

SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Prosthesis, Hip, Semi-Constrained, Ceramic-on-Metal Articulation

Device Trade Name: Pinnacle[®] CoMplete[®] Acetabular Hip System

Applicant's Name and Address: DePuy Orthopaedics, Inc.
700 Orthopaedic Drive
Warsaw, IN 46582

Date(s) of Panel Recommendation: August 18, 2009

Premarket Approval Application (PMA) Number: P090002

Date of FDA Notice of Approval: June 13, 2011

Expedited: Not applicable

II. INDICATIONS FOR USE

The Pinnacle[®] CoMplete[®] Acetabular Hip System is a single use device intended for uncemented fixation. The Pinnacle[®] CoMplete[®] Acetabular Hip System is intended as a primary joint replacement prosthesis in total hip arthroplasty for skeletally mature patients suffering at least moderate pain in the hip joint from non-inflammatory degenerative joint disease (NIDJD) and its composite diagnoses of osteoarthritis (OA) or post-traumatic arthritis.

Pinnacle[®] CoMplete[®] Acetabular Hip System's inserts (Pinnacle[®] Ultamet[®]) are only intended for use with DePuy's femoral and acetabular components having matching outer and inner diameters.

III. CONTRAINDICATIONS

The Pinnacle[®] CoMplete[®] Acetabular Hip System should not be implanted in patients with the following conditions:

- Active or recent joint or systemic sepsis
- Insufficient bone stock, osteoporosis, severe osteopenia
- Marked atrophy or deformity in the upper femur
- Skeletal immaturity, or where loss of musculature or neuromuscular disease would render the procedure unjustifiable

- The presence of any known neoplastic or metastatic disease in the subject
- Chronic renal impairment or failure
- Known metal hypersensitivity
- Females of childbearing potential due to the unknown effects of potentially elevated metal ions on the fetus.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Pinnacle® CoMplete® Acetabular Hip System labeling.

V. DEVICE DESCRIPTION

The Pinnacle® CoMplete® Acetabular Hip System is comprised of a highly polished cobalt-chromium-molybdenum alloy (CoCrMo) metal insert (Pinnacle® Ultamet®) designed to fit within a compatible titanium alloy (Ti6Al4V) acetabular shell/cup which articulates with a compatible ceramic (BIOLOX *delta*® alumina) femoral head attached to a femoral stem as part of a primary total hip joint replacement system.



Femoral Head

The BIOLOX *delta*® ceramic heads are available in 28mm and 36mm outer diameters with both 12/14 and 11/13 internal tapers. Each taper corresponds to a specific set of head sizes and neck offset lengths. Both the head and the liner articulating surfaces are highly polished to a minimum of 0.02µm R_a. The diametrical clearance of the 28mm and 36mm femoral head and the accompanying liners ranges from 40 - 160µm.

Femoral Stems

The S-ROM® Modular Hip System includes both stems and sleeves made from titanium alloy. The femoral stems are manufactured from titanium alloy conforming to ASTM F136¹ or ASTM F620² dependent on femoral stem size. The S-ROM® femoral sleeve is

¹ASTM F136 Standard Specification for wrought Titanium-6 Aluminum-4 Vanadium ELI (extra low interstitial) Alloy for Surgical Implant Applications

manufactured from titanium alloy conforming to ASTM F136. The stems have a variety of neck lengths, lateral offsets, and head center heights. The stems are designed to interface with a femoral head implant at the proximal end, and with a sleeve for the S-ROM® system along the proximal end of the stem under the neck. The S-ROM sleeves contain the S-ROM coating and are available in a variety of shapes and sizes.

The Summit™ Porocoat tapered femoral stem system includes a press-fit porous coated hip stem made from titanium alloy (ASTM F620) in a range of sizes and in two styles: standard and high offset. The distal region of the main body is tapered and has a grit blast surface. The proximal region of the main body has a Porocoat® porous coating, which is also present on the acetabular shells.

Metal Insert

The Pinnacle® Ultamet® Metal Inserts consist of a metal acetabular bearing insert manufactured from high carbon CoCrMo (ASTM F1537³). The bearing insert components are available with either 28mm or 36mm inner diameters, to accommodate the two different femoral head components and the compatible metal insert sizes for each of the femoral heads has a corresponding set of sizes to mate with the available acetabular shells.

Acetabular Shell

The Pinnacle® Acetabular Cup System includes shells made from cast titanium alloy (ASTM F136) in a range of sizes and in three different styles: a 100 series, a 300 series, and a Sector series. The shells have a hole at the apex and an outer surface that has a Porocoat® porous coating.

The 100 Series style shells have a solid surface interface and are available in 44mm – 66mm (2mm increments) outer diameter sizes; the 300 series style shells have three spikes and are available in 44mm – 66mm (2mm increments) outer diameter sizes; and the Sector style shells have three holes at one side that can be used with fixation screws and are available in 44mm – 66mm (2mm increments) outer diameter sizes.

Cancellous Bone Screws

The Pinnacle® CoMplete® Acetabular Hip System includes 6.5mm Pinnacle® cancellous bone screws that are manufactured of Ti-6Al-4V titanium alloy (ASTM F136) and are available in lengths ranging from 15 to 70mm. The self-tapping screws have four-point cutting flutes with a blunt tip. The screws also have a hex head and are inserted into the acetabulum using a hex screwdriver for additional fixation if necessary.

2 ASTM F620 Standard specification for alpha plus beta titanium alloy forgings for surgical implants

3 ASTM F1537 Standard Specification for wrought Cobalt-28 Chromium-6Molybdenum Alloys for Surgical Implants

System Compatibility

Below is a listing of all available components for use in the Pinnacle® CoMplete® Acetabular Hip System.

Table 1: Pinnacle® CoMplete® Acetabular Hip System Compatibility

Acetabular Cup
Pinnacle 100 Acetabular Porocoat Cups 48mm - 66mm
Pinnacle 300 Acetabular Porocoat Cups 48mm - 66mm
Pinnacle Sector II Acetabular Porocoat Cups 48mm - 66mm
Metal Liner
28mm ID, 44 – 50mm OD
36mm ID, 50 – 66mm OD
Femoral Head
BILOX <i>delta</i> Ceramic Head 11/13 28mm and 36mm (+0, +3, +6 heads only)
BILOX <i>delta</i> Ceramic Head 12/14 28mm (+1.5, +5, +8.5 heads only)
BILOX <i>delta</i> Ceramic Head 12/14 36mm (+1.5, +5, +8.5, +12 heads only)
Femoral Stem
Summit Porous standard offset
Summit Porous high offset
S-ROM stems and porous sleeves standard offset
S-ROM stems and porous sleeves high offset
Cancellous Bone Screws
6.5mm Pinnacle cancellous bone screws (15 – 70mm)

