual strength of the ceramic insert after fatigue testing is important. The burst test was repeated on samples after completion of fatigue testing to measure the residual strength.

The FDA *Draft Guidance Document for the Preparation of Premarket Notifications for Ceramic Ball Hip Systems* (January 10, 1995) has a post fatigue burst test requirement of no less than 20 kN for ceramic femoral heads. Since these inserts are loaded by a ceramic head they must meet at least the same requirement as the ceramic head.

All of the 24 samples from the fatigue test had a post-fatigue test burst strength significantly greater than 20 kN.

#### Post Fatigue Push Out

The self locking tapered insert under physiological pressures could exert forces tending to disassociate the tapered insert from the shell. These small forces have components that are not directly along the axis of symmetry of the insert. These off axis force components could loosen the self locking of the taper system and overcome the components of physiological force along the axis of the taper system. The axial fatigue test does not test any of these off axis forces consequently it does not challenge the self locking capability. As a result, a fatigue test with a more anatomical 45 degree orientation of the loading force to the axis of the insert was devised. The measure of the resistance of the insert to push out from the shell after the fatigue loading measures the retention of the self locking capability of the system.

Selection of a worst case was based on the results of the initial push out testing done without any fatigue preloading. Although not statistically significant, the 70 mm diameter shell had slightly lower push out resistance than smaller sizes. A 68 mm diameter shell was selected for this testing because it accommodates the largest ceramic insert, but has a slightly thinner shell. The smallest and largest of both the 28mm (n=16) and 32mm (n=9) inserts were tested in both the cluster hole and multi hole shell designs.

The inserts were preloaded in the shells at 2 kN. The assemblies were tested at peak loads of 7.6 kN, an internal anatomic fatigue performance load for 2 million cycles. Two-million cycles is considered sufficient for any loosening effects to appear. The average of 1.19 kN is above the push out values of the samples that were not fatigue preloaded.

#### Anatomic Fatigue Testing (Insert and Head)

In the axial fatigue test, the forces are transmitted directly along the axis of symmetry of the insert. In clinical use, loads are transferred through the insert system at a variety of angles depending on the patient's activities. These loads are usually far off the axis of symmetry of the insert. These off-axis loads create nonsymmetrical forces in the ceramic insert and consequently put the ceramic material in stress states different than the axial fatigue test. However, these forces are limited because they must be carried by the neck of the femoral prosthesis in bending.

The smallest insert sizes for the two articulating surface diameters were selected as worst case. Two of each size were loaded at 45 and 60 degrees to simulate different acetabular placements. To fulfill the worst case requirement for the ceramic heads, the longest offset head for each of the diameters was used for this test. The fatigue test used a peak fatigue load of 7.6 kN. All samples of both the heads and inserts had to pass 10 million cycles at that peak load without fracture. All of the samples met the performance requirement.

#### Wear Testing (Insert and Head)

The ceramic insert functions as part of a ceramic-on-ceramic articulation. Consequently, wear of both surfaces of the articulation is a concern. Zimmer performed a simulator wear test using AMTI Hip simulators. These simulators put the articulating surfaces in an anatomic orientation and apply anatomic loads and motions. The standard peak load used for wear testing was 3.2 kN. The lubricant was undiluted bovine serum. Six of both the 28mm and 32mm diameter systems were tested. The amount of wear on the head and the insert was measured and combined to determine the wear rate.

Although there is a requirement for wear testing in *The FDA Draft Guidance Document for the Preparation of Premarket Notifications for Ceramic Ball Hip Systems* (January 10, 1995), there is no performance requirement. The selected requirement for this wear test is that the insert and head should produce significantly less wear than Ultra High Molecular Weight Polyethylene (UHMWPE) liners articulating against Co-Cr-Mo heads in a similar simulator wear test.

The wear rate for the 28mm head and insert was 0.0148mm<sup>3</sup>/million cycles and a slightly higher, but not statistically significantly different wear rate of 0.0184mm<sup>3</sup>/million cycles for the 32mm components. These values are less than, but similar to other 28mm alumina on alumina wear test results in the literature. The results passed the requirement of a significant decrease in the wear volume of conventional UHMWPE on metal with a decrease in wear volume of more than two orders of magnitude.

