SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Prosthesis, Total Hip System, Semi-constrained, Metal/Ceramic/Ceramic/Metal, Cemented or Uncemented

Device Trade Name: Ceramax® Ceramic Total Hip System

Device Procode: MRA

Applicant's Name and Address: DePuy Orthopaedics, Inc.
700 Orthopaedic Drive
Warsaw, Indiana 46581-0988

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P070026/S004

Date of FDA Notice of Approval: April 2, 2013

Expedited: Not applicable

The original PMA (P070026) was approved on December 23, 2010 and is indicated for noncemented use in skeletally mature individuals undergoing primary total hip replacement surgery for rehabilitation of hips damaged as a result of noninflammatory degenerative joint disease (NIDJD) or any of its composite diagnoses of osteoarthritis, avascular necrosis, and post-traumatic arthritis. The SSED to support the indication is available on the CDRH website and is incorporated by reference here:
http://www.accessdata.fda.gov/cdrh_docs/pdf7/P070026b.pdf
The current supplement was submitted for a line extension to include the 36 Millimeter BIOLOX *delta* Ceramic Femoral Head and BIOLOX *delta* Acetabular Insert Components and Additional Pinnacle® Sector II and Pinnacle® 100 Acetabular Shells and Porocoat® Summit™ and S-ROM® Hip Femoral Prosthesis System Components

II. INDICATIONS FOR USE

The Ceramax® Ceramic Total Hip System is indicated for noncemented use in skeletally mature individuals undergoing primary total hip replacement surgery for rehabilitation of hips damaged as a result of noninflammatory degenerative joint disease (NIDJD) or any of its composite diagnoses of osteoarthritis, avascular necrosis, and post-traumatic arthritis.

III. CONTRAINDICATIONS

Use of the DePuy Ceramax® Ceramic Total Hip System is contraindicated in the following situations:

- Skeletally immature patients (tibial and femoral epiphyses not closed);
- Evidence of active infections that may spread to other areas of the body (e.g., osteomyelitis, pyrogenic infection of the hip joint, overt infection, urinary tract infection, etc.);
- The presence of any known neoplastic (tumor-causing) or metastatic (spread of cancerous cells) disease;
- Significant neurologic or musculoskeletal disorders or diseases that may adversely affect gait, weight bearing or postoperative recovery (e.g., muscular dystrophy, multiple sclerosis);
- Presence of highly communicable disease(s) that may limit follow-up (e.g., immunocompromised conditions, hepatitis, active tuberculosis, etc.);
- Any condition that may interfere with postoperative recovery (e.g., Paget's disease, Charcot's disease);
- Poor skin coverage around the hip joint;
- Use in patients with known allergies to the implant materials;
- Inadequate bone stock to support the device (e.g., severe osteopenia or osteoporosis).
- Marked atrophy (muscle and/or tissue loss) or deformity in the upper femur such as a birth defect affecting the leg bones.
- Inflammatory degenerative joint disease (like rheumatoid arthritis)
- Joint instability

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the DePuy Ceramax® Ceramic Total Hip System labeling.

V. DEVICE DESCRIPTION

The DePuy Ceramax® Ceramic Total Hip System is a modular system consisting of a ceramic on ceramic acetabular bearing couple (alumina composite matrix ceramic femoral head and alumina composite ceramic matrix acetabular liner) combined with a compatible metal shell (cup) and screws and titanium alloy femoral stems identified below. Both the femoral head and acetabular liner components are manufactured from BIOLOX *delta* alumina (Al_2O_3) matrix composite ceramic by CeramTec AG. All implantable devices are supplied sterile (see sterilization section) for single use. The 28mm BIOLOX *delta* components and corresponding components were approved in P070026. Please refer to the device description provided in the original SSED for additional details. This submission is for the addition of the 36mm BIOLOX *delta* Ceramic Femoral Head and the 36mm BIOLOX *delta* Acetabular Insert Components to the system. The 36mm femoral heads are compatible with the following femoral stems: Porocoat® Summit™ and S-ROM® Hip Femoral Prosthesis System Components. The 36mm liners are compatible with the following acetabular shells: the Pinnacle® Sector II

and the Pinnacle® 100 Acetabular Shells; Porocoat® Summit™ and S-ROM® Hip Femoral Prosthesis System Components.

36mm BIOLOX® *delta* ceramic femoral heads

The alumina composite matrix ceramic heads have an 11/13 taper and are offered in three (+0 mm, +3 mm and +6 mm) neck lengths. The 36mm alumina composite matrix ceramic heads are also available with a 12/14 taper and four (+1.5 mm, +5 mm, +8.5 mm and +12mm,) neck lengths. DePuy BIOLOX® *delta* ceramic femoral heads are only compatible with the DePuy femoral prostheses identified here and in Table 1.

36mm BIOLOX® *delta* ceramic liner (insert)

The alumina composite matrix ceramic acetabular liners are offered in eight sizes with an internal diameter of 36mm. The eight sizes are offered in outer diameters of 52-66 mm in 2 mm increments. A taper-fit connection allows assembly into the mating metal acetabular shell components.

Pinnacle® acetabular cups

The Pinnacle® 100 and Pinnacle® Sector II acetabular cups are hemispherical type replacement prostheses with a single apex hole. The Sector II has three screw holes that allow for adjunctive fixation with 6.5mm diameter bone screws. The metal outer acetabular shell components are manufactured from Ti-6Al-4V (ASTM F620). A porous coating of commercially pure (CP) titanium beads (ASTM F1580) covers the outer surfaces of the shells. The metal outer shells are available with 52, 54, 56, 58, 60, 62, 64, 66 mm outer diameters.

Bone Screws

The DePuy 6.5mm diameter cancellous bone screws are optional, and are available in titanium alloy (ASTM F136) in sizes ranging in lengths from 15-70 mm.

DePuy Femoral Stems

The DePuy Ceramax® Ceramic Total Hip System uses the commercially available DePuy S-ROM® and Porocoat® Summit™ titanium alloy (ASTM F136) femoral stem components.

The titanium alloy femoral stems, S-ROM® with 11/13 trunnions and Porocoat® Summit™ with 12/14 trunnions, are for cementless use. The S-ROM® stems are available in standard and lateralized versions. The Summit™ stems are available with standard and high offsets. The stems are partially coated with a commercially pure titanium porous coating.

Table 1. 36 mm Ceramax® System Component Compatibility

Femoral Stem	BIOLOX *delta* femoral head (OD, neck lengths, internal tapers)	Ceramax® ceramic acetabular insert (ID X OD)	Pinnacle® 100 and Sector II acetabular shells (OD)	6.5mm diameter Pinnacle® Cancellous Bone Screws
S-ROM® Modular Hip	**36mm +0, +3, and +6 (11/13 taper)**	**36 x 52, 36x 54, 36x 56, 36x 58, 36x 60, 36x 62, 36x 64, 36x 66mm**	**52 – 66mm**	**15-70mm**
Porocoat® Summit™	**36mm +1.5, +5, +8.5, and +12 (12/14 taper)**	**36 x 52, 36x 54, 36x 56, 36x 58, 36x 60, 36x 62, 36x 64, 36x 66mm**	**52 – 66mm**	**15-70mm**

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the correction of noninflammatory degenerative joint disease (NIDJD) of the hip, including:

- The use of other commercially available total hip replacement implants. Other bearing surface alternatives used in total hip replacement include ceramic on ultra-high molecular weight polyethylene (UHMWPE), metal on metal, ceramic on metal and metal on UHMWPE bearing articulations;
- Non-surgical treatment such as reduced activity and/or pain medication; and
- Other surgical treatments that do not involve the use of an implant, such as hip joint fusion.

Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

DePuy Orthopaedics has marketed the Ceramax® Ceramic Total Hip System worldwide since 2003 in the following countries: Australia, Austria, Belgium, China (Hong Kong), Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, India, Ireland, Israel, Italy, Korea, Malaysia, Middle East countries, New Zealand, Netherlands, Philippines, Poland, Portugal, Russia, Singapore, Slovakia, Spain, Slovenia, South Africa, Sweden, Switzerland, Thailand, Turkey and the United Kingdom. These devices have not been withdrawn from marketing in any country for reasons of safety and effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the DePuy Ceramax® Ceramic Total Hip System.

Reported Device Related Adverse Effects

The most commonly reported adverse events related to the DePuy Ceramax® Ceramic Total Hip System device are:

1. Trochanteric bursitis
2. Wound problems
3. Musculoskeletal problems
4. Dislocations

Potential Adverse Effects

The following adverse effects may occur in association with any hip replacement surgery, including the Ceramax® Ceramic Total Hip System:

- Device failure because the components cannot be expected to indefinitely withstand the activity level and loads of normal healthy bone.
- Surgical complications including, but not limited to: vascular disorders, including thrombus; bronchopulmonary disorders, including emboli; myocardial infarction or death.
- Hematoma or damage to blood vessels resulting in large blood loss.
- Delayed wound healing.
- Superficial or deep infection. Infections may occur months to years after surgery. These infections are difficult to treat and may require reoperation with removal surgery and replacement at a later time.
- Temporary or permanent nerve damage resulting in pain or numbness of the affected limb.
- Metal sensitivity reactions, allergic reactions, or metallosis.
- Possible detachment of the coating(s) on the femoral stem or acetabular shell components, potentially leading to increased debris particles;
- Dislocation and subluxation leading to postoperative joint instability (which may be caused by malpositioning of the implants or muscle/fibrous tissue laxity).
- Loosening of hip replacement components can occur. Early mechanical loosening may result from inadequate initial fixation, malalignment, latent infection, premature loading of the prosthesis, or trauma. Late loosening may result from trauma, infection, biological complications (including osteolysis), or mechanical problems, with the subsequent possibility of bone erosion and/or pain.
- Limb length discrepancy.
- Traumatic arthrosis of the hip from intraoperative positioning of the extremity.
- Device related noise such as, clicking, popping, squeaking or grinding.
- Increased hip pain and/or reduced hip function.
- Fatigue fracture of the implants as a result of excessive loading, malalignment, or trauma.
- Osteolysis and/or other peri-prosthetic bone loss.

- Bone perforation or fracture (occurring either intra-operatively or occurring post-operatively as a result of trauma, excessive loading, osteolysis or osteoporosis).
- Periarticular calcification or ossification.
- Wear and deformation of the articular surface (as a result of excessive loading or implant malalignment).
- Inadequate range of motion due to improper selection or positioning of components, by femoral impingement, and periarticular calcification; and
- Death.

Any of these adverse effects may require medical or surgical intervention. In rare cases, these adverse effects may lead to death.

For the specific adverse events that occurred in the clinical studies, please see Section X below.

IX. SUMMARY OF PRECLINICAL STUDIES

A battery of preclinical laboratory tests were conducted on the alumina composite matrix ceramic material used to manufacture the ceramic components. The metal components that comprise the rest of this system are made from materials that have been used for many years in total hip replacement (THR) surgery.

Non clinical laboratory testing was provided in support of the Ceramax® Ceramic Total Hip System including the information regarding:

- Femoral Head Testing: burst strength, fatigue strength, post-fatigue burst strength, axial pull-off strength
- Acetabular Liner Testing: burst strength, fatigue strength, post-fatigue burst strength, push-out strength, torsional strength, lever-out strength
- Bearing Couple: range of motion, wear
- Surface Coating Characterization

A. Laboratory Studies

Test	Purpose/Methods	Acceptance Criteria	Results
Ceramic Head Static Burst Testing	Static burst or 'crush' testing was performed to evaluate the ability of the individual ceramic head components and the system as a whole to withstand static axial compression. Static burst testing of Biolox delta ceramic ball heads used for the DePuy Ceramax® Ceramic Total Hip System was conducted. Twelve	The Ceramic Ball guidance document suggests a minimum average burst strength of 46kN with no individual failure below 20 kN, so the construct tested met the acceptance	The average load to fracture for the 36-11/13 (+12 mm) heads was 105 kN, with no head fracturing below 68kN. The average load to fracture for the 36-12/14 (+12 mm) heads was 58 kN, with no head fracturing below 46kN.