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the reduction or relief of pain due structural damage in the hip joint from non-inflammatory degenerative joint disease and its composite diagnoses of osteoarthritis or post-traumatic arthritis including:

- The use of other commercially available total hip replacement systems already approved or cleared by the FDA. Commonly used implant bearing materials for total hip arthroplasty include metal on ultra-high molecular weight polyethylene (UHMWPE), ceramic on UHMWPE, metal on metal, and ceramic on ceramic;
- 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 a hip 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

Use of the ceramic-on-metal articulation has been marketed outside of the United States since 2006. At the time of the PMA submission, the ceramic-on-metal system is being sold in over forty (40) countries. (Australia, Austria, Belgium, Canada, China, Cyprus, Czech Republic, Denmark, Dubai, Egypt, England, Estonia, Finland, Germany, Greece, Hong Kong, Hungary, India, Indonesia, Iran, Iraq, Israel, Italy, Korea, Latvia, Lithuania, Luxemburg, Malaysia, Malta, Netherlands, New Zealand, Northern Ireland, Pakistan, Philippines, Poland, Portugal, Republic of Ireland, Russia, Scotland, Singapore, Slovakia, Slovenia, South Africa, Spain, Sweden, Switzerland, Taiwan, Thailand, Turkey, Wales, and Vietnam). 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

Reported Device Related Adverse Effects

The most commonly reported adverse events related to the Pinnacle[®] CoMplete[®] Acetabular Hip System device are:

- Trochanteric bursitis
- Wound problems
- Musculoskeletal problems
- Dermatological problems
- Pain

Potential Adverse Effects

The following adverse effects may occur in association with any hip replacement surgery, including the Pinnacle[®] CoMplete[®] Acetabular 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).
- Pseudotumor.
- Aseptic Lymphocyte Dominated Vasculitis Associated Lesion (ALVAL).

Any of these adverse effects may require medical or surgical intervention. In rare cases, these adverse effects may lead to death. The potential long-term biological effects of metal wear debris and metal ion production are not known.

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

IX. SUMMARY OF PRECLINICAL STUDIES

A. Laboratory Studies

Non clinical laboratory testing was provided in support of the Pinnacle[®] CoMplete[®] Acetabular Hip System including the information regarding:

- Femoral Stem Component: stem fatigue strength
- Femoral Head Component: burst strength, fatigue strength, axial pull-off strength
- Acetabular Liner: locking strength
- Acetabular Bone Screws
- Bearing Couple: wear including micro-separation during the swing phase, ion level measurements, frictional torque, and range of motion; and
- Surface Coating Characterization

1. Femoral Stem Components

Femoral Stem Fatigue Strength

Method: To determine fatigue performance of the smallest size S-ROM and Summit Porocoat femoral stems, testing was performed per FDA's Guidance Document for Femoral Stem Prostheses⁴, in accordance with ISO 7206-4.

Results: Stems were tested at their respective endurance limits with no failures occurring to 5 million cycles. The results of these tests demonstrate that the femoral stem should withstand predicted *in vivo* loads.

2. Femoral Head Component

Worst Case Testing: Testing was conducted on the 28mm 12/14L taper and 28mm 11/13L taper BIOLOX *delta* heads because this size represents the smallest diameter femoral head with the longest neck length and results in the least amount of taper engagement with the femoral stem trunnion

Pre-Fatigue Burst Strength

Purpose: Static burst or 'crush' testing was performed to evaluate the ability of the individual ceramic head components to withstand static axial compression.

Method: Static burst testing was performed on 7 ball heads according to ISO 7206-10⁵

Acceptance Criteria: Average pre-fatigue burst strength shall exceed 46kN. No ball shall fail at less than 20kN according to FDA's Guidance Document for the Preparation of Premarket Notifications for Ceramic Ball Hip Systems⁶

Results: The average pre-fatigue burst strength of the 28mm 12/14L taper was 95kN with no head fracturing below 80kN. The average pre-fatigue burst strength of the 28mm 11/13L taper was 61kN with no head fracturing below 42kN. The specimens tested met the acceptance criteria.

Fatigue Strength

Method: Fatigue testing of three 28 – 11/13 and three 28 – 12/14 taper Biolox *delta* ceramic ball heads on titanium alloy tapers was conducted. The applied load was cycled to a maximum of 14.0 to minimum of 0.5kN at a frequency of 10 Hz in Ringers solution at ambient temperature for 10 million cycles

Acceptance Criteria: All samples shall survive 10 million cycles with no macroscopically visible component failure, according to FDA's Guidance Document for the Preparation of Premarket Notifications for Ceramic Ball Hip System

4 FDA's Guidance Document for Industry and FDA Staff – Non-clinical Information for Femoral Stem Prostheses, September 17, 2007.

5 ISO 7206-10 Implants for surgery – Partial and total hip-joint prostheses – Determination of resistance to static load of modular femoral heads

6 FDA's Guidance Document for the Preparation of Premarket Notifications for Ceramic Ball Hip Systems, January 10, 1995

Results: All femoral head components survived 10 million cycles without failure

Post-Fatigue Burst Strength

Method: Following fatigue testing, burst testing of the three 28 – 11/13 and three 28 – 12/14 taper Biolox *delta* ceramic ball heads was performed according to ISO 7206-10.

Acceptance Criteria: No post-fatigue fractures below 20kN, according to FDA's Guidance Document for the Preparation of Premarket Notifications for Ceramic Ball Hip System

Results: The minimum post-fatigue burst strength of the 28mm 12/14L taper femoral head was 71kN and the minimum post-fatigue burst strength of the 28mm 11/13L taper femoral head was 66kN minimum. These values exceed the 20kN requirement for the post-fatigue burst strength suggested by the FDA Ceramic Ball Guidance.

Axial Head Pull-off Strength

Method: Three 28 – 11/13 and three 28 – 12/14 taper Biolox *delta* ceramic ball heads were tested for pull-off loads according to FDA's Guidance Document for the Preparation of Premarket Notifications for Ceramic Ball Hip Systems

Acceptance Criteria: Axial pull-off strength shall be greater than 250N

Results: The average axial pull-off strength of the 28mm 12/14L taper femoral head is 1369N and the average axial pull-off strength of the 28mm 11/13L taper femoral head is 1627N. The ceramic head testing results indicate that the ceramic heads possess sufficient strength to perform as intended under expected *in vivo* loading conditions.

3. Acetabular Liner

Worst Case: To capture the entire size range, test samples included the 28 x 48mm, 36 x 52mm, and 36 x 66mm liners. The metal liners were assembled into Pinnacle shells.

Push-Out Force

Acceptance Criteria: Push-out force shall exceed 50 lbs

Method: For the push-out testing, two different methods of assembling the insert to the shell were used: compressive force or impaction.