#### Range of Motion

A Computer Aided Design (CAD) Model was developed to mimic maximum component range of motion for each stem/head combination and ceramic insert combination. For each combination, the model stem was mated with a femoral head and the head/stem geometry was mated with a ceramic insert. The metal shell face is designed to be at the same height as the flat equatorial face of the ceramic insert.

To determine the range of motion (ROM), an initial position was set for each combination. The polar axis of the femoral head/neck taper geometry was aligned coincident with the polar axis of the insert/shell geometry. The shell was rotated to the posterior point of contact on the stem geometry and the angle of the plane of the flat equatorial face of the insert at that position was noted.

The angle between the anterior zero position and the posterior contact position was considered to be the range of motion.

The minimum range of motion was found to be 120° when using a 28mm femoral head with a -3.5mm offset and the maximum range of motion was found to be 147° when using a 28mm femoral head with a +3.5mm offset. This range of motion is comparable to other approved total hip replacement systems.

### **Ceramic Femoral Head Testing:**

The purpose of this testing was to evaluate the performance of the *Trilogy AB* ceramic femoral heads paired with Zimmer femoral stem tapers. Ceramic heads of “worst-case” geometry (as defined below) were tested for static burst strength, pull-off strength, fatigue strength and post-fatigue strength.

#### **Head Burst**

The heads mounted on mating femoral stem tapers will be subjected to modest impact loads during implantation and peak loads that occur with patient events such as stumbles or stepping off a curb without being aware. These events will place higher loads on the head that it must be capable of resisting without failure.

Five samples of each size and diameter of ceramic heads were tested to failure on two different taper materials. The FDA *Draft Guidance Document for the Preparation of Premarket Notifications for Ceramic Ball Hip Systems* (January 10, 1995) places a requirement of 46 kN average and no single failure less than 20 kN on ceramic femoral heads.

All of the samples met the 46kN ceramic head average burst strength requirement except for the 28mm +3.5mm offset Co-Cr-Mo taper. The average burst strength of these components was 45.6kN. However, all single values were well above the 20kN requirement. Therefore, FDA determined that there was not a significant safety concern.

#### **Head Pull Off**

The head has a self locking taper socket to hold it on a mating femoral stem taper. Dislocation, impingement, and other forces at extremes of motion supply forces that could remove the heads from their mating tapers.

Worst case was determined to be the smallest contact area between the head taper socket and the mating femoral stem taper. This smallest contact area is on the longest offset head. Five samples of the longest offset head in both sizes were tested on two different stem taper materials.

Although the FDA *Draft Guidance Document for the Preparation of Premarket Notifications for Ceramic Ball Hip Systems* (January 10, 1995) asks that the test be performed, it does not identify a performance requirement. The average pull-off resistance was 0.97 kN (49% of the push-on force) or larger, which is comparable to other commercially available ceramic on ceramic systems.

#### Femoral Head Fatigue

In clinical use, the femoral head will transfer physiological loads between the leg and the upper torso. These loads are dynamic and repeatable in nature and could cause fatigue fractures of the head.

The longest offset heads in each diameter had the lowest burst strength and were selected as the worst case sizes. Five samples of the 28 mm diameter heads and three samples of the 32 mm diameter heads were tested on two different taper materials.

The FDA *Draft Guidance Document for the Preparation of Premarket Notifications for Ceramic Ball Hip Systems* (January 10, 1995) has a fatigue test requirement of a peak load of 14 kN for 10 million cycles for ceramic femoral heads.

All of the samples passed a minimum of 10 million cycles at 14 kN peak load without fracture or cracking.

#### Post Fatigue Head Burst

These systems are intended for long term clinical service. Fatigue testing for 10 million cycles is a demanding test, but some clinical cases may see even more cycles. Consequently, the measurement of the residual strength of the ceramic insert after fatigue testing is important. A measure of the residual strength is determined by a repeat of the burst test on samples following completion of the fatigue test. Both 28mm and 32mm femoral heads with +3.5mm offsets were tested on Ti-6Al-4V and Co-Cr-Mo tapers.

The FDA *Draft Guidance Document for the Preparation of Premarket Notifications for Ceramic Ball Hip Systems* (January 10, 1995) has a post fatigue burst test requirement of no less than 20 kN for ceramic femoral heads.

All of the samples from the fatigue test had a post-fatigue test burst strength significantly greater than 20 kN.

