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
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

Date of FDA Notice of Approval: December 23, 2010

Expedited: Not applicable

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, pyogenic 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 heads 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.

BIOLOX® *delta* ceramic femoral heads

The alumina composite matrix ceramic heads have a 11/13 taper and are offered with outside diameters of 28mm in three (+0 mm, +3 mm and +6 mm) neck lengths . DePuy BIOLOX® *delta* ceramic femoral heads are only compatible with the DePuy femoral prostheses identified below.

BIOLOX® *delta* ceramic liner (insert)

The alumina composite matrix ceramic acetabular liners are offered in ten sizes with an internal diameter of 28mm. The ten sizes are offered in outer diameters of 48-66 mm in 2 mm increments. A taper-fit connection allows assembly into the mating metal acetabular shell components.

Pinnacle acetabular cups

The Pinnacle 100 acetabular cups are hemispherical type replacement prostheses with a single apex hole. The metal outer acetabular shell component is manufactured from Ti-6Al-4V (ASTM F620). A porous coating of commercially pure (CP) titanium beads (ASTM F1580) covers the outer surface of the shell. The metal outer shells have 48, 50, 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 titanium alloy (ASTM F136) femoral stem components.

The S-ROM titanium alloy femoral stems are for cementless use and are available in standard and lateralized versions with 11/13 trunnions. The stems are partially coated with a commercially pure titanium porous coating.

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, 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 2004 in the following countries: Australia, Austria, Belgium, China (Hong Kong), Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, India, Ireland, Israel, Italy, Korea, Malaysia, New Zealand, Netherlands, Philippines, Poland, Portugal, Russia, Singapore, Slovakia, Spain, Switzerland, 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 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: genitourinary disorders; gastrointestinal disorders; 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.
- 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.
- 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. A. Laboratory Studies

Ceramic Femoral Head Testing

Testing of the ceramic femoral heads was conducted in accordance with FDA's Ceramic Ball Guidance.[1]

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. Seven tests were

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1 FDA *Guidance Document for the Preparation of Premarket Notifications for Ceramic Ball Hip Systems* (January 10, 1995) available at: *http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080786.pdf*

performed using 28-11/13 (+6 mm) Biolox *delta* ceramic ball heads on titanium alloy trunnions from DePuy stems representing the worst case combination. The results showed that the average load to fracture for the 28-11/13 (+6 mm) heads was 61 kN, with no head fracturing below 42kN. The Ceramic Ball guidance document suggests a minimum average burst strength of 46kN with no individual failure below 20N, so the construct tested met the acceptance criteria.

Ceramic Head Fatigue Testing

Fatigue testing of three 28-11/13 (+6 mm) Biolox *delta* ceramic ball heads on titanium alloy 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. All specimens reached 10 million cycles without failure or formation of macroscopically detectable defects, meeting the requirements suggested by the FDA Ceramic Ball Guidance.[1]

Post-Fatigue Burst Testing

Following fatigue testing, burst testing of the three 28-11/13 (+6 mm) samples was performed, with a resulting average burst test value of 79 kN and a minimum value of 71 kN. These values exceed the 20kN requirement for the post-fatigue burst strength suggested by the FDA Ceramic Ball Guidance.[1]

Ceramic Head Axial Pull-off Testing

Three 28-11/13 (+6 mm) Biolox *delta* ceramic ball heads were tested for pull-off loads using titanium alloy trunnions. The average pull-off load for the 28-11/13 (+6 mm) samples was 1627 N. The ceramic head testing results indicate that the ceramic heads possess sufficient strength to perform as intended under expected *in vivo* loading conditions.

Ceramic Liner Testing

Testing of the Ceramax™ Ceramic Total Hip System ceramic inserts was conducted by DePuy, and the test protocol was modeled on FDA Ceramic Ball Guidance.[1]

Ceramic Liner Burst Test

The purpose of this test was to determine the minimum burst strength (static axial compression fracture load) for the smallest ceramic liners. Seven worst case 28/48 mm ceramic liner/48 mm acetabular metal shell assemblies were static burst tested using Biolox *delta* (zirconia composite) ceramic heads. The acceptance criterion was defined as average burst strength greater than 46 kN with no single sample below 25 kN. The minimum burst value criterion is based upon that suggested for ceramic femoral heads in the FDA Ceramic Ball Guidance[1] (no requirements currently exist for ceramic liners).

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1 FDA *Guidance Document for the Preparation of Premarket Notifications for Ceramic Ball Hip Systems* (January 10, 1995) available at: *http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080786.pdf*

The mean static axial compressive fracture load for the DePuy ceramic insert was > 247 kN with no values below 215 kN. Three ceramic inserts did not fail at 260 kN, the highest load attainable by the test machine. Four inserts failed by chipping at the edge of the insert. This result exceeds the acceptance criteria. The ceramic liner burst testing demonstrates that the liners possess adequate strength to perform as they are intended under expected *in vivo* loading conditions.

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 28/48 mm ceramic liner/48 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. No failures or fractures occurred.

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 per the DePuy qualification procedure.

Fatigued alumina composite matrix liners were then burst tested using systems comprised of the Biolox *delta* ceramic heads and liners. The mean post fatigue burst strength for the DePuy ceramic insert was 200 kN with no values below 116 kN. This result exceeds the acceptance criterion and the 20 kN value suggested for ceramic femoral heads in the FDA Ceramic Ball Guidance[1] (no requirements currently exist for ceramic liners). The ceramic liner testing demonstrates that the liners possess adequate strength to perform as they are intended under expected *in vivo* loading conditions.

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. Three worst case smallest (28/48 mm ceramic liner/48 mm acetabular metal shell) assemblies underwent pre-fatigue push-out force testing.

The acceptance criterion required an average push-out value greater than 200 N. The mean pre-fatigue push-out force for the 28/48 mm liner/48 mm shell was 1345 N with no values below 1272 N. The subject pre-fatigue push-out strength is greater than the 200N criterion value.

The integrity of the ceramic liner/shell connection (i.e., locking mechanism) of the acetabular system as tested in pre-fatigue push-out demonstrates that the ceramic/metal shell construct locking mechanism exceeds the 200N acceptance criterion and should perform as intended under expected *in vivo* loading conditions.

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 28/48 mm ceramic liner/48 mm acetabular metal shells underwent torsional testing. The 28/48 mm liner/48 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 criterion was defined as an average torsional force greater than 4 N*m (400 N*cm). The mean rotational moment (torque) of the acetabular construct was 2994 N*cm with no values below 2911 N*cm.

The integrity of the ceramic liner/shell connection (i.e., locking mechanism) of the acetabular system as tested in torsion demonstrates that the ceramic/metal shell construct locking mechanism exceeds the 400 N*cm acceptance criteria, and therefore, should perform as intended under expected *in vivo* loading conditions.

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 28/48 mm ceramic liner/48 mm acetabular metal shells underwent lever-out testing.

The 28/48 mm liner/48 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 acetabular construct was 14,532 N*cm with no values below 12,229 N*cm. The integrity of the ceramic liner/shell connection (i.e., locking mechanism) of the acetabular system as tested in lever-out testing demonstrates that the ceramic liner/metal shell construct locking mechanism exceeds the 3000 N*cm acceptance criterion, and therefore, should perform as intended under expected *in vivo* loading conditions.

Range of Motion, Head/Liner Constraint

The DePuy Ceramax™ Ceramic Total Hip System is a semi-constrained total hip system in that it limits movement in one or more planes due to the geometry of its articulating surfaces. 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 representing worst case scenarios to establish the worst case (minimum) ROM values.

The acceptance criterion was defined as ROM > 112° in the anterior/posterior direction. The worst case (least ROM) combination of implants was determined to be the 28 mm x 54 mm ceramic insert with the S-ROM (11/13 taper) femoral stems. This combination yielded 130° minimum ROM in the anterior/posterior direction with the DePuy S-ROM femoral stem. The minimum ROM in the medial/lateral direction was determined to be 122°. All construct combinations exceeded the established acceptance criterion.

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 28mm Biolox *delta* (28/48 mm acetabular shell) ceramic-on-ceramic couple (n=3) to that of a 36 mm (36/52 mm acetabular shell) metal-on-metal couple (n=2). The acceptance criterion for this wear test was lower volumetric wear generated by the 28 mm Biolox *delta* ceramic-on-ceramic couple than for a 28 mm metal-on-crosslinked polyethylene couple (stated to be 4 mm^3 per million cycles).