Inserts of each size were initially assembled by the compressive force method and the push-out force was recorded. Those same inserts were then reassembled into their shells using the impaction assembly method and the push-out force was again recorded. Finally, three new samples of the 36 x 66mm liners were assembled using the impaction assembly method and the push-out force were recorded.

Results: Using the compressive assembly method, the minimum push-out force for the liners was 148.4lbs. Using the impaction assembly method, the minimum push-out force for the liners was 361.9 lbs. Using the new samples assembled using the impaction assembly method, the minimum push-out force of the insert was 483.3 lbs.

Torque-Out Strength

Acceptance Criteria: Torque-out force shall exceed 53in-lbs

Method: The metal inserts were assembled into the shells using the compressive force method. The inserts were torqued out and the torque required to loosen the insert from the shell was recorded.

Results: The minimum torque-out force for the liners tested was 336.7 in-lbs.

4. Acetabular Bone Screws

Torsional Strength

Method: Using a hex key, a torsional load was applied to the screw at a rate of 50lbf-in/min, while applying an axial compression load of 10lbf.

Results: The failure mode for all samples was the rounded hex, with a minimum peak torque of 90.7lb-in.

5. Bearing Couple

Wear Testing

a. 28mm High Clearance Wear Simulation

Worst Case Rationale: In hard-on-hard bearings, the smallest bearing diameter generally represents the worst-case testing scenario. Therefore, to simulate the worst case scenario the smallest bearing (28mm) with the highest diametrical clearance allowed per the engineering drawings was tested.

Materials: BIOLOX *delta* heads articulating with metal Ultamet liners

Method: The wear test was performed on a 10-station hip joint simulator using the Paul-type physiological loading (3000 N max loading cycle, $\pm 23^\circ$ biaxial rocking motion at 1 Hz). The interface was lubricated with 25% bovine serum. The wear test was run for a total of 5 million cycles.

Results: The mean bedding-in wear rate (taken to be 0 – 1.5M cycles) was $0.11\text{mm}^3/10^6$ cycles and the mean steady state wear rate (taken to be 1.5 – 5M cycles) was $0.01\text{mm}^3/10^6$ cycles.

b. 36mm Wear Simulation

Materials: BIOLOX *delta* heads articulating with metal Ultamet liners

Method: The cups were mounted anatomically above the heads at an angle of 35° to the horizontal. The synchronized load and motion cycles were applied at 1 Hz.

The load cycle was a dual-peak cycle with maximum of 3kN, the valley of 1kN and swing phase load of approximately 50N which is applied over 40% of the cycle. The motion applied was +30°/-15° on the swing and ±10° on the internal/external rotation with sinusoidal curves as a simplified cycle. The bearings were immersed in a 25% new-born calf serum solution throughout the test.

Results: The mean bedding-in wear rate, (taken to be from 0 to 1.5M cycles) for the 36mm ceramic-on-metal bearing was 0.095 mm³/10⁶ cycles. The mean steady state wear rate for the bearing was 0.02mm³/10⁶ cycles.

c. 36mm Wear Simulation Using Scratched Cups

Method: The 36mm bearings were previously tested on the hip simulator to 5 million cycles as described in (b.) above and deemed to be fully bedded in. Following the wear testing, the liners were scratched with a diamond stylus to simulate potential *in vivo* damage. The wear simulation was then continued for 5 million cycles on the scratched liners using the same loading protocol.

Results: The results showed no component failures out to 10 million cycles. After the metal liners had been scratched the ceramic-on-metal bearings had an average steady state wear rate of 0.001 mm³/10⁶ cycles.

d. 28mm Micro-Separation Simulation

Materials: BIOLOX *forte* ceramic head articulating with Ultima metal insert. The Ultima liner follows the same manufacturing specifications as the Ultamet liner; however the surface roughness and spherical diameter are different. The BIOLOX *forte* ceramic head articulating with metal underwent wear testing that demonstrated this combination produced wear at a higher rate than the BIOLOX *delta* combination. This makes the BIOLOX *forte* articulating with the Ultima liners a more worst-case scenario. Please note the BIOLOX *forte* ceramic femoral heads are not a compatible component of the Pinnacle[®] CoMplete[®] Acetabular Hip System.

Method: The components were tested in a 10-station hip simulator. The wear test introduced micro-separation of the femoral head compared to the insert ranging from 0 – 4mm for each component. The tests were carried out in 25% bovine serum; all stations were run at 1 Hz for 5 million cycles.

Results: The ceramic-on-metal bearing pair had an average wear rate of 0.256mm³/10⁶ cycles.

e. 28mm Debris Morphology Simulation

Materials: BIOLOX *forte* ceramic head articulating with Ultima metal insert. The Ultima liner follows the same manufacturing specifications as the Ultamet liner; however the surface roughness and spherical diameter are different. The BIOLOX *forte* ceramic head articulating with metal underwent wear testing that

demonstrated this combination produced wear at a higher rate than the BIOLOX *delta* combination. This makes the BIOLOX *forte* articulating with the Ultima liners a more worst-case scenario. Please note the BIOLOX *forte* ceramic femoral heads are not a compatible component of the Pinnacle[®] CoMplete[®] Acetabular Hip System.

Method: The implants were tested in a physiological hip joint simulator with the cup in the superior position to the head and inclined in the anatomical position at 45° to the vertical axis. A single axis twin peak Paul type loading curve was applied. Two directions of motion were applied, flexion-extension and internal-external rotation. The motions were 90° out of phase. Tests were carried out in 25% bovine serum; the implants were tested for 5 million cycles.

Results: Majority of the particles were oval to round in shape, and appeared as clumps or aggregates when observed using transmission electron micrographs, which may have occurred during sample preparation. The mean particle sizes at one million cycles were $17.57 \pm 1.37\text{nm}$ and at five million cycles the mean particle sizes were $6.11 \pm 0.40\text{nm}$.

Ion Level Testing

a. Measurement of Ion release in serum – 28mm bearing

Purpose: To compare the levels of Co, Cr and Mo ions released into serum from COC, COM (*forte*/Ultima), and MOM bearings during hip simulator testing under micro-separation conditions.

Materials: The 28mm bearing described in the Micro-Separation Wear Simulation summary above, were used to measure ion release

Method: Serum from the hip simulator test ran to determine micro-separation was prepared in the following way: 20ml of serum for each bearing type was taken at 1.7Mcycles and centrifuged at 1500rcf for 50 minutes, approximately 5ml of the mixture was sent for analysis.

Samples were analyzed in the following way: Levels of Co and Cr in the supernatant measured using graphite furnace atomic absorption spectroscopy; Mo ions were determined by inductively coupled plasma mass spectrometry

Results: The results (**Table 2**) demonstrated that serum cobalt, chromium and molybdenum ion levels from the COM bearing combination were lower than the corresponding MOM levels by a factor of at least 5.