Test	Purpose/Methods	Acceptance Criteria	Results
	tests were performed using 36-11/13 (+12 mm) Biolox delta ceramic ball heads on trunnions from DePuy stems representing the worst case combination. Seven tests were performed using 36-12/14 (+12 mm) Biolox delta ceramic ball heads on trunnions from DePuy stems representing the worst case combination.	criteria.	
Ceramic Head Fatigue Testing	Fatigue testing of three 36-11/13 (+12 mm) Biolox delta ceramic ball heads on DePuy stem tapers and three 36-12/14 (+12 mm) Biolox delta ceramic ball heads on DePuy stem tapers was conducted. The applied load was cycled to 14.0 to 0.5kN at a frequency of 10 Hz in Ringers solution at ambient temperature.	No cracks or ball fracture after 10 million cycles.	All specimens reached 10 million cycles without failure or formation of macroscopically detectable defects.
Post-Fatigue Burst Testing	Following fatigue testing, Burst testing of the three 36-11/13 (+12 mm) samples and three 36-12/14 (+12 mm) samples was performed.	Greater than 20kN as required for the post-fatigue burst strength suggested by the FDA Ceramic Ball Guidance.[1]	The 36-11/13 samples had an average burst test value of 78 kN and a minimum value of 67 kN. The 36-12/14 samples had an average burst test value of 65 kN and a minimum value of 52 kN.
Ceramic Head Axial Pull-off Testing	Five 36-11/13 (+12 mm) and five 36-12/14 (+12 mm) Biolox *delta* ceramic ball heads were tested for pull-off loads using DePuy stem trunnions.	No universal acceptance criteria. Compared to in-vivo conditions	The average pull-off load for the 36-11/13 (+12 mm) samples was 1309 N. The average pull-off load for the 36-12/14 (+12 mm) samples was 1094 N.
Ceramic Liner Burst Test	The purpose of this test was to determine the minimum burst	An average burst strength greater	The mean static axial compressive fracture

Test	Purpose/Methods	Acceptance Criteria	Results
	strength (static axial compression fracture load) for the smallest ceramic liners. Seven worst case 36/52 mm ceramic liner/52 mm acetabular metal shell assemblies were static burst tested using 36mm Biolox delta (zirconia composite) ceramic heads.	than 46 kN with no single sample below 25 kN.	load for the DePuy 36 millimeter ceramic insert was > 285 kN with no values below 285 kN. All inserts were loaded up to the machine capacity without failing.
Ceramic Liner Fatigue/Post-Fatigue Burst Test	The purpose of this test was to determine the minimum burst strength for the worst case liner assembly after cyclic fatigue testing. Three worst case 36/52 mm ceramic liner/52 mm acetabular metal shell assemblies were fatigue tested in axial compression using an applied load cycled from 14.0 kN to 0.5 kN at a frequency of 10 Hz in Ringers solution at ambient temperature for 20 million cycles.	The acceptance criteria required the ceramic liner samples to pass 20 million cycles at 14kN with no macroscopically visible component failure and have no post-fatigue burst strength below 25 kN.	No failures or fractures occurred. The mean post fatigue burst strength for the DePuy 36 mm ceramic insert was 290 kN with no values below 290 kN. All inserts were loaded up to the machine capacity without failing.
Ceramic Liner Push-out Testing	The purpose of this push-out testing was to evaluate the integrity of the liner/shell connection (i.e., locking mechanism) of the acetabular system. Five worst case 36/52 mm ceramic liner/52 mm acetabular metal shells underwent push-out testing.	The acceptance criterion required an average push-out value greater than 200 N.	The mean pre-fatigue push-out force for the 36/52 mm liner/52 mm shell was 1595 N with no values below 1550 N
Acetabular Liner Rotational Stability (Torsional Test)	The purpose of this torsional test was to evaluate the integrity of the liner/shell connection (i.e., locking mechanism) of the acetabular system by determining the torsional force required to dissociate the taper-fit between a ceramic liner and an acetabular shell. Three worst case 36/52 mm ceramic liner/52	The acceptance criterion was defined as an average torsional force greater than 4 N*m (400 N*cm).	The mean rotational moment (torque) of the 36mm acetabular construct was 3408 N*cm with no values below 760 N*cm.

Test	Purpose/Methods	Acceptance Criteria	Results
	mm acetabular metal shells underwent torsional testing. The 36/52 mm liner/52 mm metal shell assembly was determined to be the worst case for the testing because it has the least amount of taper surface contact area within the DePuy implant system under consideration.		
Acetabular Liner Lever-Out Test	The purpose of this test was to evaluate the integrity of the liner/shell connection (i.e., locking mechanism) of the acetabular system by determining the lever-out force required to dissociate the taper-fit between a ceramic liner and an acetabular shell. Three worst case 36/52 mm ceramic liner/52 mm acetabular metal shells underwent lever-out testing. The 36/52 mm liner/52 mm metal shell assembly was determined to be the worst case for the testing because it has the least amount of taper surface contact area within the DePuy implant system under consideration.	The acceptance criteria was defined as an average lever-out strength greater than 3000 N*cm.	The mean lever-out force of the 36 mm acetabular construct was 10,199 N*cm with no values below 9443 N*cm.
Range of Motion, Head/Liner Constraint	A computer aided design (CAD) range of motion (ROM) analysis of the total hip construct was performed to measure the constraint of the DePuy Ceramax® Ceramic Total Hip System with the S-ROM® femoral stems. ROM measurements in the anterior/posterior (A/P) and medial/lateral (M/L) directions were made for each DePuy femoral stem, femoral head and acetabular cup combination	The acceptance criterion was defined as ROM > 112° in the anterior/posterior direction	The 36mm combination yielded 148^{o} minimum ROM in the anterior/posterior direction. The minimum ROM in the medial/lateral direction was determined to be 142^{o}.

Test	Purpose/Methods	Acceptance Criteria	Results
	representing worst case scenarios to establish the worst case (minimum) ROM values. The worst case (least ROM) combination of 36mm implants was determined to be the 36 mm x 54 mm ceramic insert with the S-ROM® (11/13 taper) femoral stems.		
Wear of Alumina Composite Matrix Ceramic-on-Ceramic Hip Bearings	The purpose of this test was to assess the amount of wear debris produced from the ceramic-on-ceramic articulation. A wear test was designed to replicate an in vivo condition, comparing the amount of wear debris produced by the 36 mm (36/62 mm acetabular shell) ceramic-on-ceramic couple (n=3) against a control group with 36 mm (36/52 mm acetabular shell) metal-on-metal couple (n=2). The motion was flexion/extension of +30/-15°, internal/external rotation of +10/-10°. The components were subjected to a repetitive Paul type stance phase loading (ISO 14242-1) with a maximum load of 3kN and swing phase load minimum of 300N. The lubricant used was 25% new born calf serum (75% v/v deionized water) with sodium azide and EDTA additions. The lubricant was changed regularly throughout the test at intervals of approximately 300,000 cycles. The wear was assessed gravimetrically at intervals of 0.5 million cycles from 0 to 2 million and thereafter every 1	The acceptance criterion for this wear test was lower volumetric wear generated by the 36 mm Biolox delta ceramic-on-ceramic couple than for a 36 mm metal-on-metal couple.	There was no measurable difference in diameter of the component before or after the test. The total wear at 6 million cycles was measured as 1.72 mm3 for 36mm metal-on- metal and –0.108 mm3 for 36mm ceramic-on-ceramic. However, the measurement conditions were not accurate enough to measure the small weight changes experienced during simulation as wear rates were very low when articulating with Biolox delta ceramic.

Test	Purpose/Methods	Acceptance Criteria	Results
	million cycles up to a maximum of 6 million cycles.		
Surface Coating Characterization	The purpose of this testing was to characterize the femoral stem and acetabular shell porous-surface coatings with regard to coating thickness, bead morphology, pore size, porosity, and bond strength characteristics in accordance with the FDA Orthopedic Device Coating Guidance.[2]	In accordance with the guidance and standards	The S-ROM® femoral stem commercially pure (CP) titanium coating has: a mean coating thickness of 229 μm; a spherical bead shape; a mean pore diameter of 125 μm; a mean volume percent porosity of 34%; a mean shear strength of 46.1 MPa; and, a mean tensile pull-off strength of 70.0 MPa. The Porocoat® Summit™ femoral stem and Pinnacle® acetabular cup porous coating has; a mean coating thickness of 762 μm; a spherical bead shape; a mean pore diameter of 275 μm; a mean volume percent porosity of 51%; a mean shear strength of 25.5 MPa; and, a mean tensile pull-off strength of 21.1 MPa.

B. Animal Studies

No animal studies have been performed. Animal studies were not deemed necessary to determine the safety and effectiveness of the DePuy Ceramax® Ceramic Total Hip System.

C. Additional Studies

Biocompatibility

The materials for use in the Ceramax® Ceramic Total Hip System are standard materials used in permanently, implanted orthopaedic implants, including titanium alloy (ASTM F136, ASTM F620) and Biolox *delta* ceramic.

Sterilization

DePuy ceramic femoral heads and ceramic liners are sterilized by gamma radiation sterilization (Cobalt 60 Source) at a dose of 25kGy (2.5Mrad). The process is validated per the requirements of ISO 1113734[3] to yield a minimum Sterility Assurance Level (SAL) of 10^{-6}. The product is not labeled "pyrogen free". The components are packaged in Tyvek/PETG trays to maintain sterility.

Shelf-Life

Shelf life testing was performed to verify sterile packaging integrity equivalent to 11 years for the Ceramax® Ceramic Total Hip System.

X. SUMMARY OF PRIMARY CLINICAL STUDIES

The applicant performed a two-armed clinical study to establish a reasonable assurance of safety and effectiveness of total hip arthroplasty with the DePuy Ceramax® Ceramic Total Hip System for non-inflammatory degenerative joint disease in the US under IDE #G030075. One study arm investigated the 28mm sizes of ceramic components and the second arm the 36mm ceramic components. Please see the original SSED for details on 28mm ceramic clinical study arm. Data from the 36mm clinical study, along with a *post hoc* subgroup analysis of only the subset of components the applicant is proposing to market (DePuy S-ROM® femoral stems, Porocoat® Summit™ femoral stems, DePuy Pinnacle® 100 and Pinnacle® Sector II acetabular cups), were the basis for the PMA approval decision. A summary of the 36mm clinical study is presented below.

A. 36MM Study Design

Patients were treated between April 12, 2006 and August 29, 2007. The database for this PMA reflected data collected from April 2006 to March 2011 and included 264 patients. The first surgery occurred on October 28, 2003 and the last surgery on December 28, 2005. There were five investigational sites and 11 surgeons.

The study was a prospective, multi-center, nonrandomized, controlled clinical study of the 36mm ceramic-on-ceramic hip components of the DePuy Ceramax® Ceramic Total Hip System (COC36) compared to a conventional 28mm ceramic-on -polyethylene articulation hip system (COP28).

The investigational group (n=168 subjects) received commercially-available cementless porous coated acetabular cup prosthesis (Pinnacle®™) and an investigational ceramic

3 *Sterilization of health care products - Requirements for validation and routine control - Radiation sterilization* using AAMI TIR27 Sterilization *of health care products – Radiation sterilization – substantiation of 25kGy as a sterilization dose – Method* VD_{max}

bearing insert (Ceramax®) with a 36mm inner diameter. The control group (n=74 subjects) received commercially-available cementless porous-coated acetabular cup prosthesis (Pinnacle®™) and a commercially-available polyethylene bearing insert (Marathon™) with a 28mm inner diameter. Both treatments received a commercially available femoral stem. The control group was an active treatment with a legally marketed alternative with similar indications for use.

Femoral stem components used in this investigation consisted of implantations with Porocoat® Summit™, Summit™ Duofix, S-ROM®, Prodigy™, AML, and Corail™ hip stems. Pinnacle® 100, Pinnacle® 300 and Pinnacle® Sector II acetabular cups were used. Commercially available 28mm and 36mm Biolox® ceramic femoral heads were used on all femoral stems. In PMA P070026, the applicant is only seeking marketing approval for the following subset of the 36mm Ceramax® components studied in the IDE: S-ROM® femoral stems, Porocoat® Summit™ stems, Pinnacle® 100 and Pinnacle® Sector II acetabular cups.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the DePuy Ceramax® Ceramic Total Hip System investigational study was limited to patients who met the following inclusion criteria:

- Cementless total hip replacement in skeletally mature (tibial and femoral epiphyses are closed) individuals 20 to 75 years of age at the time of surgery undergoing primary hip surgery for noninflammatory degenerative joint disease (NIDJD)
- Composite diagnoses of NIDJD include osteoarthritis, avascular necrosis, posttraumatic arthritis, slipped capital femoral epiphysis (SCFE), fracture of the pelvis, and developmental dysplasia
- Patients with a previous total hip replacement of the contralateral leg that has a pain rating of none or slight and who are at least one year post arthroplasty are eligible for participation in the study
- Preoperative Harris Hip Total score of less than or equal to 70
- Preoperative Harris Hip Total Pain score at least Moderate
- Radiographic evaluation confirms the presence of NIDJD
- Radiographic evaluation confirms that there is sufficient femoral and acetabular bone stock, regarding strength and shape, and is suitable to receive the implants

Patients were not permitted to enroll in the DePuy Ceramax® Ceramic Total Hip System investigational study if they met any of the following exclusion criteria:

- Presence of a previous prosthetic hip replacement device (any type, including surface replacement arthroplasty, endoprosthesis, etc.) in the hip joint to be operated
- Previous Girdlestone procedure (resection arthroplasty) or surgical fusion of the hip to be operated
- Acute femoral neck fracture
- Above knee amputation of the contralateral and/or ipsilateral leg

- Patients with bilateral degenerative joint disease requiring staged or simultaneous hip replacements
- Patients with an existing total hip arthroplasty in the contralateral hip with a Harris Hip pain rating of mild, moderate marked or totally disabled
- Patients who have undergone total hip arthroplasties in their contralateral hips within the past 12 months
- Patients with a known allergy to metal (e.g., jewelry)
- Skeletally immature patients (tibial and femoral epiphyses are not closed)
- Evidence of active infections that may spread to other areas of the body (e.g., osteomyelitis, pyogenic infection of the hip joint, overt infection, urinary tract infection, etc.)
- The presence of highly communicable disease or diseases that may limit followup (e.g., immuno-compromised conditions, hepatitis, active tuberculosis, etc.)
- Presence of known metastatic or neoplastic disease
- Significant neurologic or musculoskeletal disorders or disease that may adversely affect gait or weight bearing, (e.g., muscular dystrophy, multiple sclerosis)
- Conditions that may interfere with the total hip arthroplasty‘s survival or outcome, (e.g., Paget's disease, Charcot's disease)
- Any patient believed to be unwilling or unable to comply with a rehabilitation program for a cementless total hip replacement or who indicates difficulty or inability to return for follow-up visits prescribed by the study protocol
- Patient is known to be pregnant, a prisoner, mentally incompetent, and/or alcohol or drug abuser
- Any systemic steroid therapy, excluding inhalers, within three months prior to surgery
- Patients carrying the diagnosis of inflammatory degenerative arthritis (IDJD) to include the following composite diagnoses: rheumatoid arthritis, systemic lupus erythematosus, pigmented villonodular synovitis, juvenile rheumatoid arthritis and other arthritic processes of inflammatory or autoimmune etiology
- Patients requiring structural bone grafts in order to support the prosthetic component(s) or to shape the bone to receive the implant(s)
- Patients who refuse to provide consent to participate in the clinical investigation
- Surgical replacement requires the use of an acetabular liner and femoral head greater or smaller than a 36mm diameter.