A 10-station ProSim simulator was used to perform the test. The cups were mounted anatomically above the head at an angle of 35° to the horizontal. The synchronized load and motion cycles were applied at 1Hz. The test was carried out in 25% concentration of newborn calf serum, changed approximately every 350,000 cycles. Nine measurement intervals were taken during the test out to 5 million cycles. Wear was measured via gravimetric wear assessment at each interval.

The average wear rate for the 28 mm Biolox *delta* ceramic-on-ceramic articulation was calculated to be 0.0101 mm^3 per million cycles. This is lower than both the acceptance criterion (5 mm^3 per million cycles) and the wear rate for the 36 mm metal-on-metal couple (0.397 mm^3 per million cycles). 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*.

The wear results demonstrated that the ceramic-on-ceramic articulation surfaces used for the DePuy Ceramax™ Ceramic Total Hip System produce no significant wear after five million cycles.

The results of *in vitro* simulation have not been proven to directly correlate with clinical device performance and wear mechanisms.

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]

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 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 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, including packaging seal and integrity, accelerated aging, and real-time aging testing, was performed to verify sterile packaging integrity equivalent to 11 years for the Ceramax™ Ceramic Total Hip System.

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2 *FDA Guidance Document for Testing Orthopedic Implants with Modified Metallic Surfaces Apposing Bone or Bone Cement* (April 28, 1994) available at: http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm081247.pdf

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}

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a 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. Data from this 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, DePuy Pinnacle 100 acetabular cups), were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

Patients were treated between October 28, 2003 and December 28, 2005. The database for this PMA reflected data collected from October 2003 to February 2008 and included 264 patients. The first surgery occurred on October 28, 2003 and the last surgery on December 28, 2005. There were eight (8) investigational sites and 13 surgeons.

The study was a prospective, multi-center, randomized (2 to 1), single-blind, controlled clinical study. 28mm ceramic-on-ceramic hip components of the DePuy Ceramax™ Ceramic Total Hip System (COC28) were compared to a conventional 28mm ceramic-on -polyethylene articulation hip system (COP28).

The investigational group (n=177 patients) received commercially-available cementless porous coated acetabular cup prosthesis (Pinnacle™) and a ceramic bearing insert (Ceramax™) with a 28mm inner diameter. The control group (n=87 patients) received commercially-available cementless porous-coated acetabular cup prosthesis (Pinnacle™) and a polyethylene bearing insert (Marathon™) with a 28mm inner diameter. There was one (1) bilateral case. 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 Summit™, S-ROM®, Prodigy™, AML, and Corail™ hip stems. Pinnacle 100, Pinnacle 300 and Pinnacle Sector II acetabular cups were used. Commercially available 28mm 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 components studied in the IDE: S-ROM femoral stems and Pinnacle 100 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

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, 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 $\geq$ 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.

4. Subset Cohort of S-ROM Femoral Stems and Pinnacle 100 Acetabular Cups:
   The applicant is only currently seeking marketing approval for the S-ROM femoral stem and Pinnacle 100 acetabular cup as components for the Ceramax™ Ceramic Total Hip System. Among the 264 subjects enrolled in the IDE study, 69 received an S-ROM/Pinnacle 100 combination. Various analyses were carried out on this Subset Cohort in addition to analyses on the all enrolled cohort.

B. Accountability of PMA Cohort

All Enrolled Cohort

At the time of database lock, of 264 patients enrolled in this PMA study, 85% (148/177) of the investigational subjects and 86% (71/87) of the control patients were available for analysis at the completion of the study, the 24+ Month postoperative visit for the evaluation of the safety and effectiveness of this device. This is summarized in **Table 3** below.

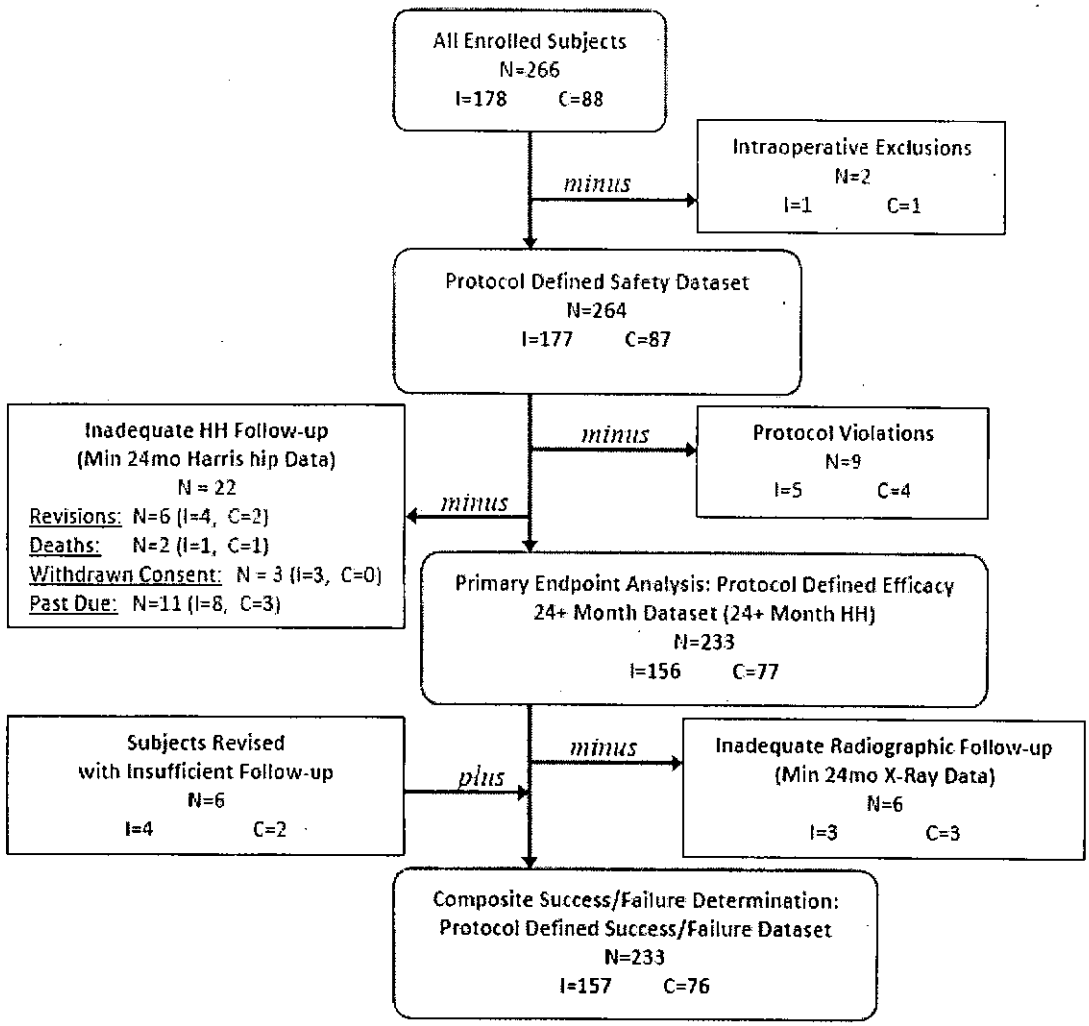
Table 3: Subject Accounting for the All Enrolled Cohort

IDE Study Cohort	Pre-Op		6 Week		6 Month		12 Month		24 Month		24+ Months	
	I	C	I	C	I	C	I	C	I	C	I	C
Theoretical Due	177	87	177	87	177	87	177	87	177	87	177	87
Expected Due	177	87	177	86	177	85	176	85	174	83	174	83
Withdrawn: Deaths (Cumulative)	0	0	0	0	0	1	0	1	1	2	1	2
Withdrawn: Components Removed/Revised (Cumulative)	0	0	0	1	0	1	1	1	2	2	2	2
Withdrawn: Consent (Cumulative)	0	0	0	0	1	0	1	0	2	0	3	0
Actual	173	87	156	82	154	78	162	79	148	71	158*	76
%Follow-up = Actual / Expected Due	98%	100%	88%	95%	87%	92%	92%	93%	85%	86%	91%	92%

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+ months data had been obtained.
*2 patients were revised prior to 24 months, but continued for follow-up.