Table 2: Metal Ion Concentrations – 28mm bearing

Type	Cr (µg/L)	Co (µg/L)	Mo (µg/L)
MOM	714	2079	257
COC	6.15	0.62	1.7
COM	140.8	317.7	4.3

b. Measurement of Ion release in serum – 36mm bearing

Materials: The 36mm bearing surface described in 36mm Wear Simulation above, were used to measure ion release

Method: Serum lubricant samples were taken for each bearing combination during both the bedding-in and steady-state periods. The lubricating serum was analyzed for levels of cobalt, chromium and molybdenum ions using inductively coupled plasma mass spectrometry.

Results: The average Cr ion levels measured were 26.0 µg/L (bedding-in) and 11.4 µg/L (steady-state); Co ion levels were 110.8 µg/L (bedding-in) and 38.5 µg/L (steady-state) and Mo ion levels were 16.0 µg/L (bedding-in) and 9.1 µg/L (steady-state).

We expected that the ceramic-on-metal bearing would exhibit metal ion concentration levels somewhere between MOM and COC bearings as demonstrated by the non-clinical mechanical testing. It should be noted that although high concentration of metal ions were observed *in vitro*, the simulations were under micro-separation conditions and the metal ion levels were collected over the span of the testing; thus not accounting for any filtering of metal ions as would be seen clinically. In addition the device has been contraindicated in patients with renal insufficiency; therefore patients should be able to adequately filter metal ions released by the device.

The *in vivo* clinical analysis of metal ion concentrations, also performed by the applicant in a subset of patients enrolled in the pivotal study does not correlate with the theory that metal ion levels from the COM bearing would be statistically less than the MOM bearing. The *in vivo* clinical results demonstrate that the metal ion concentration of the COM bearing is not statistically different than the metal ion concentration in MOM bearings.

Therefore, the results of the *in vitro* simulation have not been shown to correlate with clinical device performance. As a result, we asked the applicant to examine the survivorship of the COM and MOM bearings as reported in national joint registries. (see **X.D.1.3 – Kaplan-Meier Survivorship Analysis**); the applicant will also be monitoring long term *in vivo* metal ion levels in subjects enrolled in the metal ion study through a post-approval study (see **XIII - CDRH Decision**).

Frictional Torque Testing

Acceptance Criteria: The torque generated by the bearing couple was compared to the results of other hard-on-hard total hip replacement bearings.

a. 28mm flexion/extension unworn

Method: Components were tested with a flexion-extension motion of $\pm 25^\circ$ applied to the femoral head. Tests were performed at 1Hz, with a simple sinusoidal waveform through 60% of each cycle to apply a dynamic load, with a peak load of 2kN, and a swing phase load of 25N, 100N and 300N. Water, 25% (v/v) and 100% newborn bovine serums were used as lubricants. Each test was performed in a forward, and a reverse direction, and a mean taken. Lubricant was removed, and the prostheses cleaned between each test.

Results: In all lubricants tested and at all swing phase loads tested the mean friction factor for the ceramic-on-metal bearing couple are summarized below in **Table 3:**

Table 3: Friction Factor during flexion/extension – 28mm unworn bearing

100% Serum				
		25N	100N	300N
COM bearing	Mean (95% CI of Mean)	0.052 (0.006)	0.065 (0.012)	0.065 (0.013)
25% Serum				
COM bearing	Mean (95% CI of Mean)	0.040 (0.008)	0.047 (0.010)	0.049 (0.010)
Water				
COM bearing	Mean (95% CI of Mean)	0.015 (0.006)	0.017 (0.008)	0.021 (0.017)

95% CI of mean refers to the 95% confidence interval

b. 36mm flexion/extension unworn

Method: Components were tested in an inverted position, with a flexion-extension motion of $\pm 25^\circ$ applied to the femoral head. Tests were performed at 1Hz, with a simple sinusoidal waveform through 60% of each cycle to apply a dynamic load, with a peak load of 2kN, and a swing phase load of 300N. Lubricants were 100% bovine serum and water. Each test was performed in a forward, and reverse direction, and a mean taken.

Results: In all lubricants tested the mean friction factor for the ceramic-on-metal bearing couples are summarized below in **Table 4:**

Table 4: Friction Factor, Frictional Torque – 36mm flexion/extension unworn

Bearing Combination		WATER		100% SERUM	
		Friction Factor	Frictional Torque (Nm)	Friction Factor	Frictional Torque (Nm)
low clearance	Mean	0.031	1.077	0.084	3.06
	(95% CI of Mean)	(0.007)	(0.281)	(0.022)	(0.69)
high clearance	Mean	0.03	1.034	0.085	3.03
	(95% CI of Mean)	(0.006)	(0.128)	(0.011)	(0.38)

95% CI of mean refers to the 95% confidence interval

c. 28mm flexion/extension worn

Method: Implants were loaded with a dynamic loading curve for normal walking since walking is the most frequent daily dynamic loading mode of the hip joint. The cycle time was varied between 0.5, 1 and 2 seconds. Additionally, the back swing load (minimum load) of 250N at 86% of the cycle was reduced to 100N and increased to 500N. Bearing pairs labelled “worn” were subjected to 5 million loading cycles in a hip simulator before friction testing began.

Results: In all lubricants tested the mean friction factor for the ceramic-on-metal bearing couples are summarized below in **Table 5** (SD = standard deviation):

Table 5: Friction Moment during flexion/extension – 28mm worn bearing

Maximum Friction Moment for Different Back Swing Loads in Serum				
		100 N	250 N	500 N
Implant	Wear Status	Mean ± SD (Nm)		
COM – 28mm	unworn	1.7 ± 0.4	2.1 ± 0.3	2.3 ± 0.3
	worn	2.4 ± 0.3	2.5 ± 0.4	2.6 ± 0.3
Maximum Friction Moment for Different Movement Frequencies in Serum				
		0.5 Hz	1.0 Hz	2.0 Hz
Implant	Wear Status	Mean ± SD (Nm)		
COM – 28mm	unworn	2.3 ± 0.3	1.9 ± 0.4	1.9 ± 0.4
	worn	2.8 ± 0.3	2.4 ± 0.2	2.2 ± 0.2
Maximum Friction Moment for Different Resting Duration in Serum				
		10 seconds	30 seconds	
Implant	Wear Status	Mean ± SD (Nm)		
COM – 28mm	unworn	2.1 ± 0.4	2.0 ± 0.4	
	worn	2.6 ± 0.4	2.4 ± 0.2	
Maximum Friction Moments in Serum Averaged Over All Variables				
Implant	Wear Status	Mean (Nm)	SD (Nm)	
COM – 28mm	unworn	2.1	0.4	
	worn	2.5	0.3	

d. 28mm internal/external rotation worn

Method: The dynamic torque profile was measured for constant cyclic torsional rotation amplitude of $\pm 20^\circ$. A cyclic axial force as applied in phase with the motion, to simulate the joint load during gait. Bearing pairs labelled “worn” were subjected to 5 million loading cycles in a hip simulator. Loading was designed to simulate walking from stand-still to measure the start-up torque peak, and also the mean peak torque over 20 cycles. Therefore the displacement was started 100ms before the load cycle in order to simulate the start of walking from stand-still and a preload force of 650N was applied to simulate the joint load for 2 legged stance. The magnitude of the peak applied force was 2000N. The loading frequency of 1Hz is generally assumed for walking. This also was halved and doubled to investigate the effect of loading rate for 0.5Hz, 1Hz, and 2Hz. The magnitude measured for walking is 250N and the value on either side was also applied to investigate 100N, 250N, and 500N. For this experiment the resting durations of 10s and 30s were compared.