2. Follow-up Schedule

All patients were scheduled to return for follow up examination at 6-weeks, 6-months, 12-months, 24-months and then annually following their surgeries. (Table 1) In addition, beginning at 12-months postoperatively patient-reported satisfaction outcomes were collected.

Table 1: Protocol Interval Windows

Interval	Days
6 weeks = **6 weeks ± 2 weeks**	**28 – 60**
6 months = **6 months ± 4 weeks**	**150 – 210**
12 months = **12 months ± 8 weeks**	**300 – 420**
2 years = **24 months ± 12 weeks**	**630 –810**
3 years* = **36 months ± 16 weeks**	**960 –1200**
4 years* = **48 months ± 20 weeks**	**1290 - 1590**
**** After 2-year follow-up, subjects continue to be evaluated clinically and radiographically on an annual basis until all available study subjects have achieved a minimum 2-year follow-up.***	
An Interim Visit Evaluation was completed any time a subject was seen outside of the defined evaluations.	

Preoperatively, all subjects were clinically evaluated by the following: medical history and physical examination, Harris Hip Score (HHS), and subject-reported visual analog scale (VAS) to assess pain.

Postoperatively, all subjects were clinically evaluated at each interval by objective parameters to measure the clinical effectiveness of the device. Clinical effectiveness of this device was measured by Harris Hip Score, VAS pain scale, subjective self report questionnaire, and independently reviewed radiographs. Adverse events and complications were recorded at all visits. (**Table 2**)

Table 2: Study Evaluation Tools

Evaluation Tool	Details	Interval					
		Preop	**Oper-ative**	**6 W**	**6M**	**12M**	**24M**
Medical History	Collects subject contact information, demographics, preoperative medical history including concomitant medical conditions, medications, and allergies. This information provided baseline data.	X					
Harris Hip Score	Hips were evaluated using the modified Harris Hip Score to allow an assessment of pain, function, activities, deformity and range of motion. Range of motion was measured with a goniometer. Range of motion was not collected at the 6-week interval to protect against dislocation in the immediate postoperative period.	X		X	X	X	X
VAS Pain Scale	Subjects self-reported their pain at each interval using a 100mm visual analog scale (VAS) in which 0 indicated "No Pain" and 100 indicated "Severe Pain". The subjects placed a mark on the scale to indicate their level of pain.	X		X	X	X	X
Operative Detail	Information regarding the devices used, surgical technique, intraoperative complications and hip randomization were recorded.		X				
Subject Self-Reported Data	Subjects self-reported their satisfaction (on a CRF) with hip function.					X	X
Radio-graphic Data	No radiographic data were collected preoperatively. Three radiographic views (anteroposterior pelvis, anteroposterior femur and lateral femur) were collected postoperatively. An independent radiographic reviewer reviewed the images to assess radiographic outcomes. The independent radiographic reviewer reviewed the acetabular component position, cup migration, polyethylene liner wear, and bone-implant interface at all intervals.			X	X	X	X
Adverse Events	Postoperatively, all adverse events, device-related or not, were collected.			X	X	X	X
Interim Visits	Interim Visits were documented and included the reason for the visit. These visits included the spectrum from routine postoperative visits to visits where a subject was evaluated and/or treated for adverse events.			X	X	X	X

The key timepoints are shown above in Tables 1 and 2 summarizing safety and effectiveness.

3. Clinical Endpoints

Per the protocol, all subjects were to be evaluated at the 24 Month (or longer) endpoint.

With regard to safety, the following data were collected on all subjects: revisions, adverse events, and survivorship.

With regard to effectiveness, the following data were collected on all subjects:

- Primary Outcomes: Harris Hip Scores, Radiographic Outcomes; Secondary Outcomes: Harris Hip Score Longitudinal Analysis, and Visual Analog Scale scores for pain (VAS).

With regard to success/failure criteria, the primary endpoint of the study was determined at 24 Month (or longer) based upon a comparison of Harris Hip mean scores between the investigational and control group with a 5 point non-inferiority margin. A subject was considered to be a success if all of the following criteria were met at the 24 Month (or longer) endpoint.

Clinical Criteria for Success:

- Harris Hip total score ≥ 80 points.

Radiographic Criteria for Success:

- No radiolucencies greater than 2 mm in any zone.
- No acetabular cup migration greater than 4 mm.
- No change in inclination greater than 40 degrees.
- No osteolysis.

Revision Criteria for Success: No component removal. In addition, any subject that underwent a reoperation where any device component (acetabular or femoral components) was removed or replaced was considered a revision; and classified as a failure.

B. Accountability of 36MM PMA Cohort

36mm All Enrolled Cohort

At the time of database lock for the 36mm PMA cohort study, 90% (150/167) of the investigational subjects and 96% (68/71) of the control subjects had radiographs, a scorable (complete) Harris Hip CRF and a complete radiographic CRF at the completion of the study, the 24-month or later postoperative visit, for the evaluation of the safety and effectiveness of this device. This is summarized in **Table 3** below.

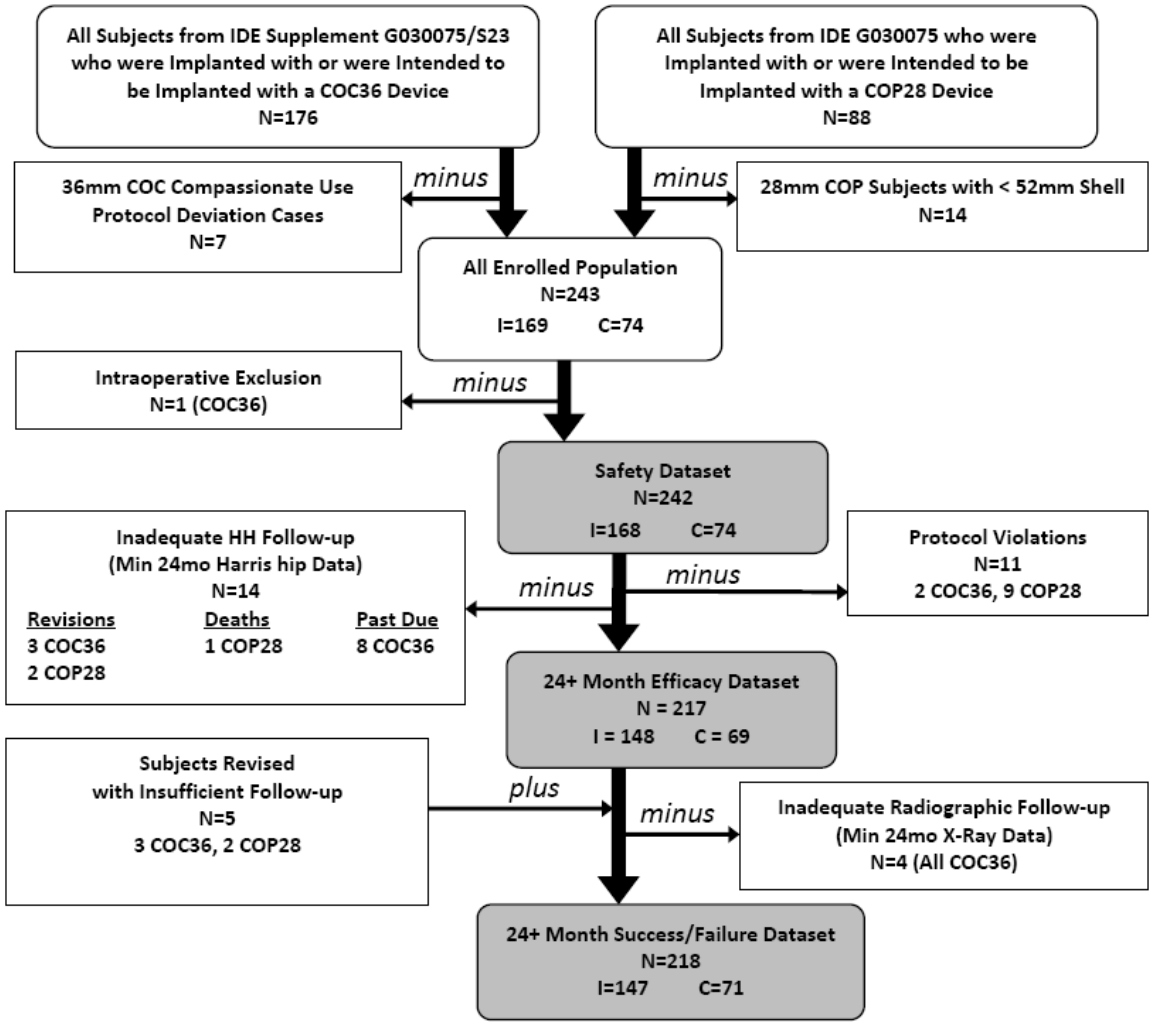
Table 3: Subject Accounting for the 36mm All Enrolled Cohort

IDE Study Cohort	Pre-Op		6 Week		6 Month		12 Month		24 Month		24 Month+	
	I	C	I	C	I	C	I	C	I	C	I	C
Theoretical Due	168	74	168	74	168	74	168	74	168	74	168	74
Expected Due	168	74	168	73	168	72	168	72	167	71	167	71
Withdrawn: Deaths (Cumulative)	0	0	0	0	0	1	0	1	0	1	0	1
Withdrawn: Components Removed/Revised (Cumulative)	0	0	0	1	0	1	0	1	1	2	3	2
Withdrawn: Consent (Cumulative)	0	0	0	0	0	0	0	0	0	0	0	1
Actual	168	74	163	69	141	65	151	67	131	61	150	68
%Follow-up = Actual / Expected Due	100%	100%	97%	95%	84%	90%	90%	93%	78%	86%	90%	96%

Theoretical Due: The number of implants that have entered the beginning of each interval window at the time of database lock.
Expected Due: Theoretical due subjects with complete follow-up minus study withdrawals for death or revision.
% Follow-up: % of hips with radiographs, a scorable (complete) Harris Hip CRF and a complete radiographic CRF.
Withdrawn: Consent (Cumulative): does not include subjects who withdrew consent after complete 24 Month+ data had been obtained.

Figure 1 below is a dataset flowchart which shows all COC36 and COP28 enrolled subjects, how the 242 patients in the 36mm Study Safety Dataset were obtained, and the order in which they were excluded, from top to bottom, to obtain the 24+ Month Efficacy and the 24+ Month Success/Failure datasets; revisions were retained for composite success analysis regardless of exclusion criteria. The primary endpoint non-inferiority test of 24+ Month HH mean scores was carried out on the 24+ Month Efficacy Dataset.

Figure 1: Patient Accounting Dataset Flowchart: 36mm All Enrolled Cohort



Subset Cohort of 36mm Study Patients with S-ROM® and Summit™ Porocoat® Femoral Stems and Pinnacle® 100 (Porocoat®) and Sector II (Porocoat®) Acetabular Cups

The primary analysis was based on six femoral stem types and two acetabular cup types. Marketing approval was sought for the S-ROM® and Summit™ Porocoat® femoral stems and Pinnacle® 100 (Porocoat®) and Sector II (Porocoat®) acetabular cups as components for the 36mm DePuy Ceramax® Ceramic Total Hip System. At the time of database lock, 89 investigational and 38 control subjects in the 36mm Subset Cohort of subjects with these components had a scorable (complete) Harris Hip CRF and a complete radiographic CRF at the 24-month or later postoperative visit. This is summarized in **Table 4** below.