Figure 1 below is a dataset flowchart which shows all 264 subjects in the Safety Dataset, and the order in which they were excluded, from top to bottom, to obtain the Efficacy 24+ Month and 24+ Month Success/Failure datasets; revisions were retained for analysis regardless of exclusion criteria. The primary endpoint non-inferiority test of 24+ Month Harris Hip score means was carried out on the Efficacy 24+ Month Dataset.

Figure 1: Subject Accounting Dataset Flowchart: All Enrolled Cohort



Subset Cohort of Subjects with S-ROM Femoral Stems and Pinnacle 100 Acetabular Cups

The primary analysis was based on five femoral stem types and three acetabular cup types; however, the applicant is only currently seeking marketing approval for the S-ROM femoral stems and Pinnacle 100 acetabular cups as components for the Ceramax™ Ceramic Total Hip System. There were 45 investigational and 24 control subjects in the Safety Dataset who received an S-ROM stem and Pinnacle 100 cup. At the time of database lock, complete 24+ Month postoperative Harris Hip data (study endpoint) was available on 42 investigational and 23 control subjects in the Subset Cohort who received the S-ROM femoral stem and Pinnacle 100 acetabular cup. This is summarized in **Table 4** below.

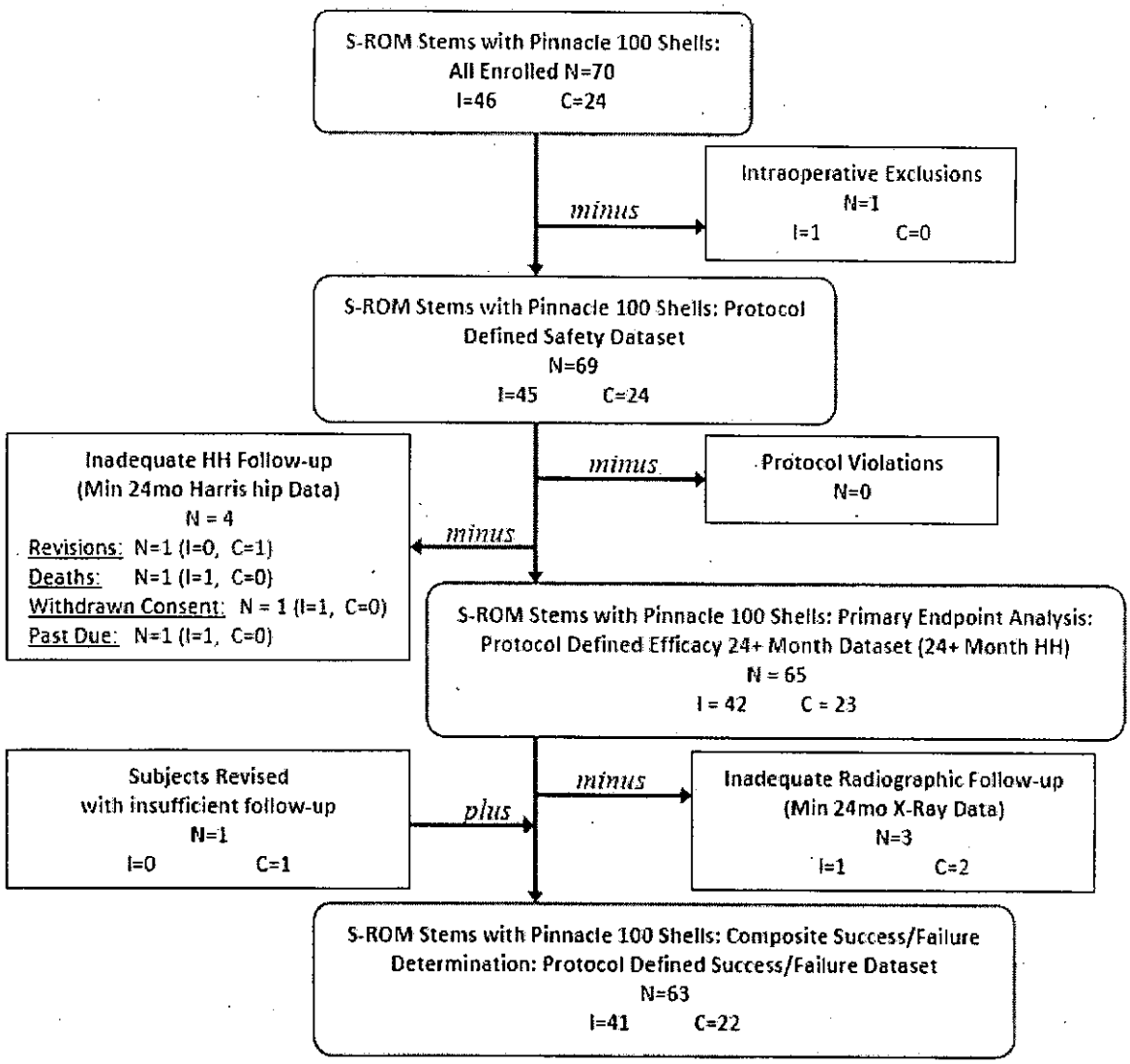
Table 4: Subject Accounting for the Subset Cohort

Subset Cohort	Pre-Op		6 Week		6 Month		12 Month		24 Month		24+ Months	
	I	C	I	C	I	C	I	C	I	C	I	C
Theoretical Due	45	24	45	24	45	24	45	24	45	24	45	24
Expected Due	45	24	45	23	45	23	45	23	44	23	43	23
Withdrawn: Deaths (Cumulative)	0	0	0	0	0	0	0	0	1	0	1	0
Withdrawn: Components Removed/Revised (Cumulative)	0	0	0	1	0	1	0	1	0	1	0	1
Withdrawn: Consent (Cumulative)	0	0	0	0	0	0	0	0	0	0	1	0
Actual	45	24	40	22	35	21	41	22	34	18	40	21
%Follow-up = Actual / Expected Due	100%	100%	89%	96%	78%	91%	91%	96%	77%	78%	91%	91%

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 69 S-ROM and Pinnacle 100 subjects in the Safety Dataset, and the order in which they were excluded, from top to bottom, to obtain the Subset Cohort of subjects in the Efficacy 24+ Month and 24+ Month Success/Failure datasets; revisions were retained for composite success analysis, regardless of exclusion criteria.

Figure 2: Subject Accounting Dataset Flowchart: Subset Cohort



C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a total hip replacement study performed in the U.S. Clinical study data was collected on 264 hips implanted. There were 177 investigational hip implantations and 87 control hip implantations in the Protocol Defined Safety Dataset for the 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 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: Baseline Demographics for the All Enrolled Cohort

Demographic Element		Investigational N=177	Control N=87	Investigational vs. Control p-values
Enrollment	Number of procedures	177	87	-
	Number of patients	177	87	-
Age in years	Mean Age	56.4	57.3	0.537
	Minimum Age	20	29	
	Maximum Age	75	77	
Gender	Females	87 (49%)	40 (46%)	0.695
	Males	90 (51%)	47 (54%)	
Body Mass Index [kg / m^2]	Mean BMI	30.1	29.8	0.787
	Minimum BMI	18.5	18.2	
	Maximum BMI	53.1	51.0	
Primary Diagnosis	Avascular Necrosis	12 (7%)	4 (5%)	0.591
	Developmental Dysplasia	5 (3%)	1 (1%)	0.667
	Epiphyseal Defect	0 (0%)	2 (2%)	0.108
	Osteoarthritis	155 (88%)	78 (90%)	0.689
	Post Traumatic Arthritis	5 (3%)	2 (2%)	1.000
Harris Hip Score	Mean Pre-Op HH Score	50.6	50.7	0.960
	Minimum Pre-Op HH Score	21.0	26.0	
	Maximum Pre-Op HH Score	71.0	76.0	
Harris Hip Pain Category (Range 0-44)	Mean Pre-op HH Pain	14.3	13.6	0.265
	Minimum Pre-op HH Pain	10.0	10.0	
	Maximum Pre-op HH Pain	20.0	30.0	
Harris Hip Function Score (Range 0-33)	Mean Pre-op HH Function	20.0	19.8	0.785
	Minimum Pre-op HH Function	0.0	5.0	
	Maximum Pre-op HH Function	30.0	30.0	
Harris Hip Activity Score (Range 0-14)	Mean Pre-op HH Activity	8.2	8.7	0.127
	Minimum Pre-op HH Activity	2.0	1.0	
	Maximum Pre-op HH Activity	12.0	14.0	
Harris Hip Deformity Score (Range 0-4)	Mean Pre-op HH Deformity	3.5	3.8	0.107
	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	0.223
	Minimum Pre-op HH ROM	3.4	3.4	
	Maximum Pre-op HH ROM	5.0	5.0	

The demographics of the subset cohort (subjects who received an S-ROM femoral stem and Pinnacle 100 acetabular cup) study population are typical for a total hip replacement

study performed in the U.S. and consistent with the demographics of the 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 Subset Cohort of the 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 6** below.