## X. SUMMARY OF CLINICAL STUDIES

As previously stated, the *Trilogy AB* Acetabular System is similar to the previously approved TRANSCEND Ceramic Hip System (P010001). Zimmer references the clinical data from P010001, under a licensing agreement, as clinical support for the safety and effectiveness of the *Trilogy AB* Acetabular System. The clinical data are relevant because the ceramic acetabular inserts of the *Trilogy AB* Acetabular System are the same as a subset of the ceramic acetabular inserts of the TRANSCEND Ceramic Hip System (P010001) and the ceramic femoral heads of the *Trilogy AB* Acetabular System have identical articulating surfaces to the ceramic femoral heads of the previously approved system. The *Trilogy AB* Acetabular System uses Zimmer's own acetabular shells (designed to mate with the ceramic inserts) and a subset of Zimmer's femoral stems. The two systems were shown to perform similarly on the bench.

### A. Published Literature

Published literature on early results of the TRANSCEND Ceramic Hip System discusses significant improvement in average Harris Hip Scores and SF-12 scores when compared to pre-operative scores. No fractures of the ceramic components were reported in these articles.<sup>34</sup>

### B. Pivotal Clinical Study

The study was a prospective, multi-center, non-masked clinical trial of 959 procedures in 848 patients, comparing the referenced ceramic hip system to a historical control group.

Although the primary efficacy endpoint in the clinical study was the survivorship of the ceramic hip (as assessed at the two-year postoperative interval), for the purpose of the clinical study, the primary efficacy endpoints included Harris Hip Score (HHS) and radiographic assessments at 2 years, as well. In addition, patient satisfaction was assessed by the SF-12 at two years.

Complication rates were the primary safety endpoint.

#### Study Design

The study was a prospective, multi-center, historical control, clinical trial. The historical control group was later selected as the population of patients implanted with a metal on polyethylene hip consisting of non-inflammatory degenerative joint disease cases. Study patients consisted of individuals over 21

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<sup>3</sup>Garino, Jonathan P., M.D. "Modern Ceramic-on-Ceramic Total Hip Systems in the United States." *Clinical Orthopedics and Related Research* 2000; 379:41-47.

<sup>4</sup>Murphy, Stephen B., M.D., and Wael K. Barsoum, M.D. "Ceramic-Ceramic Bearings in Total Hip Arthroplasty: Preliminary Clinical Results." *The Orthopaedic Journal at Harvard Medical School* 2001;3:92-94.

years of age presenting for total hip arthroplasty due to osteoarthritis, congenital hip dysplasia, traumatic arthritis and avascular necrosis. A total of 329 procedures have been performed with the referenced ceramic hip system in the original clinical population (Original Clinical Population). An additional 630 devices were implanted under Continued Access. The total number (Original Clinical Population and Continued Access) meeting the inclusion/exclusion criteria as required by the protocol is 959 procedures in 848 patients. Over a two-year period, 211 hip prostheses (179 patients) with metal femoral stems and plastic cups were implanted in the control group.

**Pivotal Clinical Patient Assessment**

Each patient was evaluated at the immediate and 6, 12, and 24-month post-operative intervals, unless otherwise indicated by complications. At each follow-up visit, a Harris Hip Score and SF-12 was administered as well as obtaining AP and lateral radiographs. Radiographs were reviewed by the implanting surgeon. There were no pre-specified success/failure criteria in the pivotal clinical study.

**Demographics**

For the study population, there were a total of 965 procedures performed in 854 patients at 12 sites by 19 surgeons. Six of these patients did not meet study inclusion criteria (one procedure enrolled as a replacement for a previously implanted total hip replacement (THR) and five procedures performed in patients with rheumatoid arthritis). These six procedures are excluded from this analysis. Therefore, the primary analysis sample included 959 procedures for first hip replacements performed in 848 patients.

The patient accounting and Baseline Demographics are summarized in Tables 1 and 2. Note that there were 9 deaths, none of which were related to the study or to the device.