Results: In all testing conditions the maximum torque for the ceramic-on-metal bearing couples are summarized below in **Table 6**:

Table 6: Maximum Torque – 28mm worn bearing

Maximum Torque in Serum Averaged Over All Variables				
Implant	Wear Status	Mean (Nm)	SD (Nm)	
COM – 28mm	unworn	0.49	0.04	
	worn	0.49	0.04	
Maximum Torque in Water Averaged Over All Variables				
Implant	Wear Status	Mean (Nm)	Std (Nm)	
COM – 28mm	unworn	0.06	0.01	
	Worn	0.22	0.03	
Maximum Torque for Different Movement Frequencies in Serum				
		0.5 Hz	1.0 Hz	2.0 Hz
Implant	Wear Status	Mean \pm SD (Nm)	Mean \pm SD (Nm)	Mean \pm SD (Nm)
COM – 28mm	unworn	0.48 \pm 0.03	0.49 \pm 0.04	0.51 \pm 0.06
	worn	0.55 \pm 0.03	0.49 \pm 0.04	0.54 \pm 0.05
Maximum Torque for Different Back Swing Loads				
		100N	250N	500N
Implant	Wear Status	Mean \pm SD	Mean \pm SD	Mean \pm SD
COM – 28mm	unworn	0.34 \pm 0.11	0.49 \pm 0.04	0.51 \pm 0.51
	worn	0.40 \pm 0.02	0.49 \pm 0.04	0.58 \pm 0.01

SD = standard deviation

Range of Motion

Worst Case: The Summit Size 10 Stem is worst-case for impingement since it has the largest neck geometry. However it was unclear whether the standard or high offset stem option would be the worst-case scenario, therefore the analysis was performed on both offset options.

The size 30 standard S-ROM® femoral stem was selected as the worst-case femoral component since it provides the largest neck geometry with the least offset of all S-ROM stems. The largest available mating sleeve used with the S-ROM® stem is the size 18F XXL.

Method: Range of motion was evaluated using CAD models following a procedure that is based on that which is outlined in ISO 21535.

Acceptance Criteria: As outlined in ISO 21535 “Specific Requirements for Hip-joint Replacement Implants” the minimum allowable angle of flexion/extension is 100°, abduction/adduction is 60° and internal/external rotation is 90°.

Results: For the Summit Size 10 standard offset the worst case flexion/extension motion was 138°, the worst case abduction/adduction motion was 133°, and the worst case internal/external rotation motion was 217°. For the Summit Size 10 high offset the worst case flexion/extension motion was 140°, the worst case abduction/adduction motion was 132°, and the worst case internal/external rotation motion was 212°. For the S-ROM stem the worst case flexion/extension motion was 134°, the worst case abduction/adduction motion was 93.5°, and the worst case internal/external rotation motion was 186°.

6. Surface Coating **S-ROM Coating**

Method: The coating was characterized with regard to coating thickness, bead morphology, pore size, porosity, and bond strength characteristics and outlined in FDA’s *Guidance Document for Testing Orthopedic Implants with Modified Metallic Surfaces Apposing Bone or Bone Cement*⁷, dated April 28, 1994.

Results: The results of the coating characterization are summarized below in **Table 7**:

⁷ FDA’s *Guidance Document for Testing Orthopedic Implants with Modified Metallic Surfaces Apposing Bone or Bone Cement*, dated April 28, 1994.

Table 7: S-ROM Coating Characterization

Mean Coating Thickness	229 µm
Bead Shape	Spherical
Mean Pore Diameter	125 µm
Mean Volume Percent Porosity	34%
Mean Shear Strength	46.1 MPa
Mean Tensile Pull-off Strength	70.0 MPa

Porocoat Porous Coating

Acceptance Criteria: The criteria for porous-coated components are described in FDA's *Guidance Document for Testing Orthopedic Implants with Modified Metallic Surfaces Apposing Bone or Bone Cement*, dated April 28, 1994.

Method: The porous coating was characterized with regard to coating thickness, bead morphology, pore size, porosity, and bond strength characteristics.

Results: The results of the porous coating characterization are summarized below in **Table 8**:

Table 8: Porocoat Porous Coating Characterization

Mean Coating Thickness	762 µm
Bead Shape	Spherical
Mean Pore Diameter	275 µm
Mean Volume Percent Porosity	51%
Mean Shear Strength	25.5 MPa
Mean Tensile Pull-off Strength	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 Pinnacle[®] CoMplete[®] Acetabular Hip System.

C. Additional Studies

Biocompatibility

The materials for use in the Pinnacle[®] CoMplete[®] Acetabular Hip System are standard materials used in permanently, implanted orthopaedic implants, including cobalt-chromium-molybdenum alloy (ASTM F1537), titanium alloy (ASTM F136, ASTM F620,) and BIOLOX *delta* ceramic.

Sterilization

The components of the Pinnacle[®] CoMplete[®] Acetabular Hip System are sterilized by gamma irradiation (Cobalt 60 source). The sterilization process has been validated to achieve a sterility assurance level (SAL) of 10^{-6} at a minimum dose of 25kGy (2.5 Mrad) in compliance with the requirements of ISO 11137-1⁸. The product is not labeled "pyrogen free". The components are packaged in an inner and outer Tyvek pouch to maintain sterility.

Shelf-Life

Shelf life testing was performed to verify sterile packaging integrity equivalent to five years for the S-ROM femoral stems and to ten years for all other components.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of total hip replacement with the Pinnacle[®] CoMplete[®] Acetabular Hip System for skeletally mature patients suffering severe pain and disability due to structural damage in the hip joint from non-inflammatory degenerative joint disease (NIDJD) and its composite diagnoses of osteoarthritis (OA) or post-traumatic arthritis in the US under IDE G050078. 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 and Summit Porocoat femoral stems, DePuy Pinnacle Sector II Porocoat, and Pinnacle 100 and 300 Series Porocoat acetabular cups), were the primary basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

Patients were treated from August 2005 – October 2006. The first surgery was performed on August 4, 2005 and the final surgery was performed on October 10, 2006. The database for this PMA reflected data collected through November 25, 2008 and included 390 subjects. There were 11 investigational sites.