Table 6: Baseline Demographics for the Subset Cohort

Demographic Element		**Investigational N=45**	**Control N=24**	**Investigational vs. Control p-values**
Enrollment	Number of procedures	45	24	-
	Number of patients	45	24	-
Age in years	Mean Age	58.7	57.6	0.607
	Minimum Age	33	45	
	Maximum Age	75	75	
Gender	Females	19 (42%)	11 (46%)	0.803
	Males	26 (58%)	13 (54%)	
Body Mass Index [kg / m^2]	Mean BMI	27.3	27.8	0.683
	Minimum BMI	18.5	18.8	
	Maximum BMI	36.2	38.7	
Primary Diagnosis	Avascular Necrosis	1 (2%)	0 (0%)	1.000
	Developmental Dysplasia	1 (2%)	0 (0%)	1.000
	Epiphyseal Defect	0 (0%)	0 (0%)	-
	Osteoarthritis	43 (96%)	24 (100%)	0.540
	Post Traumatic Arthritis	0 (0%)	0 (0%)	-
Harris Hip Score	Mean Pre-Op HH Score	52.0	48.8	0.100
	Minimum Pre-Op HH Score	36.0	34.0	
	Maximum Pre-Op HH Score	66.0	63.0	
Harris Hip Pain Category (Range 0-44)	Mean Pre-op HH Pain	14.2	12.1	0.077
	Minimum Pre-op HH Pain	10.0	10.0	
	Maximum Pre-op HH Pain	20.0	20.0	
Harris Hip Function Score (Range 0-33)	Mean Pre-op HH Function	21.1	20.1	0.291
	Minimum Pre-op HH Function	10.0	7.0	
	Maximum Pre-op HH Function	27.0	24.0	
Harris Hip Activity Score (Range 0-14	Mean Pre-op HH Activity	8.9	8.3	0.161
	Minimum Pre-op HH Activity	5.0	3.0	
	Maximum Pre-op HH Activity	12.0	10.0	
Harris Hip Deformity Score (Range 0-4)	Mean Pre-op HH Deformity	3.1	3.5	0.333
	Minimum Pre-op HH Deformity	0.0	0.0	
	Maximum Pre-op HH Deformity	4.0	4.0	
Harris Hip	Mean Pre-op HH ROM	4.6	4.6	0.465

Demographic Element		Investigational N=45	Control N=24	Investigational vs. Control p-values
Range of Motion Score (Range 0-5)	Minimum Pre-op HH ROM	3.5	3.8	
	Maximum Pre-op HH ROM	5.0	5.0	

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the following:

- Adverse events
- A Kaplan-Meier survivorship analysis of revisions

The analysis of safety was based on all 264 enrolled subjects (177 investigational and 87 control cohorts) followed over the 24+ Month evaluation.

The key safety outcomes for this study are presented below in **Tables 7** through **20**.

Adverse events that occurred in the 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 4 revisions (2.3%) reported out of 177 procedures in the investigational cohort and 2 revisions (2.3%) reported out of 87 procedures in the control cohort at 24+ months. **Table 7** provides a summary of the revision procedure, treatment group, age, gender, primary diagnosis, duration of implantation and reason for revision for each subject. There appears to be no clinically meaningful difference in rates of revision between the investigational and control treatments.

Table 7: 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
S,I	Investigational	70 / M	Osteoarthritis	9 months	Deep infection diagnosed in operative hip
S, H, I	Investigational	57 / F	Osteoarthritis	18 months	Acetabular liner failure
F, H	Investigational	53 / M	Osteoarthritis	12 months	Femoral component loosening
F, H	Investigational	41 / M	Post-traumatic Arthritis	22 months	Stem revision due to patient fall
H, I	Control	68 / F	Osteoarthritis	20 months	Recurrent dislocations
H, I	Control	62 / 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 97.6 % survivorship (95% confidence interval: 93.7%-99.1%) for the investigational subjects at 3.2 years and a 97.6 % survivorship (95% confidence interval: 90.9%-99.4%) for the control hips at 2.9 years. There was no clinically or statistically significant difference between investigational and control subjects (log-rank p-value =0.992).

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

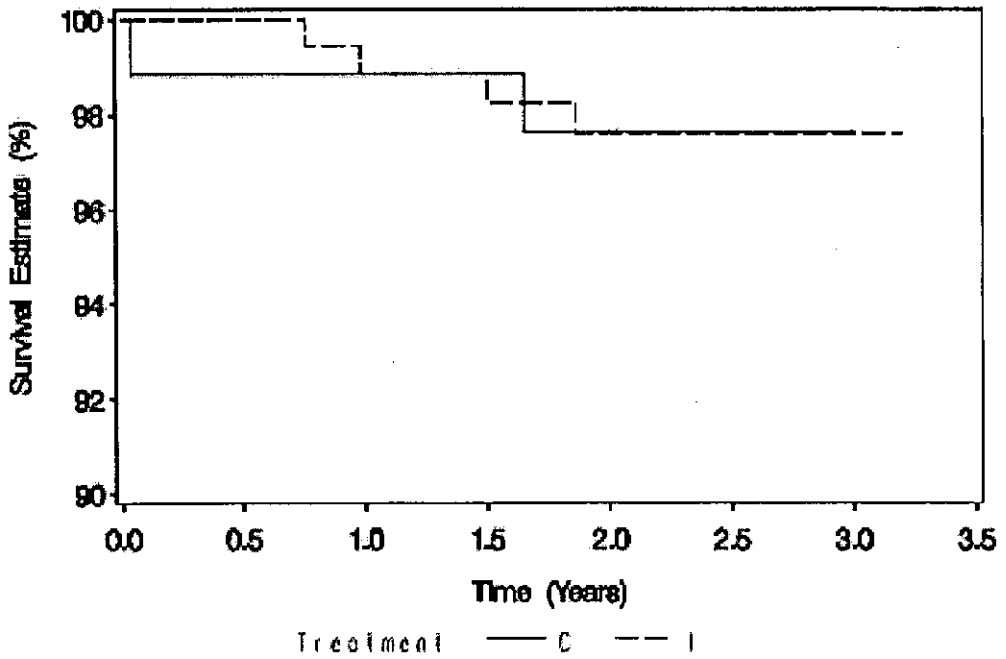
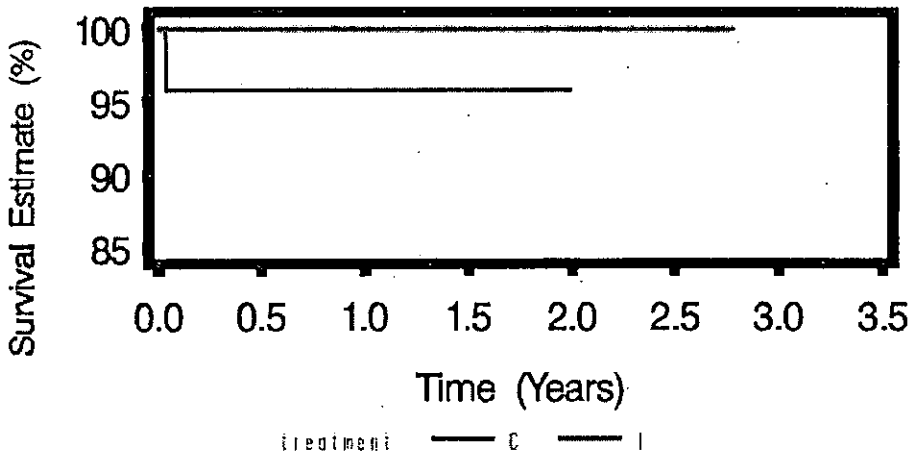