**Table 1: Patient Accounting**

Evaluation Interval	Original Clinical Patient Population (n=329)			Continued Access Population (n=630)		
	TFU	EFU	AFU(%)	TFU	EFU	AFU(%)
Pre-Op	329	329	100% (n=329)	630	630	100% (n=630)
6 months	329	323	93% (n=300)	602	602	71% (n=430)
12 months	329	321	91% (n=293)	443	442	53% (n=233)
24 months	329	321	94% (n=302)	151	150	0% (n=0)

TFU = Theoretical Follow-Up; EFU = Expected Follow-Up (Theoretical Follow-Up minus deaths and removals without replacement); AFU = Actual Follow-up

**Table 2: Baseline and Demographics**

Values	Total Study Procedures (n=959)	Historical Control Group (n=211)
Mean Age in Years	51.4 Years (range 20-80)	62.7 years (range 22-87)
Gender	595 (62%) Males 364 (38%) Females	112 (53%) Males 99 (47%) Females
Mean Body Mass Index (kg/m <sup>2</sup> )	28.8 (range 17.7-65.8)	27.1 (range 22.8-40.9)
Diagnosis		
Osteoarthritis	692 (72.2%)	180 (85.3%)
Avascular Necrosis	189 (19.7%)	31 (14.7%)
Traumatic Arthritis	36 (3.8%)	0
Congenital Hip Dysplasia	42 (4.4%)	0
Mean Baseline Total HHS (range 1-100)	45.1 (range 8.3-95.9)	42.7 (range 11-79)
Mean Baseline Pain HHS (range 0-44)	12.9 (range 0-44)	13.2 (range 0-30)
Mean Baseline Harris ROM <sup>o</sup> (range 0-5)	3.8 (range -3.1-4.88)	4.1 (range not available)

**Safety and Effectiveness Data****Safety Results**

The adverse events related to total hip replacement surgery reported in the pivotal clinical study of 959 are listed in Table 3.

**Table 3: Reported Adverse Events**

Event	Clinical Study (n=959)		Historical Control Group (n=211)	
	Freq.	% of Pop.	Freq.	% of Pop.
<b>Systemic</b>				
Deaths	9	0.9%	0	0%
Pulmonary Embolism	2	0.2%	2	0.9%
Deep Vein Thrombosis	4	0.4%	0	0%
<b>Local</b>	<b>Freq.</b>	<b>% of Pop.</b>	<b>Freq.</b>	<b>% of Pop.</b>
Revisions/Removals <sup>1</sup>	11	1.1%	8	3.8
Breakage/Fracture of Component <sup>2</sup>	5	0.5%	2	0.9%
Dislocation (single) of Component <sup>3</sup>	8	0.8%	3	1.4%
Dislocation (recurrent) of Component <sup>4</sup>	2	0.2%	0	0%
Femoral Fracture	18	1.9%	9	4.3%
Hematoma	2	0.2%	0	0%
Heterotopic Ossification	1	0.1%	1	0.5%
Infection: Deep, Early <1 year	2	0.2%	0	0%
Infection: Deep, Late > 1 year	1	0.1%	0	0%
Infection: Superficial	7	0.7%	0	0%
Loosening of Component	3	0.3%	2	0.9%
Migration of Component	2	0.2%	0	0%
Persistent Foot Drop	2	0.2%	0	0%
Pain	10	1.0%	0	0%
Perforation of Femur During Reaming	2	0.2%	0	0%
Wear of Component	1	0.1%	0	0%
Subsidence of Component	3	0.3%	2	0.9%
Soft Tissue Trauma	0	0%	0	0%
Wound Problems	2	0.2%	0	0%
Other Local Complication <sup>5</sup>	10	1.0%	0	0%
<b>Local-Hip</b>	<b>Freq.</b>	<b>% of Pop.</b>	<b>Freq.</b>	<b>% of Pop.</b>
Trochanteric Bursitis	16	1.7%	1	0.5%
Trochanteric Non-union	0	0%	0	0%
Trochanteric Avulsion	4	0.4%	0	0%

**Notes:**

- <sup>1</sup> See details in the following Table 4 for n=959.
- <sup>2</sup> Clinical Study: Chipping of ceramic acetabular liner during placement requiring intraoperative revision.  
Historical Control Group: Broken metal peg of acetabular cup.
- <sup>3</sup> 2 were revised for this reason.
- <sup>4</sup> 1 was revised for this reason.
- <sup>5</sup> Consisted of: 3 cases of irritation/inflammation; 2 cases where patients fell; 1 case of component mismatch; 1 case of liner malposition; 1 case where the acetabular shell seated too deeply in the reamed cavity; 1 case of hip flexor weakness; and 1 case where the anterior abductor pulled off.

**Revisions and Removals**

Eleven devices out of the 959 procedures in the trial have been revised or removed. Table 4 summarizes the clinical information pertaining to these cases.