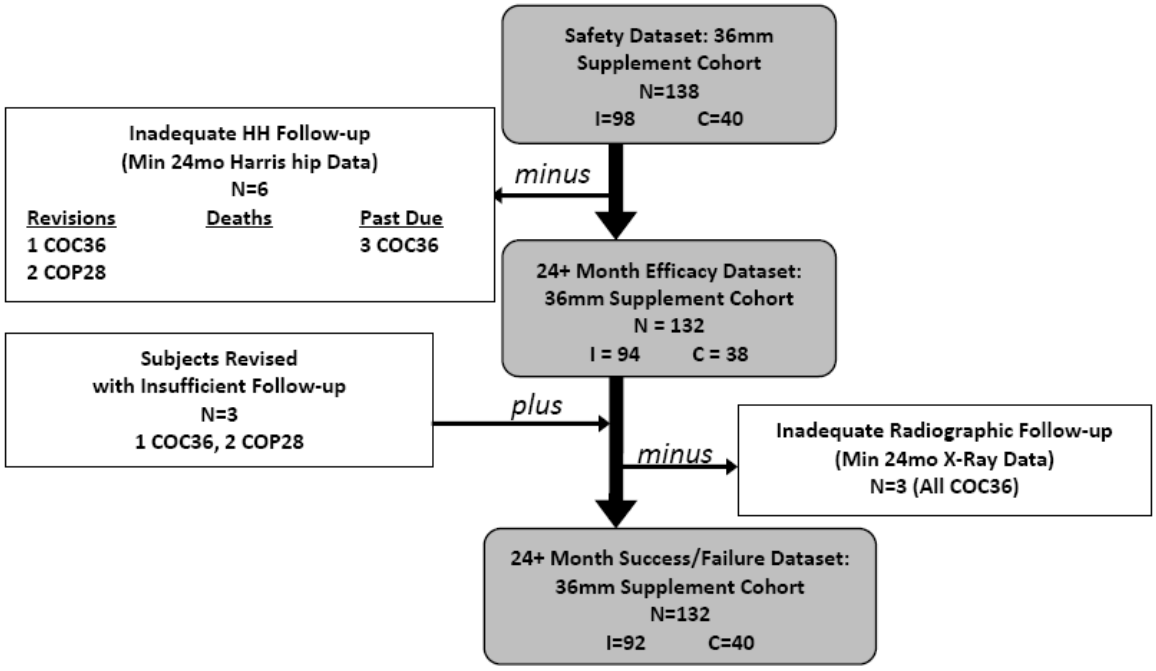
Table 4: Subject Accounting for the 36mm Subset Cohort

36mm Subset Cohort	Pre-Op		6 Week		6 Month		12 Month		24 Month		24 Month+	
	I	C	I	C	I	C	I	C	I	C	I	C
Theoretical Due	98	40	98	40	98	40	98	40	98	40	98	40
Expected Due	98	40	98	39	98	39	98	39	98	38	98	38
Withdrawn: Deaths (Cumulative)	0	0	0	0	0	0	0	0	0	0	0	0
Withdrawn: Components Removed/Revised (Cumulative)	0	0	0	1	0	1	0	1	0	2	1	2
Withdrawn: Consent (Cumulative)	0	0	0	0	0	0	0	0	0	0	0	0
Actual	98	40	94	37	83	36	87	37	77	32	89	38
%Follow-up = Actual / Expected Due	100%	100%	96%	95%	85%	92%	89%	95%	79%	84%	91%	100%

Theoretical Due: The number of implants that have entered the beginning of each interval window at the time of database lock.
Expected Due: Theoretical due subjects with complete follow-up minus study withdrawals for death or revision.
% Follow-up: % of hips with radiographs, a scorable (complete) Harris Hip CRF and a complete radiographic CRF.
Withdrawn: Consent (Cumulative): does not include subjects who withdrew consent after complete 24 Month+ data had been obtained.

Figure 2 below is a dataset flowchart which shows all 138 36mm Study subjects with S-ROM® and Summit™ Porocoat® Femoral Stems and Pinnacle® 100 (Porocoat®) and Sector II (Porocoat®) Acetabular Cups in the Safety Dataset, and the order in which they were excluded, from top to bottom, in order to obtain the 36mm Subset Cohort of subjects in the Efficacy Dataset and in the Success/Failure Dataset; revisions were retained for composite success, regardless of exclusion criteria.

Figure 2: Study Subject Accounting Dataset Flowchart: 36mm Subset Cohort



C. 36mm PMA Study Population Demographics and Baseline Parameters

The demographics of the 36mm PMA Study population are typical for a total hip replacement study performed in the U.S. Clinical study data was collected on 242 hips implanted. There were 168 investigational hip implantations and 74 control hip implantations in the 36mm Protocol Defined Safety Dataset for the 36mm All Enrolled Cohort.

Comparisons were performed to determine whether the subject populations for the treatment groups were equivalent prior to study treatment. Comparisons were conducted using the 36mm Safety Dataset: means were compared with a t-test, and proportions were compared with Fisher's exact test. Results of these analyses are provided in **Table 5** below.

Table 5: Study Baseline Demographics for the 36mm Safety Dataset

Demographic Element		**Investigational N=168**	**Control N=74**	**Investigational vs. Control p-values**
Enrollment	Number of procedures	168	74	-
	Number of patients	168	74	-
Age in years	Mean Age	57.3	56.9	0.781
	Minimum Age	24	29	
	Maximum Age	75	74	
Gender	Females	76 (45%)	27 (36%)	0.259
	Males	92 (55%)	47 (64%)	
Body Mass Index [kg / m^2]	Mean BMI	29.0	29.9	0.318
	Minimum BMI	18.4	18.8	
	Maximum BMI	51.1	47.1	
Primary Diagnosis	Avascular Necrosis	13 (8%)	4 (5%)	0.597
	Developmental Dysplasia	3 (2%)	1 (1%)	1.000
	Epiphyseal Defect	2 (1%)	2 (3%)	0.588
	Osteoarthritis	148 (88%)	65 (88%)	1.000
	Post Traumatic Arthritis	2 (1%)	2 (3%)	0.588
Harris Hip Score	Mean Pre-Op HH Score	52.9	52.1	0.564
	Minimum Pre-Op HH Score	18.0	26.0	
	Maximum Pre-Op HH Score	70.0	76.0	
Harris Hip Pain Category (Range 0-44)	Mean Pre-op HH Pain	14.9	14.1	0.252
	Minimum Pre-op HH Pain	0.0	10.0	
	Maximum Pre-op HH Pain	20.0	30.0	
Harris Hip Function Score (Range 0-33)	Mean Pre-op HH Function	20.9	20.6	0.702
	Minimum Pre-op HH Function	2.0	5.0	
	Maximum Pre-op HH Function	30.0	30.0	
Harris Hip Activity Score (Range 0-14)	Mean Pre-op HH Activity	8.6	8.9	0.373
	Minimum Pre-op HH Activity	0.0	1.0	
	Maximum Pre-op HH Activity	14.0	14.0	
Harris Hip	Mean Pre-op HH Deformity	3.9	3.7	0.332

Demographic Element		Investigational N=168	Control N=74	Investigational vs. Control p-values
Deformity Score (Range 0-4)	Minimum Pre-op HH Deformity	0.0	0.0	
	Maximum Pre-op HH Deformity	4.0	4.0	
Harris Hip Range of Motion Score (Range 0-5)	Mean Pre-op HH ROM	4.6	4.6	0.652
	Minimum Pre-op HH ROM	0.0	3.4	
	Maximum Pre-op HH ROM	5.0	5.0	

The demographics of the 36mm Subset Cohort (subjects who received S-ROM® and Summit™ Porocoat® Femoral Stems and Pinnacle® 100 and Sector II Acetabular Cups) study population are typical for a total hip replacement study performed in the U.S. and consistent with the demographics of the 36mm All Enrolled cohort.

Comparisons were performed to determine whether the patient populations for the treatment groups were equivalent prior to study treatment. Comparisons were conducted using the subset of subjects from the 36mm Safety Dataset with S-ROM® and Porocoat® Summit™ femoral stems and Pinnacle® 100 and Pinnacle® Sector II acetabular cups: means were compared with a t-test, and proportions were compared with Fisher's exact test. Results of these analyses are provided in **Table 6** below.

Table 6: Baseline Demographics for the 36mm Subset Cohort of Safety Dataset Subjects

Demographic Element		Investigational N=98	Control N=40	Investigational vs. Control p-values
Enrollment	Number of procedures	98	40	-
	Number of patients	98	40	-
Age in years	Mean Age	58.1	58.5	0.849
	Minimum Age	32	39	
	Maximum Age	75	74	
Gender	Females	32 (33%)	13 (33%)	1.000
	Males	66 (67%)	27 (68%)	
Body Mass Index [kg / m^2]	Mean BMI	29.3	30.3	0.406
	Minimum BMI	18.4	18.8	
	Maximum BMI	49.5	45.9	
Primary Diagnosis	Avascular Necrosis	4 (4%)	0 (0%)	0.323
	Developmental Dysplasia	0 (0%)	0 (0%)	1.000
	Epiphyseal Defect	0 (0%)	0 (0%)	1.000
	Osteoarthritis	93 (95%)	40 (100%)	0.321
	Post Traumatic Arthritis	1 (1%)	0 (0%)	1.000
Harris Hip Score	Mean Pre-Op HH Score	51.6	49.7	0.347
	Minimum Pre-Op HH Score	18.0	26.0	
	Maximum Pre-Op HH Score	70.0	68.0	
Harris Hip	Mean Pre-op HH Pain	14.2	13.2	0.211

Demographic Element		Investigational N=98	Control N=40	Investigational vs. Control p-values
Pain Category (Range 0-44)	Minimum Pre-op HH Pain	0.0	10.0	
	Maximum Pre-op HH Pain	20.0	20.0	
Harris Hip Function Score (Range 0-33)	Mean Pre-op HH Function	20.4	19.7	0.436
	Minimum Pre-op HH Function	2.0	5.0	
	Maximum Pre-op HH Function	30.0	27.0	
Harris Hip Activity Score (Range 0-14	Mean Pre-op HH Activity	8.5	8.7	0.735
	Minimum Pre-op HH Activity	2.0	2.0	
	Maximum Pre-op HH Activity	14.0	14.0	
Harris Hip Deformity Score (Range 0-4)	Mean Pre-op HH Deformity	3.7	3.6	0.429
	Minimum Pre-op HH Deformity	0.0	0.0	
	Maximum Pre-op HH Deformity	4.0	4.0	
Harris Hip Range of Motion Score (Range 0-5)	Mean Pre-op HH ROM	4.6	3.7	0.555
	Minimum Pre-op HH ROM	0.9	3.8	
	Maximum Pre-op HH ROM	5.0	5.0	

D. 36mm Study Safety and Efficacy Results

1. Safety Results

The analysis of safety was based on the following:

- Adverse Events
- Kaplan-Meier survivorship analysis of revisions

The analysis of safety was based on all 242 enrolled subjects (168 investigational and 74 control cohorts) followed over the 24+ Month evaluation.

The key safety outcomes for this study are presented below in **Tables 5** through **20**.

Adverse events that occurred in the 36mm PMA clinical study:
The Safety Dataset was used to compare:

1) Revisions,
2) Intraoperative complications,
3) Postoperative, systemic adverse events and
4) Postoperative, operative site adverse events

between investigational and control treatment groups.

a. Adverse Events

1. Revisions

Revision was defined as a reoperation where any component (acetabular or femoral) was removed or replaced. There were a total of 3 revisions (1.8%) reported out of 168 procedures in the investigational cohort and 2 revisions (2.7%) reported out of 74 procedures in the control cohort at 24+ months. **Table 7** provides a summary of the revision procedure, treatment group, age, gender, and primary diagnosis, duration of implantation and reason for revision for each patient. There appears to be no clinically meaningful difference in rates of revision between the investigational and control treatments.

Table 7: 36mm PMA Study Investigational and Control Device Revisions

Revision Procedure(s): F = Femoral Stem S = Acetabular Shell H = Femoral Head I = Acetabular Insert	Treatment Group	Age / Gender	Primary Diagnosis	Duration of Implantation	Reason for Revision / Removal
H, I	COC36	26/F	Avascular Necrosis	3.53 yrs	Deep infection
H, I	COC36	59/F	Osteo-arthritis	1.67 yrs	Ceramic liner fracture observed on radiograph
1st revision: F, H (0.58 years), Subject not withdrawn from study 2nd revision: S, I (2.92 years)	COC36	52/M	Osteo-arthritis	0.58 yrs	Femoral component loosening (revised at 0.58 years); Acetabular component loosening (revised/withdrawn at 2.92 years)
H, I	COP28	68 / F	Osteoarthritis	20 months	Recurrent dislocations
H, I	COP28	63 / M	Osteoarthritis	13 days	Recurrent dislocations

Kaplan-Meier Survivorship Analysis

Kaplan-Meier analyses were carried out to determine the expected rate of revision for any reason for both treatment groups. Revision was defined as a reoperation where any component (acetabular or femoral) was removed or replaced. The 'years' variable was calculated using time from surgery to revision for any reason. Subjects not having a revision had their time calculated one of two ways: 1) time from surgery to last clinical or radiographic evaluation, or 2) time from surgery to death. Subjects not having a revision had their time variable censored.

The results are presented graphically in **Figure 3** and in tabular form across time in **Table 8.** When revision was defined as the endpoint for survivorship, the results demonstrated a 97.5 % survivorship (95% confidence interval: 91.9%-99.2%) for the investigational subjects at 4.1 years and a 97.3% survivorship (95% confidence interval:

89.6%-99.3%) for the control hips 5.6 years. There was no clinically or statistically significant difference between investigational and control subjects (log-rank p-value =0.734).

Survivorship analyses for the 36mm Subset Cohort (subjects who received S-ROM® and Summit™ Porocoat® Femoral Stems and Pinnacle® 100 and Sector II Acetabular Cup) are presented graphically in **Figure 4** and in tabular form across time in **Table 9**. Results for the 36mm Subset Cohort demonstrated a 99% survivorship (95% confidence interval: 92.8%-99.9%) for the investigational subjects at 4.1 years and a 95.0% survivorship (95% confidence interval: 81.5%-98.7%) for the control hips at 5.2 years. There was no clinically or statistically significant difference between investigational and control subjects (log-rank p-value =0.153).