Table 8: Safety Dataset - Survival Estimates Across Time: All Enrolled Cohort

	Timecourse						
Treatment	0 months	6 months	1 year	1.5 years	2 years	2.5 years	3 years
Investigational: Survival Estimate	100%	100%	98.9%	98.2%	97.6%	97.6%	97.6%
Investigational: # Hips Remaining	177	175	171	161	126	82	57
Control: Survival Estimate	100%	98.9%	98.9%	97.6%	97.6%	97.6%	97.6%
Control: # Hips Remaining	87	84	83	81	65	42	23

Survivorship analyses for the Subset Cohort (subjects who received S-ROM and Pinnacle 100 components only) are presented graphically in **Figure 4** and in tabular form across time in **Table 9**. Results for the Subset Cohort demonstrated a 100% survivorship (95% confidence interval: not evaluable because of no observed failures) for the investigational subjects at 2.8 years and a 95.8% survivorship (95% confidence interval: 73.9%-99.4%) for the control hips at 2.0 years. There was no clinically or statistically significant difference between investigational and control subjects (log-rank p-value =0.171). Note that the curves were terminated at the point where evaluable hips were equal to 20, due to the inaccuracy of survivorship beyond this point.

Figure 4: Kaplan-Meier Survivorship Estimates: Subgroup Cohort



Event=Revision for any reason

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

	Timecourse					
Treatment	0 months	6 months	1 year	1.5 years	2 years	2.5 years
Investigational: Survival Estimate	100%	100%	100%	100%	100%	100%
Investigational: # Hips Remaining	45	45	44	42	34	22
Control: Survival Estimate	100%	95.8%	95.8%	95.8%	95.8%	95.8%
Control: # Hips Remaining	24	23	23	23	20	15

Adverse events reported from the clinical study of 264 hip procedures are listed in **Tables 7, 10, 12, 14, 16,** and **18-20** below.

Adverse Events by Subject

In **Tables 10** through **15** below, every unique adverse event was reported once per subject, 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 femoral bone fracture, which was observed in 2.8% of investigational subjects (5/177). There was no statistically or clinically meaningful difference in the proportions of observed intraoperative adverse events across treatment groups (see **Table 10** below). Fisher's exact test was used to compare proportions across the two treatment groups.

Table 10: Comparison of Frequency of Intraoperative Adverse Events for the All Enrolled Cohort

	Investigational N=177		Control N=87		
Adverse Events at 24+ Months	**AEs (%)**	**95% Confidence Levels**	**AEs (%)**	**95% Confidence Levels**	**p-value**
Fracture of Femur	5 (2.8%)	0.9 – 6.5	1 (1.1%)	0.0 – 6.2	0.667
Difficulty Seating Femoral Component	1 (0.6%)	0.0 – 3.1	1 (1.1%)	0.0 – 6.2	0.551
Nerve Damage	1 (0.6%)	0.0 – 3.1	0 (0.0%)	-	1.000
Hematological	1 (0.6%)	0.0 – 3.1	0 (0.0%)	-	1.000
Genitourinary	1 (0.6%)	0.0 – 3.1	0 (0.0%)	-	1.000
Musculoskeletal*	1 (0.6%)	0.0 – 3.1	0 (0.0%)	-	1.000
Liner Fracture During Surgery**,†	2 (1.2%)	0.1 – 4.1	0 (0.0%)	-	1.000
Difficulty Seating Liner w/o Fracture**	1 (0.6%)	0.0 – 3.1	0 (0.0%)	-	1.000
Difficulty Seating Liner**,†,‡	3 (1.7%)	0.3 – 4.8	0 (0.0%)	-	0.553
Dermatological	0 (0.0%)	-	1 (1.1%)	0.0 – 6.2	0.330
Blemish on Ceramic Component	0 (0.0%)	-	1 (1.1%)	0.0 – 6.2	0.330
Total	12 (6.8%)	-	4 (4.6%)	-	-

** One investigational subject had difficulty in broaching the femoral canal (musculoskeletal) and difficulty seating the femoral component.*

***Three subjects experienced difficulty seating the liner; 2 of these experienced a ceramic liner fracture upon attempted removal of the mal-positioned liner.*

† N = 178 for the investigational group, consisting of 177 enrolled investigational subjects + 1 intent to treat subject who received a polyethylene liner subsequent to intraoperative ceramic liner fracture.

‡Difficulty Seating Liner includes 1 subject w/o fracture, which is also listed separately in this table.

There were three (3) intraoperative complications among subjects in the S-ROM/Pinnacle 100 Subset Cohort, 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 for the Subset Cohort

	Investigational N=45		Control N=24		
Adverse Events at 24+ Months	**AEs (%)**	**95% Confidence Levels**	**AEs (%)**	**95% Confidence Levels**	**p-value**
Dermatological	0 (0.0%)	-	1 (4.2%)	0.1 – 21.1	0.348
Liner Fracture During Surgery*,†	1 (2.2%)	0.1 – 11.5	0 (0.0%)	-	1.00
Difficulty Seating Liner*,†	1 (2.2%)	0.1 – 11.5	0 (0.0%)	-	1.00
Total	2 (4.4%)	-	1 (4.2%)	-	-

**One subject experienced difficulty seating the liner, and also experienced a ceramic liner fracture upon attempted removal of the mal-positioned liner.*

† N = 46 for the investigational group, consisting of 45 enrolled subjects + 1 intent to treat subject who received a polyethylene liner subsequent to intraoperative ceramic liner fracture.

3. Postoperative-Systemic Adverse Events

For both the investigational and control treatments the most commonly reported postoperative systemic complication was musculoskeletal. Frequently reported adverse events also included: cardiovascular, genitourinary, gastrointestinal, respiratory, and dermatological.

There was no statistically or clinically meaningful difference in the proportion of postoperative systemic adverse events (see **Table 12** below).

Although no patient complaints about audible 'squeaking' throughout the 24+ months time course were reported, this study did not directly address this issue; therefore, this clinical concern cannot be reported on at this time.

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

	Investigational N=177			Control N=87			
Adverse Events at the 24+ Months	**AEs**	**%**	**95% Confidence Levels**	**AEs**	**%**	**95% Confidence Levels**	**p-value**
Cancer	5	2.8	0.9 – 6.5	2	2.3	0.3 – 8.1	1.000
Cardiovascular	12	6.8	3.5 – 11.5	6	6.9	2.6 – 14.4	1.000
Central Nervous System	3	1.7	0.3 – 4.9	3	3.4	0.7 – 9.8	0.339
Dermatological	7	4.0	1.6 – 8.0	2	2.3	0.3 – 8.1	0.722
Endocrine/Metabolic	4	2.3	0.6 – 5.7	5	5.7	1.9 – 12.9	0.161
Gastrointestinal	9	5.1	2.3 – 9.4	5	5.7	1.9 – 12.9	0.779
Genitourinary	14	7.9	4.4 – 12.9	7	8.0	3.3 – 15.9	1.000
Heent	2	1.1	0.1 – 4.0	2	2.3	0.3 – 8.1	0.600
Hematological	3	1.7	0.3 – 4.9	4	4.6	1.3 – 11.4	0.223
Musculoskeletal	84	47.5	44.9 – 60.1	43	49.4	38.5 – 60.4	0.794
Neurological	2	1.1	0.1 – 4.0	0	0.0	-	1.000
Other*	13	7.3	4.0 – 12.2	7	8.0	3.3 – 15.9	0.810
Peripheral Nervous System	4	2.3	0.6 – 5.7	1	1.1	0.0 – 6.2	1.000
Psychological	1	0.6	0.0 – 3.1	0	0.0	-	1.000
Respiratory System	9	5.1	2.3 – 9.4	4	4.6	1.3 – 11.4	1.000
Thrombosis / Thrombophlebitis	2	1.1	0.1 – 4.0	1	1.1	0.0 – 6.2	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.