**Table 4: Summary of Revisions and Removals**

Procedures	Age/ Gender	Diagnosis	Duration of Implantation	Reason for Revision/Removal
Revision of acetabular component with bone graft and cage implantation	50/F	AVN	84 days	Migration of acetabular component
Revision of femoral head with a longer neck	29/F	Congenital hip dysplasia	1 day	Dislocation
Replaced acetabular component to larger size (32mm) and replaced femoral head to 35mm	43/M	Severe osteoarthritis with mild hip dysplasia	1 day	Dislocation
Replacement of acetabular component, liner, and femoral head. Repair of abductor mechanism.	62/M	Osteoarthritis	38 days	Persistent dislocation following closed reduction, trochanteric fracture with avulsion of abductors.
Revision followed by removal and girdlestone procedure	51/M	Traumatic arthritis	210 days	Deep infection and stitch abscess
Replacement of acetabular liner	36/F	Congenital hip dysplasia	3 days	Acetabular liner disassociated from shell
Replacement of acetabular liner and femoral head	41/M	Osteoarthritis	14 days	Increasing pain, suspected infection
Replacement of acetabular liner and femoral head	58/M	Avascular necrosis	953 days	Excessive wear due to impingement on acetabular cup rim
Replacement of femoral head from 32mm to 28mm	50/M	Osteoarthritis	1 day	Liner/head size mismatch noted on postoperative film
Replacement of (uncemented) femoral stem to cemented stem	56/M	Osteoarthritis	657 days	Pain and progressive subsidence due to undersized (uncemented) femoral stem
Replacement of femoral stem and head	56/F	Osteoarthritis	786	Femoral component loosening

**Efficacy results**

Table 5, below, shows the mean and range of Harris Hip Scores for each study cohort preoperatively and two years postoperatively

**Table 5: Efficacy Results--HHS**

Primary Efficacy Assessment	Original Patient Population (n=329) <sup>1</sup>	Continued Access Population (n=630) <sup>2</sup>	Historical Control Group (n=211)
Preoperative mean HHS (range)	44.8 (13-89)	45.2 (8-96)	42.7 (11-79)
2 year postop mean HHS (range)	94.8 (34-100)	88.1 (17-100)	92.7 (39-100)
% Excellent/Good Results (HHS 80-100 points) at 2 years postop	92.2%	76.9%	88.2%

**Notes:**

<sup>1</sup> Original clinical study population includes the first 329 procedures enrolled in the pivotal clinical study. This includes replacements and removals prior to 24 months (n=9), death prior to 24 months (n=7), and cases in which only a partial Harris Hip Score at 24 months or later was available (n=4).

<sup>2</sup> The *Continued Access* sample (N=630) includes procedures performed after the original population without Month 24+ outcomes. Therefore, outcomes reported were defined on the basis of Last Observation carried Forward (LOCF) and represent the latest clinical results available for that procedure.

**Any Radiographic Lucency**

Radiolucencies were recorded at each follow-up visit based on if they involved the entire Gruen zone (7 AP femoral zones, 7 lateral femoral zones, 3 AP acetabular zones, and 3 lateral acetabular zones). Table 6 summarizes these results.

**Table 6: Any Radiolucency**

Lucency	Original Study Population (n=329)	Historical Control Group (n=211)
Femoral	18 (5.5%)	66 (31.3%)
Acetabular	9 (2.8%)	56 (26.5%)
Overall	22 (6.8%)	77 (36.5%)

In addition, any subsidence was reported for the original study population for 0.9% of the femoral stems and 0.3% of the acetabular cups. In the historical control group there were two instances of femoral stem subsidence (1.0%).

**Implant Survivorship**

Implant survivorship was the pre-specified primary endpoint in the pivotal clinical study of the referenced ceramic hip system. Kaplan-Meier cumulative survivorship is shown in Tables 7 and 8 for the referenced ceramic hip system and the historical control group over time.

The cumulative Kaplan-Meier survivorship values for the femoral or acetabular component are shown in Tables 7 and 8 based on the longest duration of follow-up available in each study cohort.