Figure 3: Kaplan-Meier Survivorship Estimates: 36mm All Enrolled Cohort

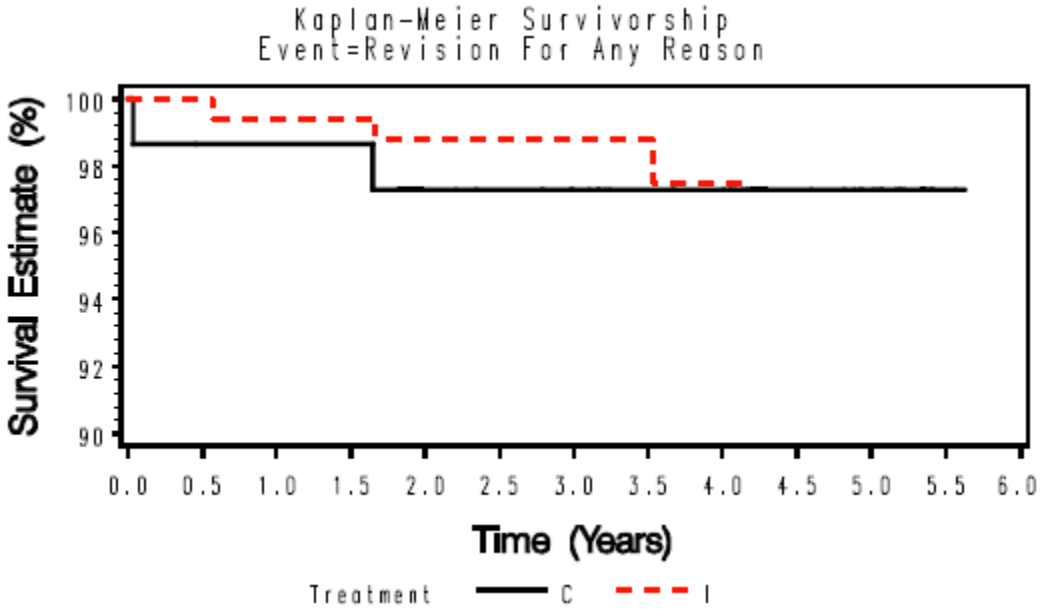


Table 8: Safety Dataset - Survival Estimates Across Time 36mm COC Study: 36mm All Enrolled Cohort

Treatment		0	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5	5.5	6
C	Survival Estimate	100.0	98.6	98.6	98.6	97.3	97.3	97.3	97.3	97.3	97.3	97.3	97.3	
C	Lower 95% Confidence Limit	100.0	90.8	90.8	90.8	89.6	89.6	89.6	89.6	89.6	89.6	89.6	89.6	
C	Upper 95% Confidence Limit	100.0	99.8	99.8	99.8	99.3	99.3	99.3	99.3	99.3	99.3	99.3	99.3	
C	Hips Remaining	74	72	72	72	67	65	60	55	53	42	36	21	<20
C	Accumulative Hips Revised	0	1	1	1	2	2	2	2	2	2	2	2	2
I	Survival Estimate	100.0	100.0	99.4	99.4	98.8	98.8	98.8	98.8	97.5				
I	Lower 95% Confidence Limit	100.0	100.0	95.8	95.8	95.2	95.2	95.2	95.2	91.9				
I	Upper 95% Confidence Limit	100.0	100.0	99.9	99.9	99.7	99.7	99.7	99.7	99.2				

Treatment		0	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5	5.5	6
I	Hips Remaining	168	166	162	159	152	133	126	78	52	<20			
I	Cumulative Hips Revised	0	0	1	1	2	2	2	2	3	3			

Figure 4: Kaplan-Meier Survivorship Estimates: 36mm Subset Cohort

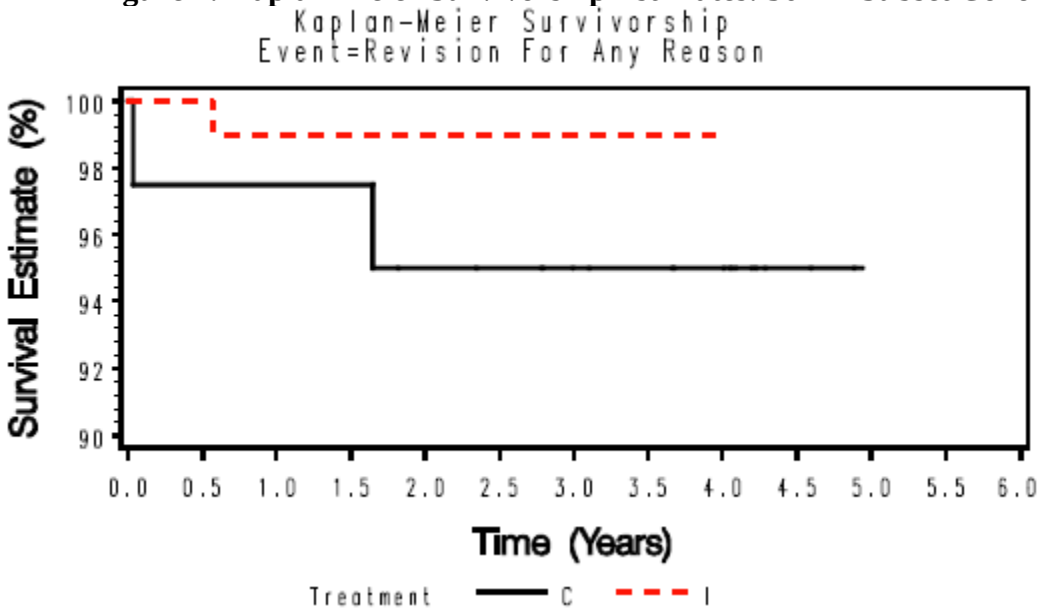


Table 9: Safety Dataset- Survival Estimates Across Time: 36mm Subset Cohort

Treatment		0	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5	5.5
C	Survival Estimate	100.0	97.5	97.5	97.5	95.0	95.0	95.0	95.0	95.0	95.0	95.0	
C	Lower 95% Confidence Limit	100.0	83.5	83.5	83.5	81.5	81.5	81.5	81.5	81.5	81.5	81.5	
C	Upper 95% Confidence Limit	100.0	99.6	99.6	99.6	98.7	98.7	98.7	98.7	98.7	98.7	98.7	
C	Hips Remaining	40	39	39	39	37	36	33	32	30	23	20	<20
C	Accumulative Hips Revised	0	1	1	1	2	2	2	2	2	2	2	2
I	Survival Estimate	100.0	100.0	99.0	99.0	99.0	99.0	99.0	99.0	99.0			
I	Lower 95% Confidence Limit	100.0	100.0	92.8	92.8	92.8	92.8	92.8	92.8	92.8			
I	Upper 95% Confidence Limit	100.0	100.0	99.9	99.9	99.9	99.9	99.9	99.9	99.9			
I	Hips Remaining	98	96	94	94	92	84	78	41	24	<20		
I	Cumulative Hips Revised	0	0	1	1	1	1	1	1	1	1		

Adverse events reported from the clinical study of 242 hip procedures are listed in **Tables 10, 12, 14, 16, 21,** and **22** below.

In **Tables 10** through **15** below, every unique adverse event was reported once per patient, regardless of whether a single subject reported more than one instance of a particular adverse event.

2. Intraoperative Complications

The most common intraoperative complication was cardiovascular, which was observed in 1.2% of investigational subjects (2/168). There was no statistically or clinically meaningful difference in the proportions of observed intraoperative adverse events across treatment groups (see **Table 8** below). Fisher's exact test was used to compare proportions across the two treatment groups.

Table 10: Comparison of Frequency of Intraoperative Adverse Events: 36mm All Enrolled Cohort

	Investigational N=168		Control N=74		
Adverse Events at the 24+ Endpoint	**AEs, (%)**	**95% Confidence Levels**	**AEs, (%)**	**95% Confidence Levels**	**p-value**
2cm non-displaced fracture of posterior femoral neck	1 (0.6%)	0.0 – 3.3	0 (0.0%)	-	1.000
Blemish on Ceramic Component	0 (0.0%)	-	1 (1.4%)	0.0 – 7.3	0.306
Broken Drill Bit	1 (0.6%)	0.0 – 3.3	0 (0.0%)	-	1.000
Cardiovascular	2 (1.2%)	0.1 – 4.2	0 (0.0%)	-	1.000
Hematological	1 (0.6%)	0.0 – 3.3	0 (0.0%)	-	1.000
Liner Fracture During Surgery†	1 (0.6%)	0.0 – 3.3	0 (0.0%)	-	1.000
Total†	**6 (3.6%)**	**1.3 – 7.6**	**1 (1.4%)**	**0.0 – 7.3**	**0.679**

† N=168 investigational subjects + 1 subject who received a metal-on-metal system subsequent to intraoperative ceramic liner fracture.

There were five (5) intraoperative complications among subjects in the 36mm Subset Cohort of subjects with S-ROM® and Porocoat® Summit™ femoral stems and Pinnacle® 100 and Pinnacle® Sector II acetabular cups, as presented in **Table 11** below. There appears to be no clinically meaningful difference in rates of intraoperative adverse events between the investigational and control treatments.

Table 11: Comparison of Frequency of Intraoperative Adverse Events: 36mm Subset Cohort

	Investigational N=98		Control N=40	
Adverse Events at the 24+ Month Endpoint	**AEs, (%)**		**AEs, (%)**	
2cm non-displaced fracture of posterior femoral neck	1 (1.0%)		0 (0.0%)	
Broken Drill Bit	1 (1.0%)		0 (0.0%)	
Cardiovascular	2 (2.0%)		0 (0.0%)	
Hematological	1 (1.0%)		0 (0.0%)	
Total	5 (5.1%)		0 (0.0%)	

3. 36mm PMA Study Postoperative-Systemic Adverse Events

The most commonly reported postoperative systemic complication reported for investigational subjects was musculoskeletal. Other frequently reported adverse events included: cardiovascular, genitourinary, gastrointestinal, dermatological, and HEENT.

There were no systemic adverse events that occurred with a higher incidence in the 36mm All Enrolled Cohort with statistical significance. The Hematological adverse event rate was significantly higher in the COP28 control group compared to the COC36 investigational group (see **Table 12** below).

Table 12: Comparison of Frequency of Postoperative Systemic Adverse Events: 36mm All Enrolled Cohort

	Investigational N=168			Control N=74			
Adverse Events at the 24+ Month Endpoint	**AEs**	**%**	**95% Confidence Levels**	**AEs**	**%**	**95% Confidence Levels**	**p-value**
Cancer	4	2.4	0.6 - 6.0	3	4.1	0.8 - 11.4	0.440
Cardiovascular	15	8.9	5.1 - 14.3	6	8.1	3.0 - 16.8	1.000
Central Nervous System	6	3.6	1.3 - 7.6	4	5.4	1.5 - 13.3	0.500
Dermatological	8	4.8	2.1 - 9.2	0	0.0	0.0 - 0.0	0.111
Endocrine/Metabolic	4	2.4	0.6 - 6.0	6	8.1	3.0 - 16.8	0.072
Gastrointestinal	8	4.8	2.1 - 9.2	6	8.1	3.0 - 16.8	0.371
Genitourinary	10	6.0	2.9 - 10.7	7	9.5	3.9 - 18.5	0.413
HEENT	7	4.2	1.7 - 8.4	6	8.1	3.0 - 16.8	0.225
Hematological	0	0.0	0.0 - 0.0	4	5.4	1.5 - 13.3	0.008
Musculoskeletal	93	55.4	47.5 - 63.0	44	59.5	47.4 - 70.7	0.576

	Investigational N=168			Control N=74			
Adverse Events at the 24+ Month Endpoint	**AEs**	**%**	**95% Confidence Levels**	**AEs**	**%**	**95% Confidence Levels**	**p-value**
Neurological	3	1.8	0.4 - 5.1	0	0.0	0.0 - 0.0	0.555
Other – Fell	5	3.0	1.0 - 6.8	3	4.1	0.8 - 11.4	0.703
Other – Insect bite	0	0.0	0.0 - 0.0	1	1.4	0.0 - 7.3	0.306
Other - Pregnancy - 7 Months Gestation	1	0.6	0.0 - 3.3	0	0.0	0.0 - 0.0	1.000
Peripheral Nervous System	4	2.4	0.6 - 6.0	3	4.1	0.8 - 11.4	0.440
Respiratory System	4	2.4	0.6 - 6.0	4	5.4	1.5 - 13.3	0.253
Thrombosis/Thrombophlebitis	5	3.0	1.0 - 6.8	1	1.4	0.0 - 7.3	0.670
Wound Problem	1	0.6	0.0 - 3.3	0	0.0	0.0 - 0.0	1.000
Every unique adverse event was reported once, regardless of whether a single hip reported more than one instance of a particular adverse event. For example, if a hip reported 'musculoskeletal', then 'musculoskeletal' was listed once for that hip. However, if that same hip also reported 'cancer', then that adverse event was listed in addition to the 'musculoskeletal' adverse event.							

The most frequent postoperative systemic adverse events for investigational subjects in the 36mm Subset Cohort were musculoskeletal, cardiovascular, gastrointestinal, HEENT, central nervous system, and genitourinary.