Additional Notes:

*** Frequency of Systemic AEs reported as "Other", Investigational:** Papular red erythema treated with hydrocortisone-1; Non-displaced patella treated with knee immobilizer-1; Bursitis treated with anti-inflammatories-2; ENNT (Pre-Glaucoma) treated with eye drops-1; Prophylactic antibiotics for dental procedure- 2; Fever that delayed discharge from hospital- 1; Weak and wobbly needing reassurance- 1; Cellulite left tibia prescribed antibiotic-1; Mild leg pain- 1; Non cardiac chest pain & degenerative disc disease- 1; Leakage of silicone breast implants and surgical removal of breast implants- 1. **Frequency of Systemic AEs reported as "Other", Control:** Prophylactic antibiotics for dental procedure- 4; Bursitis- 1; Lumbar spine and left knee pain/left knee arthroscopy and subject fall- 1; and Spider bite- 1.

For the Subset Cohort, the most frequent postoperative systemic adverse events were musculoskeletal, cardiovascular, genitourinary, and respiratory. There appears to be no clinically meaningful difference in rates of postoperative systemic adverse events between the investigational and control treatments (see **Table 13** below).

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

	Investigational N=45		Control N=24	
Adverse Events at 24+ Months	**AEs**	**%**	**AEs**	**%**
Cardiovascular	2	4.4	1	4.2
Dermatological	0	0.0	1	4.2
Gastrointestinal	1	2.2	1	4.2
Genitourinary	2	4.4	2	8.3
HEENT	1	2.2	0	0.0
Hematological	0	0.0	2	8.3
Musculoskeletal	14	31.1	9	37.5
Neurological	1	2.2	0	0.0
Peripheral Nervous System	1	2.2	0	0.0
Psychological	1	2.2	0	0.0
Respiratory System	3	6.7	1	4.2

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. Postoperative Operative Site Adverse Events

The most commonly reported postoperative operative site complications for investigational and control subjects were wound problems and bursitis, respectively. Other complications included dislocation, muscle weakness, and end of stem pain. There appear to be no statistically or clinically meaningful differences in the proportions of postoperative operative site adverse events (see **Table 14** below).

Table 14: Comparison of Frequency of Postoperative Operative Site Adverse Events: All Enrolled Cohort

	Investigational N=177			Control N=87			
Adverse Events at 24+ Months	**AEs**	**%**	**95% Confidence Levels**	**AEs**	**%**	**95% Confidence Levels**	**p-value**
Acetabular Liner Failure [1]	1	0.6	0.0 – 3.1	0	0.0	-	1.000
Bone Lysis [2]	1	0.6	0.0 – 3.1	0	0.0	-	1.000
Component Fracture[1]	1	0.6	0.0 – 3.1	0	0.0	-	1.000
Deep Infection [2,3]	2	1.1	0.1 – 4.0	0	0.0	-	1.000
Dislocation [4]	5	2.8	0.9 – 6.5	4	4.6	1.3 – 11.4	0.483
Femoral Component Loosening [5]	3	1.7	0.3 – 4.9	0	0.0	-	0.553
Fracture [6]	2	1.1	0.1 – 4.0	0	0.0	-	1.000
Heterotopic Bone Formation	1	0.6	0.0 – 3.1	0	0.0	-	1.000
Muscle Weakness	5	2.8	0.9 – 6.5	0	0.0	-	0.175
Other[7]	16	9.0	5.3 – 14.3	12	13.8	7.3 – 22.9	0.288
Other – Neurological[8]	1	0.6	0.0 – 3.1	0	0.0	-	1.000
Other - Bursitis	6	3.4	1.3 – 7.2	5	5.7	1.9 – 12.9	0.513
Other – End Of Stem Pain	4	2.3	0.6 – 5.7	0	0.0	-	0.306
Other - Iliopsoas Tendonitis	1	0.6	0.0 – 3.1	0	0.0	-	1.000
Wound Problem[9]	9	5.1	2.4 – 9.4	2	2.3	0.3 – 8.1	0.349

	Investigational N=177			Control N=87			
Adverse Events at 24+ Months	**AEs**	**%**	**95% Confidence Levels**	**AEs**	**%**	**95% Confidence Levels**	**p-value**

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 'bone lysis', then that adverse event was listed in addition to the 'deep infection' adverse event.

Additional Notes:

1 This investigational subject was seen more than one time and the adverse event was initially reported as a component fracture and at the time of revision surgery was confirmed as an acetabular liner failure.

2 Bone lysis was reported secondary to deep infection for one subject.

3 Two investigational subjects had deep infections. One subject had a resection arthroplasty. In the other subject, an I&D was performed and the components were retained.

4 Two control hips were revised to treat recurrent dislocations.

5 Two investigational hips were revised for loose femoral components. The acetabuli were retained.

6 A greater trochanter fracture was reported for 1 investigational subject secondary to recurrent dislocations and this subject was treated with open reduction internal fixation.

7 **Frequency of Operative Site AEs reported as "Other", Investigational**: Blister treated with tagaderm-1; Groin pain secondary to slipping treated conservatively-1; Hematoma secondary to fall and trochanteric bursitis-1; Groin tendonitis treated with medications-1; muscle pain treated with medication- 1; leg swelling-1; general musculoskeletal treated with medications and hip pain after a fall-2; subject fell- 1; hip/thigh pain -1; adductor strain treated conservatively-1; subject trauma treated with reduced weight bearing and medications-1; warm incision-1; Hamstring tendonitis treated with physical therapy-1; calf pain, twisted knee and thigh/buttock pain treated with NSAIDs-1; and thigh pain treated with NSAIDS-1. **Frequency of Operative Site AEs reported as "Other", Control**: Mild serous drainage treated with dressing-1; subject trauma treated with reduced weight bearing-1; trochanteric tenderness treated with injection-1; hip pain-2; trochanteric bursitis treated with multiple injections-1; and thigh pain treated with continued strengthening-1; uneven leg length treated by reassuring subject-1; leg/calf pain-1; mid thigh pain treated with medications-1; one episode of clicking-1, iliopsoas tendonitis-1.

8 Frequency of Operative Site AE reported as **"Other- Neurological"**,: Investigational: nerve damage causing footdrop treated with physical therapy, medications and a foot orthothic-1.

9 Wound problems were observed in the immediate postoperative period (0-6 weeks) except for 1 investigational case where the AE was observed between 12 and 24 months. All wound problems were treated conservatively with superficial treatment and/or antibiotics with the exception of 1 investigational case that required a superficial I&D.

For the Subset Cohort, the most frequent postoperative operative site adverse events were dislocation, muscle weakness and wound problems. There appear to be no clinically meaningful difference in rates of postoperative operative site adverse events between the investigational and control treatments (see **Table 15** below).

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

	Investigational N=45		Control N=24	
Adverse Events at 24+ Months	**AEs**	**%**	**AEs**	**%**
Dislocation[1]	2	4.4	1	4.8
Muscle Weakness	1	2.8	0	0.0
Other[2]	0	0.0	3	12.5
Wound Problem[3]	3	6.7	2	8.3

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 'bone lysis', then that adverse event was listed in addition to the 'deep infection' adverse event.

Additional Notes:
1 One control hip was revised to treat recurrent dislocations.

2 **Frequency of Operative Site AEs reported as "Other", Control:** Mid thigh pain treated with medications-1; one episode of clicking-1, iliopsoas tendonitis-1.

3 Wound problems were observed in the immediate postoperative period (0-6 weeks). All wound problems were treated conservatively with superficial treatment and/or antibiotics.

b. Complications Grouped by Type of Adverse Event

There were no statistically or clinically meaningful significant differences in the proportions of adverse events grouped by type of AE (intraoperative, postoperative operative site, or systemic) or overall across investigational and control treatment groups in the All Enrolled Cohort (see **Table 16** below). Similarly, there appears to be no clinically meaningful differences in the AE rates for the Subset Cohort (see **Table 17** below). The total number of AEs grouped by type of AE (intraoperative, postoperative, operative site, or systemic) for the All Enrolled Cohort are reported in **Table 18**.