The study was a prospective, multi-center, randomized, single blind, controlled clinical investigation of 390 procedures in 390 subjects comparing the Pinnacle[®] CoMplete[®] Acetabular Hip System (COM), the investigational ceramic-on-metal hip system, to a legally marketed metal-on-metal (MOM) articulation system. The study was designed to demonstrate non-inferiority between the investigational and control patient populations using a non-inferiority margin of 8%.

Both treatment groups received a commercially-available femoral stem. The control group was an active treatment with a legally marketed alternative bearing with similar indications for use.

⁸ ISO 11137-1 Sterilization of health care products – Requirements for validation and routine control – Radiation sterilization

Femoral stem components used in this investigation consisted of implantations with Summit™ Porocoat, Summit™ DuoFix, S-ROM®, Prodigy™, and AML systems. 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 P090002, for the Pinnacle® CoMplete® Acetabular Hip System the applicant is only seeking marketing approval for the following subset of the components studied in the IDE: S-ROM and Summit Porocoat femoral stems; and, Pinnacle 100, 300, and Sector II acetabular cups.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the study was limited to patients who met the following inclusion criteria:

- Able to (or capable of) provide consent to participate in the clinical investigation prior to the day of the surgery. However, if the informed patient consent was signed on the day of surgery, then the source documents needed to state that the subject was given adequate time prior to the date of surgery to review and give consent
- Skeletally mature (tibial and femoral epiphyses are closed) and 20 – 75 years of age at the time of surgery
- Undergoing cementless primary hip replacement surgery for non-inflammatory degenerative joint disease (NIDJD). Composite diagnoses of NIDJD include osteoarthritis, avascular necrosis, post traumatic arthritis, slipped capital femoral epiphysis (SCFE), fracture of the pelvis, and developmental dysplasia,
- Affected hip has a Harris Hip Score of ≤ 70 , and a Pain rating of \geq Moderate,
- Met the following selected radiographic parameters:
 - a. X-ray evaluation confirms the presence of NIDJD
 - b. Femoral and acetabular bone stock is sufficient regarding strength and shape, and is suitable to receive the implants
 - c. No structural bone grafts required to support the prosthetic component(s) or to shape the bone to receive the implant(s)
- Were willing to have knowledge of treatment arm (CoM or MoM) withheld for a period of 24 months postoperatively (unless disclosure is legally and/or medically necessary)
- Previous THA in contralateral hip is greater than one (1) year post-operative and had a Harris Hip pain rating less than Mild

Patients were not permitted to enroll in the study if they met any of the following exclusion criteria:

- Bilateral hip disease with an anticipated need for bilateral hip implant during study participation (i.e., within the next 24 months)
- THA required for the revision of previously failed THA
- Suffering from inflammatory arthritides (e.g., rheumatoid arthritis, juvenile rheumatoid arthritis, psoriatic arthritis, systemic lupus erythematosus, etc.)

- 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,
- Above knee amputation of the contralateral and/or ipsilateral leg,
- Known allergy to metal (e.g. jewelry)
- Evidence of active infections that may spread to other areas of the body (e.g., osteomyelitis, pyogenic infection of the hip joint, overt infection, etc.)
- The presence of highly communicable disease or diseases that may limit follow-up (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)
- 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
- Known to be pregnant, a prisoner, mentally incompetent, and/or alcohol or drug abuser
- Previous treatment for renal disease
- Any current systemic steroid therapy, excluding inhalers, or within three months prior to surgery

2. Follow-up Schedule

All subjects were scheduled to return for follow-up examinations at 4 weeks, 3 months, 12 months, 24 months and annually thereafter, unless otherwise indicated by complications.

Preoperatively, a complete medical history, Harris Hip Score and subject-reported visual analog scale to assess pain were collected.

Postoperatively at each follow-up visit, a Harris Hip Score, subject self-reported pain assessment and 3 radiographic views (anteroposterior pelvis, anteroposterior femur and lateral femur) were obtained. In addition, beginning at 12 months postoperatively, subject reported satisfaction outcomes were collected. Adverse events and complications were recorded at all visits.

On a subset of subjects, chromium, cobalt, and titanium ions were measured preoperatively, and at 3 months, 12 months and 24 months postoperatively.

Radiographs were reviewed by an independent radiographic reviewer.

The key time points that were used in the study are shown below in the tables summarizing safety and effectiveness.

3. Clinical Endpoints

Per protocol, all subjects were evaluated at the 24 month 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: Visual Analogue Scale scores for pain (VAS), and Subject Self-Reported Satisfaction and Function.

With regard to success/failure criteria, subject composite success or failure was determined at 24 months based upon a combination of clinical, radiographic, and revision criteria. A subject was considered to be a success if all of the following were met at the 24 month endpoint.

Clinical Criteria for Success:

- Harris Hip total score ≥ 80 points.
- Harris Hip Pain was Mild or better.

Radiographic Criteria for Success:

- Femoral stem subsidence, compared to 4 week baseline ≤ 2 mm.
- Acetabular shell migration, compared to 4 week baseline ≤ 2 mm.
- Acetabular shell inclination change, compared to 4 week baseline ≤ 4 degrees.
- Acetabular or femoral osteolytic lesions ≤ 5 mm in the greatest dimension.
- Acetabular or femoral radiolucencies involving $\leq 50\%$ of the visible porous coated surface of the femoral stem or acetabular cup.

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 and Summit Porocoat Stems

The applicant is only currently seeking marketing approval for the Summit Porocoat femoral stem (standard and high offset) and the S-ROM femoral stem as components for the Pinnacle[®] CoMplete[®] Acetabular Hip System. Among the 390 subjects enrolled in the IDE study, 226 received a S-ROM or Summit Porocoat stem. Various analyses were carried out on this Subset Cohort in addition to analyses on the all enrolled cohort.

5. Bilateral Patients

Per study protocol, a bilateral patient is defined as an individual that receives a contralateral hip during the study period.

B. Accountability of PMA Cohort

All Enrolled Cohort

At the time of the applicant's database lock, complete 24 month postoperative data (study endpoint) was available on 85% (85% of COM subjects and 85% of MOM subjects) of the 390 enrolled subjects in the IDE study.

This is summarized in **Table 9** below.