There were no systemic adverse events in the 36mm Subset Cohort that occurred with a higher incidence statistical significance. The hematological adverse event rate was significantly higher in the COP28 control group compared to the COC36 investigational group (see **Table 13** below).

Table 13: Comparison of Frequency of Postoperative Systemic Adverse Events: 36mm Subset Cohort

	Investigational N=98		Control N=40	
Adverse Events at the 24+ Month Endpoint	**AEs**	**%**	**AEs**	**%**
Cancer	2	2.0	1	2.5
Cardiovascular	11	11.2	4	10.0
Central Nervous System	5	5.1	3	7.5
Dermatological	3	3.1	0	0.0
Endocrine/Metabolic	1	1.0	3	7.5
Gastrointestinal	6	6.1	3	7.5
Genitourinary	4	4.1	5	12.5
HEENT	6	6.1	1	2.5
Hematological	0	0.0	3	7.5
Musculoskeletal	53	54.1	27	67.5
Neurological	1	1.0	0	0.0
Other – Fell	3	3.1	1	2.5
Other – Insect bite	0	0.0	1	2.5
Peripheral Nervous System	2	2.0	2	5.0

	Investigational N=98		Control N=40	
Adverse Events at the 24+ Month Endpoint	**AEs**	**%**	**AEs**	**%**
Respiratory System	2	2.0	3	7.5
Thrombosis/Thrombophlebitis	2	2.0	0	0.0
Every unique adverse event was reported once, regardless of whether a single hip reported more than one instance of a particular adverse event. For example, if a hip reported 'musculoskeletal', then 'musculoskeletal' was listed once for that hip. However, if that same hip also reported 'cardiovascular', then that adverse event was listed in addition to the 'musculoskeletal' adverse event.				

4. 36mm PMA Study Postoperative Operative Site Adverse Events

The most commonly reported postoperative operative site complications for investigational subjects were Trochanteric Bursitis, Musculoskeletal, Other – Squeaking, Pain, and Other – Clicking, Other – Iliopsoas Tendinitis, Pain: Thigh, and Wound Problem, respectively. There were no specific postoperative-operative site adverse events that occurred with a statistically significant higher proportion in COC36 investigational subjects. (See **Table 14** below).

Table 14: Comparison of Frequency of Postoperative Operative Site Adverse Events: 36mm PMA Study: All Enrolled Cohort

	Investigational N=168			Control N=74			
Adverse Events at the 24+ Month Endpoint	**AEs**	**%**	**95% Confidence Levels**	**AEs**	**%**	**95% Confidence Levels**	**p-value**
Acetabular Component Failure[1]	1	0.6	0.0 - 3.3	0	0.0	0.0 - 0.0	1.000
Acetabular Liner Failure[2]	1	0.6	0.0 - 3.3	0	0.0	0.0 - 0.0	1.000
Deep Infection	2	1.2	0.1 - 4.2	0	0.0	0.0 - 0.0	1.000
Dermatological	3	1.8	0.4 - 5.1	0	0.0	0.0 - 0.0	0.555
Dislocation	2	1.2	0.1 - 4.2	4	5.4	1.5 - 13.3	0.073
Femoral Component Loosening[3]	1	0.6	0.0 - 3.3	0	0.0	0.0 - 0.0	1.000
Fracture – Femoral Insertional FX[4]	1	0.6	0.0 - 3.3	0	0.0	0.0 - 0.0	1.000
Hematoma Requiring Drainage	1	0.6	0.0 - 3.3	0	0.0	0.0 - 0.0	1.000
Heterotopic Bone Formation	3	1.8	0.4 - 5.1	0	0.0	0.0 - 0.0	0.555
Muscle Weakness	4	2.4	0.6 - 6.0	0	0.0	0.0 - 0.0	0.316
Musculoskeletal	16	9.5	5.5 - 15.0	3	4.1	0.8 - 11.4	0.197
Other – Clicking	7	4.2	1.7 - 8.4	1	1.4	0.0 - 7.3	0.441
Other – Contusion	1	0.6	0.0 - 3.3	0	0.0	0.0 - 0.0	1.000

	Investigational N=168			Control N=74			
Adverse Events at the 24+ Month Endpoint	**AEs**	**%**	**95% Confidence Levels**	**AEs**	**%**	**95% Confidence Levels**	**p-value**
Other – Fell	3	1.8	0.4 - 5.1	0	0.0	0.0 - 0.0	0.555
Other – Hip Pain	2	1.2	0.1 - 4.2	1	1.4	0.0 - 7.3	1.000
Other – Hip Snapping	1	0.6	0.0 - 3.3	0	0.0	0.0 - 0.0	1.000
Other – Iliopsoas Tendinitis	6	3.6	1.3 - 7.6	3	4.1	0.8 - 11.4	1.000
Other – Squeaking	8	4.8	2.1 - 9.2	0	0.0	0.0 - 0.0	0.111
Other – Stiffness	1	0.6	0.0 - 3.3	0	0.0	0.0 - 0.0	1.000
Other – Subsidence of Femoral Component	0	0.0	0.0 - 0.0	1	1.4	0.0 - 7.3	0.306
Other – Vibration	1	0.6	0.0 - 3.3	0	0.0	0.0 - 0.0	1.000
Pain	8	4.8	2.1 - 9.2	2	2.7	0.3 - 9.4	0.728
Pain: Thigh	6	3.6	1.3 - 7.6	3	4.1	0.8 - 11.4	1.000
Subluxation	1	0.6	0.0 - 3.3	0	0.0	0.0 - 0.0	1.000
Trochanteric Bursitis	17	10.1	6.0 - 15.7	4	5.4	1.5 - 13.3	0.323
Wound Problem	6	3.6	1.3 - 7.6	1	1.4	0.0 - 7.3	0.679

Every unique adverse event was reported once, regardless of whether a single hip reported more than one instance of a particular adverse event. For example, if a hip reported 'deep infection', then 'deep infection' was listed once for that hip. However, if that same hip also reported 'trochanteric bursitis', then that adverse event was listed in addition to the 'deep infection' adverse event**.**

Additional Notes:

1 This AE was documented for the 52 year old male Subject who had acetabular components revised at 2.92 years post-op (this Subject's second revision).

2 This AE was documented for the 59 year old female Subject who was revised for an acetabular liner fracture at 1.67 years post-op.

3 This AE was documented for the 52 year old male Subject who had femoral components revised at 0.58 years post-op (this Subject's first revision; the Subject was not withdrawn from the study because acetabular components were not revised).

4 A femoral fracture diagnosed one month after index THA; date of onset was stated as the date of index THA. The investigator indicated that the AE was not directly related to the device. The recommended treatment was protected weight bearing for 6 weeks.

For the 36mm PMA Study Subset Cohort, the most frequent postoperative operative site adverse events were Trochanteric Bursitis, Musculoskeletal, Pain, Pain: Thigh, Heterotopic Bone Formation, Muscle Weakness, and Other - Squeaking. There were no specific postoperative-operative site adverse events that occurred with a statistically significant higher proportion in COC36 investigational subjects (see **Table 15** below).

Table 15: Comparison of Frequency of Postoperative Operative Site Adverse Events: 36mm Subset Cohort

	Investigational N=98		Control N=40	
Adverse Events at the 24 month+ Endpoint	**AEs**	**%**	**AEs**	**%**
Acetabular Component Failure[1]	1	1.0	0	0.0

	Investigational N=98		Control N=40	
Adverse Events at the 24 month+ Endpoint	**AEs**	**%**	**AEs**	**%**
Deep Infection	1	1.0	0	0.0
Dermatological	2	2.0	0	0.0
Dislocation	2	2.0	2	5.0
Femoral Component Loosening[2]	1	1.0	0	0.0
Hematoma Requiring Drainage	1	1.0	0	0.0
Heterotopic Bone Formation	3	3.1	0	0.0
Muscle Weakness	3	3.1	0	0.0
Musculoskeletal	7	7.1	2	5.0
Other – Clicking	2	2.0	1	2.5
Other – Contusion	1	1.0	0	0.0
Other – Fell	1	1.0	0	0.0
Other – Hip Pain	0	0.0	1	2.5
Other – Iliopsoas Tendinitis	2	2.0	2	5.0
Other – Squeaking	3	3.1	0	0.0
Other – Stiffness	1	1.0	0	0.0
Other – Subsidence of Femoral Component	0	0.0	1	2.5
Other – Vibration	1	1.0	0	0.0
Pain	4	4.1	2	5.0
Pain: Thigh	4	4.1	2	5.0
Subluxation	1	1.0	0	0.0
Trochanteric Bursitis	13	13.3	3	7.5

Every unique adverse event was reported once, regardless of whether a single hip reported more than one instance of a particular adverse event. For example, if a hip reported 'deep infection', then 'deep infection' was listed once for that hip. However, if that same hip also reported 'trochanteric bursitis', then that adverse event was listed in addition to the 'deep infection' adverse event.

Additional Notes:

1 This AE was documented for the 52 year old male Subject who had acetabular components revised at 2.92 years post-op (this Subject's second revision).

2 This AE was documented for the 52 year old male Subject who had femoral components revised at 0.58 years post-op (this Subject's first revision; the Subject was not withdrawn from the study because acetabular components were not revised).

There were no specific postoperative-operative site adverse events that occurred with a statistically significant higher proportion in 36mm PMA study, for either the 36mm All Enrolled or the 36mm Subset Cohort However, it was observed that in total there were 18 noise related postoperative-operative site adverse events (clicking, snapping, squeaking, or vibration) reported in 15 COC36 and 1 COP28 subjects. Some of these noise related AEs were deemed by the respective sites to be related to the device, and some were not, as displayed in **Table 16** below. All but one of the 12 device related noise AEs (reported in 11 COC36 subjects) were deemed by the respective investigators to be 'Mild' in severity; one instance of squeaking was reported to be 'Moderate' in severity. All but one of these 11 subjects stated satisfaction with their THA at the most recent 24+ month follow-up, and all of these 11

patients had a 24+ month Harris Hip score of 84 or higher (six had a 100).

Table 16: Distribution of Device Related vs. Not Device Related (as determined by the sites) Postoperative Operative Site Noise Adverse Events: 36mm All Enrolled Cohort

	OTHER-CLICKING	OTHER- HIP SNAPPING	OTHER-SQUEAKING*	OTHER-VIBRATION
Possibly Device Related	3 COC36		8 COC36	1 COC36
Not Device Related	4 COC36, 1 COP28	1 COC36		
*Note: After database lock, one further subject was reported to have squeaking in the study hip, for a total of 9 COC36 AEs related to squeaking. Out of these 9 hips, squeaking was only reproducible in 2 during clinical follow-up.				

The applicant acknowledged that post-operative operative site noise related adverse events that are possibly related to the COC36 investigational device occurred with a higher frequency in the COC36 investigational group than in the COP28 control group, but considered these adverse events to be mild in severity, particularly given the clinical, pain, and satisfaction outcomes of the patients that exhibited these adverse events.

b. Complications Grouped by Type of Adverse Event

When AEs were grouped by type of AE (intraoperative, postoperative operative site, or systemic) for the 36mm PMA Study All Enrolled Cohort, there was a greater proportion of subjects with postoperative-operative site AEs in the investigational group (p-value = 0.018); there was no significant difference in the proportions of hips with systemic, intraoperative, or overall AEs across treatment groups (see **Table 17** below). In the 36mm Subset Cohort, there was not a significant difference in the proportions of hips with AEs in any category (overall, intraoperative, postoperative-operative site, or post-operative systemic; **Table 18** below). The total number of AEs grouped by type of AE (intraoperative, postoperative, operative site, or systemic) for the 36mm All Enrolled Cohort are reported in **Table 19**.

Table 17: Comparison of Frequencies of Any Adverse Event (Per Hip Basis): 36mm All Enrolled Cohort

	Investigational N=168			Control N=74			
Adverse Events at 24+ Endpoint	**AEs**	**%**	**95% Confidence Levels**	**AEs**	**%**	**95% Confidence Levels**	**p-value**
Any Complication	**134**	**79.8**	**72.9 - 85.6**	**60**	**81.1**	**70.3 - 89.3**	**0.863**
Intraoperative*	**5**	**3.0**	**1.0 - 6.8**	**1**	**1.4**	**0.0 - 7.3**	**0.670**
Operative Site	**66**	**39.3**	**31.9 - 47.1**	**17**	**23.0**	**14.0 - 34.2**	**0.018**
Systemic	**117**	**69.6**	**62.1 - 76.5**	**52**	**70.3**	**58.5 - 80.3**	**1.000**

	Investigational N=168			Control N=74			
Adverse Events at 24+ Endpoint	**AEs**	**%**	**95% Confidence Levels**	**AEs**	**%**	**95% Confidence Levels**	**p-value**
Adverse events are reported on a per hip basis. Regardless of how many times a single hip had an intraoperative complication, for example, it was only counted once. * The intraoperative AE tally presented in this table does not include one subject who received a metal-on-metal system subsequent to intraoperative ceramic liner fracture.							

Table 18: Comparison of Frequencies of Any Adverse Event (Per Hip Basis): 36mm Subset Cohort

24+ Months	Investigational N=98		Control N=40	
Adverse Events	**AEs**	**%**	**AEs**	**%**
Any Complication	**78**	**79.6**	**33**	**82.5**
Intraoperative	**5**	**5.1**	**0**	**0.0**
Operative Site	**36**	**36.7**	**10**	**25.0**
Systemic	**70**	**71.4**	**30**	**75.0**
Adverse events are reported on a per hip basis. Regardless of how many times a single hip had an intraoperative complication, for example, it was only counted once.				