Table 16: Comparison of Frequencies of Any Adverse Event (Per Hip Basis): All Enrolled Cohort

	Investigational N=177			**Control N=87**			
Adverse Events at 24+Months	**AEs**	**%**	**95% Confidence Levels**	**AEs**	**%**	**95% Confidence Levels**	**p-value**
Any Complication	125	70.6	63.3 – 77.2	63	72.4	61.8 – 81.5	0.885
Intraoperative	10	5.6	2.7 – 10.1	3	3.4	0.7 – 9.8	0.555
Operative Site	38	21.5	15.7 – 28.3	19	21.8	13.7 – 32.0	1.000
Systemic	112	63.3	55.7 – 70.4	57	65.5	54.6 – 75.4	0.786

	Investigational N=177			Control N=87			
Adverse Events at 24+Months	**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.							

Table 17: Comparison of Frequencies of Any Adverse Event (Per Hip Basis): Subset Cohort

24+ Months	Investigational N=45		Control N=24	
Adverse Events	**AEs**	**%**	**AEs**	**%**
Any Complication	24	53.3	15	62.5
Intraoperative	0	0.0	1	4.2
Operative Site	5	11.1	6	25.0
Systemic	20	44.4	12	50.0
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 18: Comparison of Frequencies of Any Adverse Event (All events): All Enrolled Cohort

Adverse Events (distinct events)	**Investigational N=177**	**Control N=87**
Any Complication	342	162
Intraoperative	12	4
Operative Site	78	28
Systemic	252	130
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.		

c. Distribution of Adverse Events over Time

In **Tables 19** and **20**, time course presentations of the occurrence of post-operative systemic and operative site adverse events are 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 19: Time Course Occurrence of Postoperative Systemic Adverse Events: All Enrolled Cohort

Complication	Interval																Total	
	0D-6W		6 Week		6W-6M		6 Month		6M-12M		12 Month		12M-24M		24 Month+			
	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	I N
CANCER						1				1	2				1	5	3	7
CARDIOVASCULAR	1	4				1	1	2			2	2		2	3	1	7	12
CENTRAL NERVOUS SYSTEM	1				1	1	1					1		1			3	3
DERMATOLOGICAL	2	1				4			1			2		2		1	3	10
ENDOCRINE/METABOLIC	1					1		1			1		1	1	2	2	5	5
GASTROINTESTINAL	2	4	1			3	1		1			2				2	5	11
GENITOURINARY	4	5				2	2	3		1		3		4	2	1	8	19
HEENT	1			1							1	1		1			2	3
HEMATOLOGICAL	4	1		1		1											4	3
MUSCULOSKELETAL	2	5	5	9	9	16	12	18	4	9	7	14	10	34	23	39	72	144
NEUROLOGICAL						1								1				2
PERIPHERAL NERVOUS SYSTEM						2							1	1		1	1	4
PSYCHOLOGICAL																1		1
RESPIRATORY SYSTEM	3	4				3	1	2		1				1			4	11
THROMBOSIS/THROMBOPHLEBITIS	1	1		1													1	2
OTHER	2	4	3	1	3		1	1			1	1	1	2	1	6	12	15
Total	24	29	9	13	13	36	19	27	6	12	14	26	13	50	32	59	130	252

Table 20: Time Course Occurrence of Postoperative Operative Site Adverse Events: All Enrolled Cohort

Complication	Interval																	
	0D-6W		6 Week		6W-6M		6 Month		6M-12M		12 Month		12M-24M		24 Month+		Total	
	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	I N
ACETABULAR LINER FAILURE														1				1
BONE LYSIS														1				1
COMPONENT FRACTURE														1				1
DEEP INFECTION		1								1								2
DISLOCATION	1	2	2	3		4			2			1	2		1	1	8	11
FEMORAL COMPONENT LOOSENING												1		1		2		4
FRACTURE				2				1										3
HETEROTOPIC BONE FORMATION								1										1
MUSCLE WEAKNESS		1		1		1		1						1				5
OTHER - BURSITIS						1	2			2	1	2	1		2	1	6	6
OTHER - END OF STEM PAIN				1				2		1								4
OTHER - ILIOPSOAS TENDONITIS																1		1
WOUND PROBLEM	2	7		3										1			2	11
OTHER	2	6	2	2	3	6	2	3	1		1	5		1	1	4	12	27
Total	5	17	4	12	3	12	4	8	3	4	2	9	3	7	4	9	28	78

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 233 subjects in the 24+ Month dataset of the All Enrolled Cohort.

Since the applicant is only currently seeking marketing approval for the S-ROM femoral stem and Pinnacle 100 acetabular cup as components for the Ceramax™ Ceramic Hip System, information is presented for the All Enrolled Cohort as well as the Subset Cohort (subjects who received the S-ROM/Pinnacle 100).

Primary Analysis

The Harris Hip Score mean in the All Enrolled Cohort for the investigational group was 94.4 while the Harris Hip Score mean for the control group was 93.8. The standard error of difference was 1.31, and the non-inferiority p-value was less than 0.001. These results are summarized in **Table 21** below.

Table 21: Comparison of 24+Month Harris Hip Score Means: All Enrolled Cohort

Parameter	Treatment	N	Least Square Means	Standard Error of Difference	Non-inferiority P-value
Harris Hip Score	I	152†	94.4	1.31	<0.001
	C	77	93.8		

† This analysis was carried out with under an ANCOVA model where preoperative Harris Hip score was a significant covariate; 4 patients did not have a preoperative Total Harris Hip score on file, so the investigational group had a sample size of 152 in the final analysis. Non-inferiority results were similar (p-value < 0.001) when carried out with a t-test and full sample sizes of 156 in the investigational group and 77 in the control group.

The Harris Hip Score mean in the Subset Cohort for the investigational group was 97.5 while the Harris Hip Score mean for the control group was 94.7. The standard error of the difference was 1.99, and results for both groups are comparable. These results are summarized in **Table 22** below.

Table 22: Comparison of 24+Month Harris Hip Score Means: Subset Cohort

Parameter	Treatment	N	Least Square Means	Standard Error of Difference
Harris Hip Score	I	42	97.5	1.99
	C	23	94.7	

The primary analysis for the All Enrolled Cohort (and *post hoc* primary analysis for the 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 23** and **24**, Harris Hip Scores at different time points are presented for the All Enrolled and Subset Cohorts, respectively.

Table 23: Timecourse of Harris Hip Scores and Subscores: 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	14	8.4	2	2.4	118	76.6	57	73.1	127	78.4	62	78.5	129	85.4	61	82.4	134	81.7	64	79
Good (81-90)	0	0	0	0	49	29.5	23	27.4	18	11.7	13	16.7	16	9.9	10	12.7	8	5.3	4	5.4	11	6.7	9	11.1
Fair (71-80)	2	1.1	1	1.1	48	28.9	33	39.3	7	4.5	4	5.1	10	6.2	2	2.5	5	3.3	3	4.1	5	3	5	6.2
Poor (<71)	171	96.6	86	98.9	48	28.9	25	29.8	11	7.1	4	5.1	9	5.6	5	6.3	9	6	6	8.1	13	7.9	3	3.7

	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	%
Missing	4	2.3	0	0	7	4.2	1	1.2	0	0	0	0	0	0	0	0	0	0	0	0	1	0.6	0	0
Total	177	100	87	100	166	100	84	100	154	100	78	100	162	100	79	100	151	100	74	100	164	100	81	100

Table 24: Timecourse of Harris Hip Scores and Subscores: 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	3	7	1	4.5	28	80	17	81	36	87.8	19	86.4	30	85.7	15	83.3	38	90.5	20	87
Good (81-90)	0	0	0	0	16	37.2	8	36.4	4	11.4	2	9.5	3	7.3	1	4.5	2	5.7	1	5.6	3	7.1	1	4.3
Fair (71-80)	0	0	0	0	15	34.9	10	45.5	3	8.6	1	4.8	2	4.9	1	4.5	1	2.9	1	5.6	0	0	1	4.3
Poor (<71)	45	100	24	100	7	16.3	3	13.6	0	0	1	4.8	0	0	1	4.5	2	5.7	1	5.6	1	2.4	1	4.3
Missing	0	0	0	0	2	4.7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Total	45	100	24	100	43	100	22	100	35	100	21	100	41	100	22	100	35	100	18	100	42	100	23	100

Radiographic Assessment and Overall Success

The sponsor conducted secondary endpoint analyses related to radiographic assessment, revision rate, and Visual Analog Scale (VAS) scores. A subject was considered by the applicant to be a composite success at 24+ Months if the subject's 24+ Month Harris Hip Score values 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 All Enrolled Cohort in **Table 25**. 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 All Enrolled Cohort.