Table 9: Patient Accounting for the All Enrolled Cohort

	PreOp		4 Week		3 Month		12 Month		24 Month	
	COM	MOM	COM	MOM	COM	MOM	COM	MOM	COM	MOM
TFU	194	196	194	196	194	196	194	196	194	196
Deaths (cumulative)	0	0	0	0	0	0	0	2	0	2
Component Removal (cumulative)	0	0	1	1	1	1	1	2	2	3
EFU	194	196	193	195	193	195	193	192	192	190
AFU	194	196	186	186	174	168	174	172	164	162
% Follow-up	100%	100%	96%	95%	90%	86%	90%	90%	85%	85%
<p>TFU: Theoretical Follow-up = The number of implants that have entered the beginning of each interval window at the time of database lock.</p> <p>EFU: Expected Follow-up = Theoretical Due - [Deaths + Components Removed/Revised + Consent Withdrawn]</p> <p>AFU: Actual Follow-Up</p>										

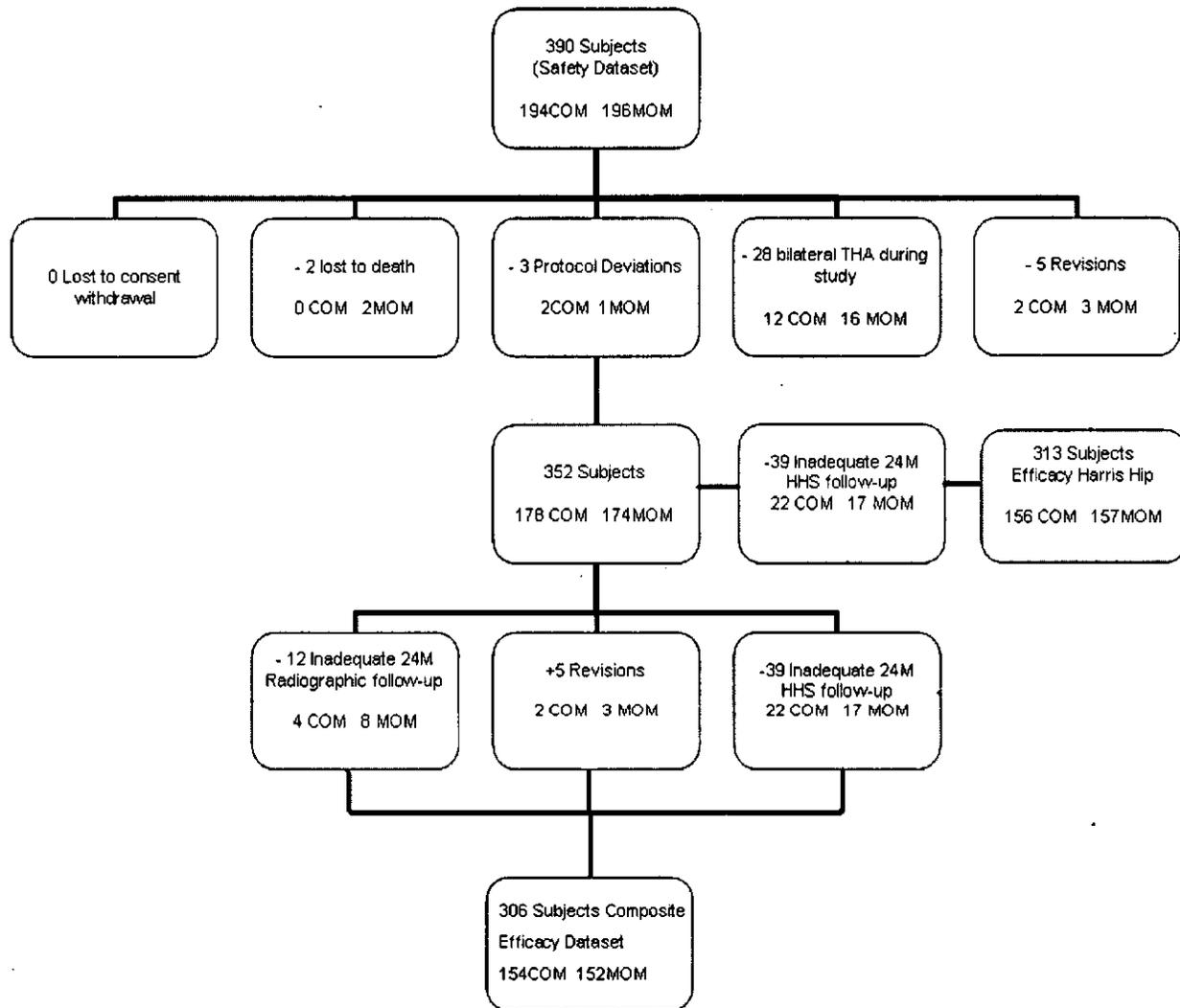
A total of 10 subjects were withdrawn from this investigation. Three of 10 were investigational and 7 of 10 were control devices. Of the 3 investigational devices, 2 were revised and 1 died. Of the 7 control devices, 3 were revised, 3 died, and 1 withdrew consent. The deaths were for reasons unrelated to the device or procedure. Two (1 I and 1 C) of the 4 deaths occurred after study endpoint (24 month postoperative follow-up) had been obtained. Study endpoint data had already been obtained for the 1 subject who withdrew consent. There was no difference in the proportion of deaths (p=0.623) or study withdrawals (p=1.000) between the investigational and control treatments (see **Table 10** below).

Table 10: Comparison of Proportion of Deaths and Consent Withdrawals

Related Events	(I) AEs	(I) Subjects	(I) %	(C) AEs	(C) Subjects	(C) %	Exact p-value
Deaths	1	194	0.52	3	196	1.53	0.623
Consent Withdrawals	0	194	0.00	1	196	0.51	1.000

Figure 1 below is a dataset flowchart which shows all 390 subjects in the Safety Dataset, and the order in which they were excluded, from top to bottom, to obtain the Efficacy Dataset; revisions were retained regardless of exclusion criteria. The primary composite success/failure endpoint analysis was carried out on the Efficacy Dataset.

Figure 1: Subject Accounting Dataset Flowchart – All Enrolled Cohort



Subset Cohort of Subjects with S-ROM and Summit Porocoat Stems

The primary analysis was based on five femoral stem types; however, the applicant is only currently seeking marketing approval for the Summit Porocoat femoral stem (standard and high offset) and the S-ROM femoral stem as components for the Pinnacle® CoMplete® Acetabular Hip System.

At the time of database lock, complete 24 month postoperative data (study endpoint) was available on 86 COM & 86 MOM (control) (80% of COM subjects and 83% of MOM subjects) of the 226 subjects in the Subset Cohort of subjects who received the S-ROM or Summit Porocoat stems.