Table 19: Comparison of Frequencies of Any Adverse Event (All events): 36mm All Enrolled Cohort

Adverse Events (distinct events)	Investigational N=168	Control N=74
Any Complication	417	237
Intraoperative	5	1
Operative Site	133	40
Systemic	279	196
In this table, adverse events are reported on a per event basis, so that adverse events which were reported multiple times for a single hip were counted each time.		

In order to understand the slightly higher proportion of post-operative operative site AEs in the investigational group, the sponsor examined those AEs which were deemed by the sites to be possibly device related, and those which were deemed by the sites not to be device related. **Table 20** below presents the number of subjects who experienced post-operative operative site adverse events which were deemed by the sites to be possibly device related, and also adverse events which were deemed to be not device related.

Table 20: Subjects with Device Related vs. Not Device Related (as determined by the (sites) Postoperative Operative Site Adverse Events: 36mm All Enrolled Cohort

Adverse Events at 24+m Endpoint	Investigational N=168		Control N = 74		Fisher's Exact test p-value
	Subjects	Percent	Subjects	Percent	
OPERATIVE SITE: Device Related	16	9.5	4	5.4	0.325
OPERATIVE SITE: Not Device Related	61	36.3	16	21.6	0.025

Out of the 16 36mm All Enrolled Cohort subjects who were deemed to have experienced device related post-operative operative site adverse events, 11 experienced noise related adverse events. The sponsor attributed the disproportion in reported non-device related AEs to an increased rigor in investigator training and monitoring at the start of the 36mm arm of the PMA study, and concludes that with the exception of noise related AEs, there is not a significant difference across treatment groups in the proportions of subjects who experienced adverse events for reasons attributable to the COC36 investigational device.

b. Distribution of Adverse Events over Time

In **Tables 21** and **22**, a time course of the occurrence of post-operative systemic and operative site adverse events is displayed. An adverse event may be reported more than once per subject in these tables if the adverse event occurred more than once across time.

Table 21: Time Course Occurrence of Postoperative Systemic Adverse Events: 36mm All Enrolled Cohort

	Interval																	
	0D-6W		6 Week		6W-6M		6 Month		6M-12M		12 Month		12M-24M		24 month+		Total	
	I	C	I	C	I	C	I	C	I	C	I	C	I	C	I	C	I	C
Complication	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
CANCER											1	1	1		2	3	4	4
CARDIOVASCULAR	7	1						1			2	1	2		7	3	18	6
CENTRAL NERVOUS SYSTEM	3	1				1		1							4	1	7	4
DERMATOLOGICAL	2		2		1						2				1		8	
ENDOCRINE/METABOLIC											1	1	1	1	2	3	4	5
GASTROINTESTINAL	2	1	1	1	1			1		1	1				3	3	8	7
GENITOURINARY	2	3			2		1	2	1				1		5	3	12	8
HEENT		1	1	2	1			1			2	1			4	1	8	6
HEMATOLOGICAL		4																4
MUSCULOSKELETAL	6	3	3	4	11	7	18	8	11	3	12	8	20	12	75	56	156	101

Complication	Interval																	
	0D-6W		6 Week		6W-6M		6 Month		6M-12M		12 Month		12M-24M		24 month+		Total	
	I N	C N	I N	C N	I N	C N	I N	C N	I N	C N	I N	C N	I N	C N	I N	C N	I N	C N
NEUROLOGICAL			1												2		3	
OTHER - FELL														1	5	1	5	2
OTHER - INSECT BITE																1		1
OTHER - PREGNANCY - 7 MONTHS GESTATION															1		1	
PERIPHERAL NERVOUS SYSTEM	1		1					1					2	1		1	4	3
RESPIRATORY SYSTEM	1	3	2					1					1				4	4
THROMBOSIS/THROMBOPHLEBITIS		1			2								1		2		5	1
WOUND PROBLEM	1																1	
Total	25	18	11	7	18	8	19	16	12	4	21	12	29	15	113	76	248	156

Table 22: Time Course Occurrence of Postoperative Operative Site Adverse Events: 36mm Subset Cohort

Complication	Interval																	
	0D-6W		6 Week		6W-6M		6 Month		6M-12M		12 Month		12M-24M		24 month+		Total	
	I N	C N	I N	C N	I N	C N	I N	C N	I N	C N	I N	C N	I N	C N	I N	C N	I N	C N
ACETABULAR COMPONENT FAILURE															1		1	
ACETABULAR LINER FAILURE													1				1	
DEEP INFECTION															1		1	
DERMATOLOGICAL	2												1				3	
DISLOCATION		3		1					2	2				2	1	5	3	13
FRACTURE - FEMORAL INSERTIONAL FX	1																1	
HEMATOMA REQUIRING DRAINAGE	1																1	
HETEROTOPIC BONE FORMATION			1		1										1		3	
MUSCLE WEAKNESS	2				1										1		4	
MUSCULOSKELETAL	5		3	1	3		3	1	1						1		16	2
OTHER - CLICKING					1	1			1		1				4		7	1
OTHER - CONTUSION													1				1	
OTHER - FELL					2		1										3	
OTHER - HIP PAIN										1					2		2	1
OTHER - HIP SNAPPING					1												1	
OTHER - ILIOPSOAS TENDINITIS									1				1		8	2	10	2
OTHER - SQUEAKING							2				2				7		11	
OTHER - STIFFNESS									1								1	
OTHER - SUBSIDENCE OF FEMORAL COMPONENT																2		2
OTHER - VIBRATION															1		1	
PAIN	1		1		2	2			2				1		2		9	2

Complication	Interval																	
	0D-6W		6 Week		6W-6M		6 Month		6M-12M		12 Month		12M-24M		24 month+		Total	
	I N	C N	I N	C N	I N	C N	I N	C N	I N	C N	I N	C N	I N	C N	I N	C N	I N	C N
PAIN: THIGH			1		1			2	1		2				2	1	7	3
SUBLUXATION															2		2	
TROCHANTERIC BURSITIS					5		1	1	1	1	3		3		4	2	17	4
WOUND PROBLEM	4	1	2														6	1
Total	16	4	8	2	17	3	7	4	10	4	8		8	2	38	12	112	31

2. Effectiveness Results

The primary analysis was a non-inferiority test of the Harris Hip Score means as assessed at the minimum 24+ Month interval, with a 5 point non-inferiority margin, as defined in the study protocol. This primary analysis non-inferiority test was carried out on the 217 subjects in the 24+Month Efficacy dataset of the 36mm All Enrolled Cohort.

Marketing approval is for the S-ROM® and Summit™ Porocoat® femoral stems and Pinnacle® 100 and Sector II acetabular cups as components for the DePuy Ceramax® Ceramic Total Hip System; information is presented for the 36mm All Enrolled Cohort as well the 36mm Subset Cohort (subjects who received S-ROM® and Summit™ Porocoat® femoral stems and Pinnacle® 100 and Pinnacle® Sector II acetabular cups).

Primary Analysis

The Harris Hip Score mean in the 36mm All Enrolled Cohort for the investigational group was 95.6 while the Harris Hip Score mean for the control group was 94.9. The standard error of difference was 1.24, and the non-inferiority p-value was less than 0.001. These results are summarized in **Table 23** below.

Table 23: Comparison of 24+ Month Harris Hip Score Means: 36mm All Enrolled Cohort

Parameter	Treatment	N	Least Square Means†	Standard Error of Difference	Non-inferiority P-value
Harris Hip Score	**COC36**	**148**	**95.6**	**1.24**	**< 0.001**
	COP28	**69**	**94.9**		
† This analysis was carried out using an ANCOVA model where preoperative Harris Hip score and weight were significant covariates.					

The Harris Hip Score mean in the 36mm Subset Cohort for the investigational group was 95.5 while the Harris Hip Score mean

for the control group was 95.3. The standard error of the difference was 1.54, and the non-inferiority p-value was less than 0.001. These results are summarized in **Table 24** below.

Table 24: Comparison of 24+ Month Harris Hip Score Means: 36mm Subset Cohort

Parameter	Treatment	N	Least Square Means†	Standard Error of Difference	Non-inferiority P-value
Harris Hip Score	**COC36**	**94**	**95.5**	**1.54**	**< 0.001**
	COP28	**38**	**95.3**		

† This analysis was carried out using an ANCOVA model where weight was a significant covariate.

The primary analysis for the 36mm PMA Study**,** 24+ Month Efficacy Dataset (and *post hoc* primary analysis for the 36mm Subset Cohort) demonstrate that the investigational group 24+Month Harris Hip score mean is non-inferior to the control group 24+Month Harris Hip score mean with a five (5) point non-inferiority margin.

Harris Hip Scores

In **Tables 25** and **26**, Harris Hip Scores at different time points are presented for the 36mm All Enrolled and 36mm Subset Cohorts, respectively.

Table 25: Timecourse of Harris Hip Scores and Subscores: 36mm All Enrolled Cohort

	Interval																							
	Pre Op				6 Week				6 Month				12 Month				24 Month				24+ Month			
	I		C		I		C		I		C		I		C		I		C		I		C	
Total Score	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Excellent (91-100)	0	0.0	0	0.0	15	9.1	2	2.8	110	75.3	51	77.3	134	87.6	55	82.1	115	84.6	53	86.9	133	83.6	59	83.1
Good (81-90)	0	0.0	0	0.0	43	26.1	21	29.6	19	13.0	8	12.1	10	6.5	8	11.9	11	8.1	1	1.6	10	6.3	4	5.6
Fair (71-80)	0	0.0	1	1.4	54	32.7	26	36.6	5	3.4	3	4.5	5	3.3	1	1.5	7	5.1	2	3.3	6	3.8	3	4.2
Poor (<71)	168	100	73	98.6	52	31.5	21	29.6	11	7.5	3	4.5	4	2.6	3	4.5	3	2.2	5	8.2	8	5.0	3	4.2
Missing	0	0.0	0	0.0	1	0.6	1	1.4	1	0.7	1	1.5	0	0.0	0	0.0	0	0.0	0	0.0	2	1.3	2	2.8
Total	168	100	74	100	165	100	71	100	146	100	66	100	153	100	67	100	136	100	61	100	159	100	71	100

Table 26: Timecourse of Harris Hip Scores and Subscores: 36mm Subset Cohort

	Interval																							
	Pre Op				6 Week				6 Month				12 Month				24 Month				24+ Month			
	I		C		I		C		I		C		I		C		I		C		I		C	
Total Score	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Excellent (91-100)	0	0.0	0	0.0	10	10.5	2	5.3	60	72.3	28	75.7	78	89.7	32	86.5	65	81.3	29	90.6	80	84.2	33	86.8
Good (81-90)	0	0.0	0	0.0	27	28.4	17	44.7	13	15.7	4	10.8	5	5.7	1	2.7	8	10.0	0	0.0	6	6.3	3	7.9
Fair (71-80)	0	0.0	0	0.0	32	33.7	11	28.9	3	3.6	1	2.7	2	2.3	1	2.7	5	6.3	1	3.1	4	4.2	1	2.6

	Interval																							
	Pre Op				6 Week				6 Month				12 Month				24 Month				24+ Month			
	I		C		I		C		I		C		I		C		I		C		I		C	
Total Score	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Poor (<71)	98	100	40	100	26	27.4	8	21.1	7	8.4	3	8.1	2	2.3	3	8.1	2	2.5	2	6.3	4	4.2	1	2.6
Missing	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	2.7	0	0.0	0	0.0	0	0.0	0	0.0	1	1.1	0	0.0
Total	98	100	40	100	95	100	38	100	83	100	37	100	87	100	37	100	80	100	32	100	95	100	38	100

Secondary endpoint analyses were related to radiographic assessment, revision rate, and Visual Analog Scale (VAS) scores. A subject was considered to be a composite success at 24+Months if the subject's 24+Month Harris Hip Score was greater than or equal to 80, if the subject was a radiographic success, and if the subject had not had a revision. The radiographic success, absence of revision, and overall success rates are reported for the 36mm PMA Study 24+ Month Success/Failure Dataset in **Table 27**. The results demonstrate no clinically or statistically significant differences between investigational and control hips for radiographic success, absence of revision, or overall success in the 36mm PMA Study 24+ Month Success/Failure Dataset.

Table 27: Comparison of Clinical Success, Radiographic Success and Revision: 36mm All Enrolled Cohort

Patient Success Criteria	COC36 147 subjects	COP28 71 subjects	Fishers Exact p-value
*Clinical Success(at 24+ months)	134 / 147 (91.2%)	64 / 71 (90.1%)	0.8060
*Total Harris Hip Score >= 80	134 / 147 (91.2%)	64 / 71 (90.1%)	0.8060
*Mild - Slight - No Pain	136 / 147 (92.5%)	68 / 71 (95.8%)	0.5565
*Radiographic Success(at 24+ months)	143 / 147 (97.3%)	69 / 71 (97.2%)	1.0000
*Radiolucencies <= 2mm	143 / 147 (97.3%)	69 / 71 (97.2%)	1.0000
*Acetabular Migration <= 4mm	144 / 147 (98.0%)	69 / 71 (97.2%)	0.6616
*Acetabular Inclination <= 4 Degrees	144 / 147 (98.0%)	69 / 71 (97.2%)	0.6616
*Osteolysis None	144 / 147 (98.0%)	69 / 71 (97.2%)	0.6616
Absence of Revision	144 / 147 (98.0%)	69 / 71 (97.2%)	0.6616
OVERALL COMPOSITE SUCCESS RATE	**133 / 147 (90.5%)**	**64 / 71 (90.1%)**	**1.0000**

* Subjects who were revised were also considered to be clinical and radiographic failures, The denominator of 147 COC36 subjects includes 3 revised subjects who did not reach the 24-Month study endpoint but are shown in this table to be clinical and radiographic failures, and the denominator of 71 COP28 subjects includes 2 revised subjects who did not reach the 24-Month study endpoint but are shown in this table to be clinical and radiographic failures.