Table 25: Comparison of Clinical Success, Radiographic Success and Revision at 24+ Months: All Enrolled Cohort

Patient Success Criteria	(I) 157 subjects	(C) 76 subjects	Fishers Exact p-value
Clinical Success	138 / 157 (87.9%)	67 / 76 (88.2%)	1.000
Total Harris Hip Score >= 80	138 / 157 (87.9%)	67 / 76 (88.2%)	1.000
Mild - Slight - No Pain	148 / 157 (94.3%)	71 / 76 (93.4%)	0.776
Radiographic Success	153 / 157 (97.5%)	74 / 76 (97.4%)	1.000
Radiolucencies <= 2mm	153 / 157 (97.5%)	74 / 76 (97.4%)	1.000
Acetabular Migration <= 4mm	153 / 157 (97.5%)	74 / 76 (97.4%)	1.000
Acetabular Inclination <= 4 Degrees	153 / 157 (97.5%)	74 / 76 (97.4%)	1.000
Osteolysis None	153 / 157 (97.5%)	74 / 76 (97.4%)	1.000
Absence of Revision	153 / 157 (97.5%)	74 / 76 (97.4%)	1.000
OVERALL SUBJECT SUCCESS RATE	138 / 157 (87.9%)	67 / 76 (88.2%)	1.000
There were 6 revisions (4I,2C) that did not meet the minimum 24-month follow-up criteria; these 6 revisions were counted as failures in all categories (clinical, radiographic, revision, and overall).			

Similarly, the radiographic success, absence of revision, and overall success rates are reported for the Subset Cohort in **Table 26**. The results demonstrate no clinically significant differences between investigational and control hips for radiographic success, absence of revision, or overall success in the Subset Cohort.

Table 26: Comparison of Clinical Success, Radiographic Success and Revision at 24+ Months: Subset Cohort

Patient Success Criteria	(I) 41 subjects	(C) 22 subjects
Clinical Success	**40 / 41 (97.6%)**	**19 / 22 (86.4%)**
Total Harris Hip Score >= 80	40 / 41 (97.6%)	19 / 22 (86.4%)
Mild - Slight - No Pain	40 / 41 (97.6%)	19 / 22 (86.4%)
Radiographic Success	**41 / 41 (100.0%)**	**21 / 22 (95.5%)**
Radiolucencies <= 2mm	41 / 41 (100.0%)	21 / 22 (95.5%)
Acetabular Migration <= 4mm	41 / 41 (100.0%)	21 / 22 (95.5%)
Acetabular Inclination <= 4 Degrees	41 / 41 (100.0%)	21 / 22 (95.5%)
Osteolysis None	41 / 41 (100.0%)	21 / 22 (95.5%)
Absence of Revision	**41 / 41 (100.0%)**	**21 / 22 (95.5%)**
OVERALL SUBJECT SUCCESS RATE	**40 / 41 (97.6%)**	**19 / 22 (86.4%)**
There was 1 revision (0I,1C) that did not meet the minimum 24-month follow-up criteria; this 1 revision was counted as a failure in all categories (clinical, radiographic, revision, and overall).		

Visual Analog Scale (VAS)

Subjects were asked preoperatively and at follow-up visits to identify their level of pain on a visual analog scale (VAS). 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 All Enrolled Cohort by treatment group over time is displayed in **Table 27**. The difference in means at 24+ months was not significant ($p = 0.324$) as displayed in **Table 28**.

Table 27: Timecourse of Visual Analog Scale Means: All Enrolled Cohort

	Event Interval											
	Pre Op		6 Week		6 Month		12 Month		24 Month		24+ Month	
	VAS		VAS		VAS		VAS		VAS		VAS	
	Mean	N	Mean	N	Mean	N	Mean	N	Mean	N	Mean	N
Treatment Type												
C	65.5	87	10.4	83	8.94	77	8.64	77	5.21	73	6.11	80
I	63.6	177	9.65	161	9.7	152	7.28	159	6.62	150	7.87	164

Table 28: Comparison of 24+Month VAS Score Means

Parameter	Treatment	N	Least Square Means	Standard Error of Difference	Non-inferiority P-value
24+Month VAS Score	**C**	**80**	**6.11**	**2.10**	**0.324**
	I	**164**	**7.87**		

A presentation of VAS pain score means for the Subset Cohort by treatment group over time is given in **Table 29**. There did not appear to be a difference in means at 24+ Months as displayed in **Table 30**.

Table 29: Timecourse of Visual Analog Scale Means: Subset Cohort

	Event Interval											
	Pre Op		6 Week		6 Month		12 Month		24 Month		24+ Month	
	VAS		VAS		VAS		VAS		VAS		VAS	
	Mean	N	Mean	N	Mean	N	Mean	N	Mean	N	Mean	N
Treatment Type												
C	60.3	24	8.73	22	7.52	21	8.18	22	5.94	17	8.32	22
I	63.7	45	8.16	38	11.7	33	4.59	41	9.62	34	9.95	42

Table 30: Comparison of 24+Month VAS Score Means: Subset Cohort

Parameter	Treatment	N	Least Square Means	Standard Error of Difference
24+Month VAS Score	C	22	8.32	4.66
	I	42	9.95	

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, randomized, single blinded, controlled Investigational Device Exemption (IDE) clinical investigation was conducted using components of the DePuy Ceramax Ceramic 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 233 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 related to the DePuy Ceramax™ Ceramic Total Hip System were musculoskeletal. There were a total of 6 revisions in this study (4 investigational; 2 control), 2.3%, reported out of 264 subjects. The Kaplan-Meier Survivorship Analysis for the All Enrolled Cohort demonstrated a 97.6 % survivorship (95% confidence interval: 93.7%-99.1%) for the investigational subjects at 3.2 years and a 97.6 % survivorship (95% confidence interval: 90.9%-99.4%) for the control hips at 2.9 years. There was no clinical or statistical difference in the proportion of adverse events between the investigational and control cohorts. With respect to the 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. There were 233 subjects in the All Enrolled 24+ Month Harris Hip dataset with an evaluable 24+ Months for Harris Hip Total score, demonstrating HHS means of 94.4 and 93.8 in the investigational and control groups, respectively. There were 69 subjects from the Subset Cohort in the 24+ Month Harris Hip dataset with an evaluable 24+ Months Harris Hip Total score demonstrating HHS means of 97.5 and 94.7 in the investigational and control groups, respectively. In both the All Enrolled cohort and the Subset Cohort (S-ROM stems and Pinnacle 100 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 All Enrolled Cohort for radiographic outcomes or VAS assessments, and the Subset Cohort results were comparable.

C. **Overall Conclusions**

The clinical data in this application support the reasonable assurance of safety and effectiveness of the 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 DePuy Ceramax™ Ceramic Total Hip System for the target population outweighs the risk of surgery when used in accordance with the directions of use.

XIV. CDRH DECISION

CDRH issued an approval order on December 23, 2010. The final conditions of approval cited in the approval order are described below.

The applicant agreed to perform a single arm, hypothesis-driven multi-center cohort post-approval study enrolling a minimum of 250 patients. The study will follow PMA patients who agree to participate in the post-approval study out to their 10^{th} year post-implantation. Additional study subjects will also be enrolled to supplement the PMA subjects and fulfill sample size requirements. The data on a minimum of 87 patients will be collected at 10-years post-implantation.

The first phase of the investigation will gather clinical, radiographic, and survivorship data for each study subject five years following implantation. The second phase immediately follows the first, starting at year six (6) of follow-up and continues until year ten (10). This phase utilizes mailings to gather device survivorship information on a yearly basis. The applicant agrees to report each adverse event including details of nature, onset, duration, severity, relationship to device, and relationship to the operative procedure and outcome. The applicant agrees to initiate this study promptly following approval of this PMA.

The applicant has agreed to submit post-approval study reports, separately for this study, every six months for the first two years, and then annually until the study is completed. The applicant has agreed to update the patient and physician labeling (via PMA supplement) to reflect the 5- and 10-year findings of the study as soon as these data are available, as well as at any other time point deemed necessary by FDA if significant new information from the study becomes available.

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.