**Table 7: Referenced Ceramic Hip System Implant Survivorship**

Interval	Number Entering Interval	Number Withdrawn	Number Revised in Interval	Cumulative Survival	Standard Error
12 months	528	69	8	0.9909	0.0041
24 months	279	78	1	0.9876	0.0066
36 months	1	0	0	0.9876	0.0562

**Table 8: Historical Control Group Implant Survivorship**

Interval	Number Entering Interval	Number Withdrawn	Number Revised in Interval	Cumulative Survival	Standard Error
12 months	234	8	3	0.9870	0.0074
34 months	223	70	1	0.9817	0.0090
36 months	152	103	1	0.9719	0.0131
48 months	48	34	3	0.8779	0.0481
60 months	11	11	0	0.8779	0.0481

**Patient Success Criteria**

Table 9 describes the proportion of patients meeting individual clinical success criteria at 2 years postoperatively.

**Table 9: Patient Success Criteria at 2 Years**

Patient Success Criteria	Original Patient Population (n=329) <sup>1</sup>	Historical Control Group (n=211)
Absence of Revision (5)	96.7% (n=318)	98.1% (n=207)
Total HHS > 70	96.8% (n=318)	95.3% (n=201)
No Complete Radiolucencies <sup>2</sup>	99.7% (n=328)	88.5% (n=184)

**Notes:**

<sup>1</sup>The *Original Patient Population* sample includes procedures in the *Complete Endpoint* (N=309) sample plus procedures with revisions, replacements, or removals prior to Month 24 (N=9); who died prior to Month 24 (N=7); or who had only a partial Harris Hip Score assessment at Month 24 or later (N=4). This sample was constructed in order to facilitate an analysis of efficacy and safety endpoints for hips that were at-risk for a complication and that 'completed the study.' For *Complete Follow-up* procedures (N=329), the Month 24+ endpoint was defined as the Month 24 value and if not available, value after Month 24 were used. Original pivotal clinical population includes the first 329 procedures enrolled in the clinical study. This includes replacements and removals prior to 24 months (n=9), deaths prior to 24 months (n=7) and cases in which only a partial Harris Hip score at 34 months or later was available (n=4).

<sup>2</sup>Absence of complete radiolucency were determined by radiographic evaluation for four views: acetabular AP view (3 regions), acetabular lateral view (3 regions) femoral stem AP view (7 regions), and femoral stem lateral view (7 regions). Complete radiolucency in a view was defined to be present if there was any radiolucency present in all zones comprising that view. Absence of complete radiolucency was defined to be present if none of these four views had complete radiolucency.

## **XI. CONCLUSIONS DRAWN FROM THE STUDIES**

The preclinical and referenced clinical data provide reasonable assurance that the *Trilogy AB* Acetabular System is safe and effective for total hip replacement in patients with osteo/degenerative arthritis, avascular necrosis, and related diagnoses.

A system comparison analysis between the *Trilogy AB* Acetabular System and the TRANSCEND Ceramic Hip System (P010001) demonstrated that the systems perform similarly on the bench and that the clinical data referenced in Section X can be used to predict the clinical outcomes for the *Trilogy AB* Acetabular System.

## **XII. PANEL RECOMMENDATIONS**

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA application was not referred to the Orthopedic 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. CDRH DECISION**

The applicant has adequately submitted all answers to the FDA's questions and comments for their PMA application. The preclinical data and similarities in device design to the previously approved ceramic hip system (P010001) provide reasonable assurance that the *Trilogy AB* Acetabular System is safe and effective when used as directed for either cemented or noncemented use in skeletally mature individuals undergoing primary surgery for rehabilitating hips damaged as a result of noninflammatory degenerative joint disease (NIDJD) such as osteoarthritis, avascular necrosis, congenital hip dysplasia, and traumatic arthritis.

In addition, the applicant has agreed to conduct 10 year post-approval study to evaluate the long term safety and effectiveness of the *Trilogy AB* Acetabular System. The study will enroll 250 patients, of which a minimum of 175 patients will be followed out to five years and a minimum of 100 patients will be followed out to 10 years. During the first five years of the study clinical, radiographic and subject self-assessment information will be collected for each subject. For the sixth through the tenth postoperative years, patients will be asked to return an outcomes questionnaire designed to determine the status of their hip replacement.

The applicant's manufacturing facilities were inspected and determined to be in compliance with the Quality System Regulation (21 CFR Part 820).

FDA issued an approval order on June 28, 2006.

#### **XIV. APPROVAL SPECIFICATIONS**

Directions for Use: See the Device Labeling

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

Post-Approval Requirements and Restrictions: See Approval Order