Similarly, the radiographic success, absence of revision, and overall success rates are reported in **Table 28** for the 36mm PMA Study 24+ Month Success/Failure Dataset Subset Cohort. The results demonstrate no clinically or statistically significant differences between investigational and control hips for radiographic success, absence of revision, or overall success in the 36mm Subset Cohort.

Table 28: Comparison of Clinical Success, Radiographic Success and Revision at 24+ Months: 36mm Subset Cohort

Patient Success Criteria	COC36 92 subjects	COP28 40 subjects	Fishers Exact p-value
Clinical Success(at 24+ months)	84 / 92 (91.3%)	36 / 40 (90.0%)	0.7541
*Total Harris Hip Score >= 80	84 / 92 (91.3%)	36 / 40 (90.0%)	0.7541
*Mild - Slight - No Pain	86 / 92 (93.5%)	38 / 40 (95.0%)	1.0000
*Radiographic Success(at 24+ months)	91 / 92 (98.9%)	38 / 40 (95.0%)	0.2179
*Radiolucencies <= 2mm	91 / 92 (98.9%)	38 / 40 (95.0%)	0.2179
*Acetabular Migration <= 4mm	91 / 92 (98.9%)	38 / 40 (95.0%)	0.2179
*Acetabular Inclination <= 4 Degrees	91 / 92 (98.9%)	38 / 40 (95.0%)	0.2179
*Osteolysis None	91 / 92 (98.9%)	38 / 40 (95.0%)	0.2179
Absence of Revision	91 / 92 (98.9%)	38 / 40 (95.0%)	0.2179
OVERALL COMPOSITE SUCCESS RATE	**84 / 92 (91.3%)**	**36 / 40 (90.0%)**	**0.7541**

* Subjects who were revised were also considered to be clinical and radiographic failures, The denominator of 92 COC36 subjects in the 36mm Supplement Cohort includes 1 revised subject who did not reach the 24-Month study endpoint but is shown in this table to be a clinical and radiographic failure, and the denominator of 40 COP28 subjects includes 2 revised subjects who did not reach the 24-Month study endpoint but are shown in this table to be clinical and radiographic failures.

Subjects were asked preoperatively and at follow-up visits to identify their level of pain on a visual analog scale. Specifically, a mark was placed on a line where one end denoted "NO PAIN" and the other denoted "SEVERE PAIN". The location of the mark on the line was proportionately converted to a 100 point scale with 0 denoting "NO PAIN" and 100 denoting "SEVERE PAIN". A presentation of VAS pain score means for the 36mm PMA Study subjects by treatment group over time is given in **Table 29**. The difference in means for 24+ Month Efficacy Dataset subjects at 24+ Months was not significant (p = 0.304) as presented in **Table 30.**

Table 29: Timecourse of Visual Analog Scale Means: 36mm All Enrolled Cohort

	Interval											
	Pre-Op		6 Week		6 Month		12 Month		24 Month		24 Month+	
	Mean	N	Mean	N	Mean	N	Mean	N	Mean	N	Mean	N
Treatment Type												
C	64.15	74	9.99	70	8.20	65	8.21	67	4.77	61	7.61	69
I	66.02	167	10.37	163	9.19	146	6.28	154	7.21	134	10.13	158

Table 30: Comparison of 24+ Month Visual Analog Scale Means: 36mm All Enrolled Cohort

Parameter	Treatment	N	Means	Standard Error of Difference	t-test p-value
24+Month VAS Score	**C**	**67**	**6.63**	**2.10**	**0.304**
	I	**146**	**8.48**		

A presentation of VAS pain score means for the 36mm Subset Cohort is given in **Table 31**. The difference in means for 24+ Month Efficacy Dataset subjects in the 36mm Subset Cohort at 24+ months was not significant (p=0.727) as presented in **Table 32**.

Table 31: Timecourse of Visual Analog Scale Means: 36mm Subset Cohort

	Interval											
	Pre-Op		6 Week		6 Month		12 Month		24 Month		24 Month+	
	Mean	N	Mean	N	Mean	N	Mean	N	Mean	N	Mean	N
Treatment Type												
C	65.78	40	8.95	38	8.65	37	9.87	38	4.22	32	5.41	37
I	67.46	97	10.43	94	9.48	83	5.93	89	8.34	78	10.14	94

Table 32: Comparison of 24+Month VAS Score Means: 36mm Subset Cohort

Parameter	Treatment	N	Means	Standard Error of Difference	t-test p-value
24+Month VAS Score	**C**	**37**	**5.41**	**2.72**	**0.080**
	I	**92**	**9.25**		

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

None.

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 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

CDRH determined that the applicant provided an adequate device description and the preclinical testing information to support a reasonable assurance of device safety.

A prospective, multi-center, non randomized, prospectively controlled Investigational Device Exemption (IDE) clinical investigation was conducted using 36 millimeter ceramic components of the DePuy Ceramax® Ceramic Total Hip System in the United States. The primary analysis was a non-inferiority test investigational group 24+ Month Harris Hip mean scores compared to the control group 24+ Month Harris Hip mean scores with a non-inferiority margin of five (5) points. This primary analysis, non-inferiority test was carried out on the 218 subjects in the 24+ Month Harris Hip dataset.

A. Safety Conclusions

The adverse effects of the investigational device were based on data collected in a clinical study conducted to support PMA approval as described above. The most commonly reported adverse events in the 36 millimeter ceramic components study related to the DePuy Ceramax® Ceramic Total Hip System were musculoskeletal. There were a total of 5 revisions in this study (3 investigational; 2 control), 2.1%, reported out of 242 subjects. The Kaplan-Meier Survivorship Analysis for the All Enrolled Cohort demonstrated a 97.5 % survivorship (95% confidence interval: 91.9%-99.2%) for the investigational subjects at 4.1 years and a 97.3 % survivorship (95% confidence interval: 89.6%-99.3%) for the control hips at 5.6 years. There was no clinical or statistical difference in the proportion of adverse events between the investigational and control cohorts. With respect to the 36mm Subset Cohort, the adverse event rates and revision rates were comparable.

B. Effectiveness Conclusions

The primary effectiveness of the investigational device was based on Harris Hip Scores (HHS). The secondary effectiveness results were based on the radiographic success, absence of revision/removal, and Visual Analog Scale (VAS) scores. In accordance with 21 CRF 860.7, the results provide a reasonable assurance of effectiveness as described above. In the 36 millimeter ceramic components study, there were 217 subjects in the 36mm All Enrolled 24+ Month Harris Hip dataset with an evaluable 24+ Months for Harris Hip Total score, demonstrating HHS means of 95.6 and 94.9 in the investigational and control groups, respectively. There were 132 subjects from the 36mm Subset Cohort in the 24+ Month Harris Hip dataset with an evaluable 24+ Months Harris Hip Total score demonstrating HHS means of 95.5 and 95.3 in the investigational and control groups, respectively. In both the 36mm All Enrolled cohort and the 36mm Subset Cohort (S-ROM® and Porocoat® Summit™ stems and Pinnacle® 100 and Pinnacle® Sector II cups), the investigational group 24+ Months Harris Hip score mean was non-inferior to the control group 24+Month Harris Hip score mean with a non-inferiority margin of five (5) points. In addition, there were no statistically significant differences between the investigational and control hips in the 36mm All Enrolled Cohort for radiographic outcomes or VAS assessments, and the 36mm Subset Cohort results were comparable.

C. Benefit-Risk Conclusions

The probable benefits of the device are also based on preclinical testing and clinical data collected in a clinical study conducted to support PMA approval as described above.

The 36mm Ceramax® Ceramic Total Hip System study was a non-inferiority study designed to test the hypothesis that the 36 millimeter performs no differently from a commercially available ceramic-on-polyethylene hip prosthesis system. Likewise, the risks to patients would be no greater than those associated with conventional ceramic-on-polyethylene hip prosthesis systems. Results from the clinical study demonstrated that the 36 millimeter Ceramax® Ceramic Total Hip System performed no differently from a commercially available ceramic-on-polyethylene hip prosthesis system, and, with the exception of device related noise, there were no differences in the reported operative and postoperative complications from the study. The inability to detect differences was limited by the design of the study. The study was also limited to patients having a specific diagnosis of noninflammatory degenerative joint disease (NIDJD) in only one hip, as well as other specific criteria including age, preoperative pain and activity levels. Use of the 36mm Ceramax® Ceramic Total Hip System was restricted to patients who met these criteria defined in the study protocol. Therefore, the safety and efficacy of the 36mm Ceramax® Ceramic Total Hip System for patients with conditions other than those that were defined by the study plan has not been established.

In conclusion, given the available information above, the data support that for the indicated patient population the probable benefits of the 36mm Ceramax® Ceramic Total Hip System outweigh the probable risks.

D. Overall Conclusions

The clinical data in this application support the reasonable assurance of safety and effectiveness of the 36mm DePuy Ceramax® Ceramic Total Hip System when used in accordance with the indications for use and indicated population. Therefore, CDRH believes that it is reasonable to conclude that the benefits of the use of the 36mm DePuy Ceramax® Ceramic Total Hip System for the target population outweighs the risk of surgery when used in accordance with the directions for use.

XIV. CDRH DECISION

CDRH issued an approval order on April 2, 2013. The final conditions of approval cited in the approval order are described below.

In addition to the conditions outlined above, you must conduct 3 post-approval studies outlined below.

1. Long-Term Follow-up of IDE COC36 patients: The applicant has to perform a single arm, multi-center (i.e., 5 IDE sites), prospective follow-up post-approval study of 80 patients implanted with the 36mm Ceramax® Ceramic-on-Ceramic

Acetabular Cup Prosthesis System. These subjects will be followed out to 10 years. A minimum of 80% of enrolled subjects will be confirmed to either have a surviving implant or to have had a revision at a minimum of 10 years post-operatively via clinical evaluation or telephone interview. The following information will be obtained at each post-op clinical visit: a Harris Hip evaluation, radiographic evaluation, subject evaluation and adverse event information. The applicant has also agreed to provide retrieval analysis for the explants made available because of the revision or removal surgeries or patient death. Device survivorship will be estimated with a Kaplan-Meier survivorship analysis at each year and at 5 years post-operatively.
Summary statistics will be provided for Harris Hip scores and change from baseline, overall and stratified by obesity. Cumulative rates for adverse events by adverse event, as well as by category (intraoperative, postoperative-operative site, systemic, and overall) will be provided.

2. Short to Mid-Term Follow-up of New COC36 Patients: The applicant has agreed to perform a single arm, multi-center (i.e., 5 IDE sites and 5 new sites), prospective follow-up post-approval study enrolling 170 new patients implanted with the 36mm Ceramax® Ceramic-on-Ceramic Acetabular Cup Prosthesis System. These subjects will be followed for a pre-op clinic visit at the time of consent, and then at 6 weeks, 1 year, 2 years, 3 years, 4 years, and 5 years. A minimum of 80% of enrolled subjects will be confirmed, either via clinical evaluation or telephone interview, to either have a surviving implant or have a revision after 5 years post-operatively. The following information will be obtained at each post-op clinical visit: a Harris Hip evaluation, radiographic evaluation, subject evaluation and adverse event information. The applicant has also agreed to provide retrieval analysis for the explants made available because of the revision or removal surgeries or patient death. Device survivorship will be estimated with a Kaplan-Meier survivorship analysis at each year and at 5 years post-operatively. Summary statistics will be provided for Harris Hip scores and change from baseline, overall and stratified by obesity. Cumulative rates for adverse events by adverse event, as well as by category (intraoperative, postoperative-operative site, systemic, and overall) will be provided.

3. COC36 PAS: UK & Australian National Joint Registry Data: The applicant has agreed to gather retrospectively and prospectively, short, medium and long-term information regarding the performance and safety of the commercially available 36mm Ceramax® Ceramic on Ceramic Total Hip System from series of subjects in the UK National Join Registry (UK NJR) and Australia Orthopaedic Association NJRR. The study will provide data 10 years post-op follow-up for all eligible patients. The applicant has agreed to provide compiled information on the device survivorship, reasons for revisions and revision data. The primary endpoint in this study is device survivorship, which will be estimated at 10 years post-operatively utilizing Kaplan Meier survival methodology.

The applicant has also agreed that progress reports will differentiate subjects who have received the approved US system (approved stem, head, liner, and shell combination), and patients who have component(s) which are not approved in the U.S. Sub-group analyses will be conducted which present survivorship analyses overall, and by sub-group cohort.

The applicant's manufacturing facilities were inspected and found to be in compliance with the device 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.