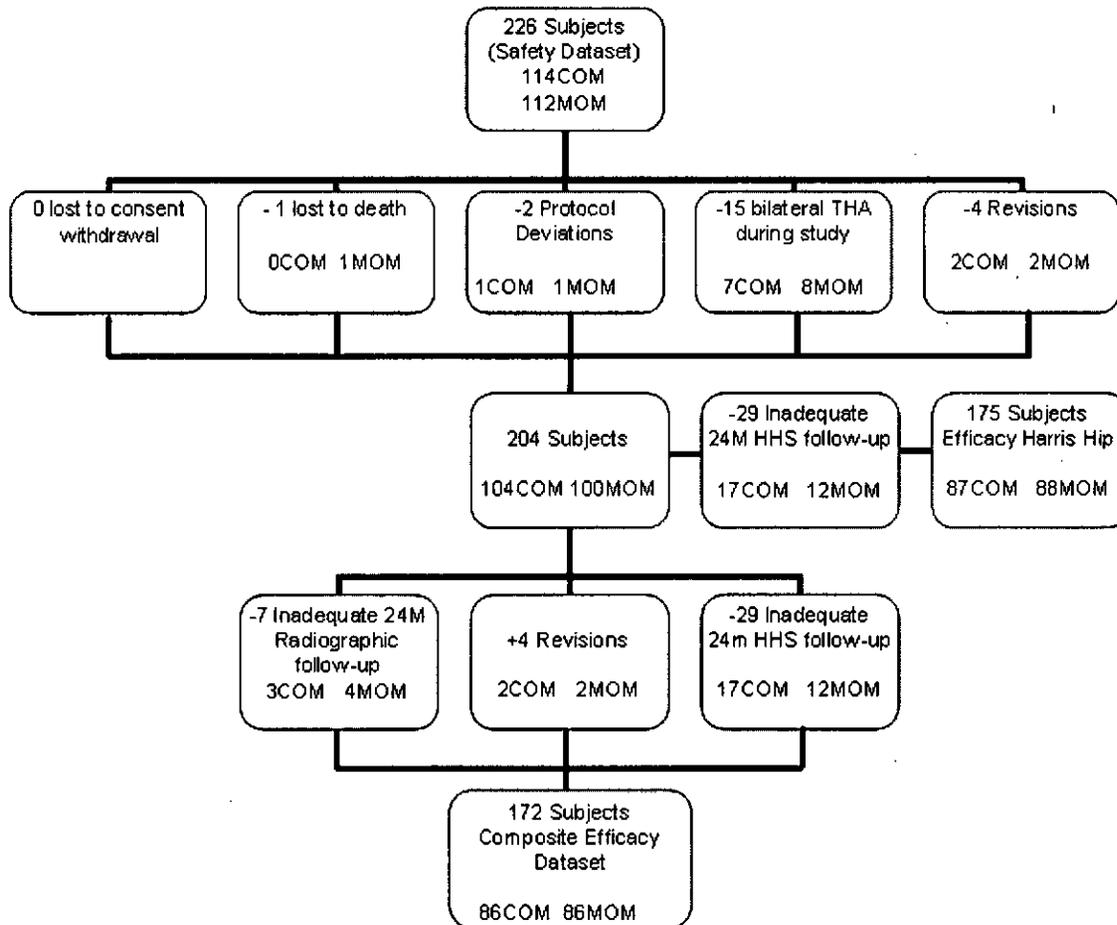
This is summarized in **Table 11** below.

Table 11: Patient Accounting for Subset Cohort of S-ROM and Summit Porocoat Stems

	PreOp		4 Week		3 Month		12 Month		24 Month	
	COM	MOM	COM	MOM	COM	MOM	COM	MOM	COM	MOM
TFU	114	112	114	112	114	112	114	112	114	112
Deaths (cumulative)	0	0	0	0	0	0	0	1	0	1
Component Removal (cumulative)	0	0	1	1	1	1	1	1	2	2
EFU	114	112	113	111	113	111	113	110	112	109
AFU	114	112	106	104	100	101	101	99	90	91
% Follow-up	100%	100%	94%	94%	88%	91%	89%	90%	80%	83%
<p>TFU: Theoretical Follow-up = The number of implants that have entered the beginning of each interval window at the time of database lock.</p> <p>EFU: Expected Follow-up = Theoretical Due - [Deaths + Components Removed/Revised + Consent Withdrawn]</p> <p>AFU: Actual Follow-Up</p>										

Figure 2 below is a dataset flowchart which shows all 226 S-ROM and Summit Porocoat stem subjects in the Safety Dataset, and the order in which they were excluded, from top to bottom, to obtain the Efficacy Dataset; revisions were retained regardless of exclusion criteria.

**Figure 2: Subject Accounting Dataset Flowchart;
Subset Cohort (S-ROM, Summit Porocoat Stems)**



C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a total hip replacement study performed in the US. Clinical study data was collected on 390 hips implanted. There were 194 investigational hip implantations and 196 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 12** below.

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Table 12: Baseline Demographics – All Enrolled Cohort

Demographic Element		COM N=194	MOM N=196	COM vs. MOM p-values
Enrollment	Number of procedures	194	196	-
	Number of patients	194	196	-
Age in years	Mean Age	58.9	59.1	0.792
	Minimum Age	24	25	
	Maximum Age	75	75	
Gender	Females	83 (43%)	91 (46%)	0.478
	Males	111 (57%)	105 (54%)	
Body Mass Index [kg / m ²]	Mean BMI	29.5	29.8	0.598
	Minimum BMI	20.2	19.2	
	Maximum BMI	49.2	48.8	
Primary Diagnosis	Avascular Necrosis	19 (10%)	8 (4%)	0.029
	Developmental Dysplasia	4 (2%)	3 (2%)	0.723
	Epiphyseal Defect	2 (1%)	1 (1%)	0.622
	Osteoarthritis	161 (83%)	174 (89%)	0.111
	Post Traumatic Arthritis	8 (4%)	10 (5%)	0.810
Harris Hip Score	Mean Pre-Op HH Score	48.5	49.2	0.588
	Minimum Pre-Op HH Score	15	23	
	Maximum Pre-Op HH Score	71	70	
Harris Hip Pain Category (Range 0-44)	Mean Pre-op HH Pain	13.1	13.5	0.491
	Minimum Pre-op HH Pain	0	0	
	Maximum Pre-op HH Pain	20	20	
Harris Hip Function Score (Range 0-33)	Mean Pre-op HH Function	19.5	19.5	0.982
	Minimum Pre-op HH Function	2	2	
	Maximum Pre-op HH Function	33	33	
Harris Hip Activity Score (Range 0-14)	Mean Pre-op HH Activity	8.1	8.4	0.110
	Minimum Pre-op HH Activity	0	2	
	Maximum Pre-op HH Activity	14	14	
Harris Hip Deformity Score (Range 0-4)	Mean Pre-op HH Deformity	3.4	3.3	0.353
	Minimum Pre-op HH Deformity	0	0	
	Maximum Pre-op HH Deformity	4	4	
Harris Hip Range of Motion Score (Range 0-5)	Mean Pre-op HH ROM	4.4	4.4	0.885
	Minimum Pre-op HH ROM	1	2	
	Maximum Pre-op HH ROM	5	5	

The demographics of the subset cohort (subjects who received S-ROM and Summit Porocoat stems) study population are typical for a total hip replacement study performed in the US 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 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 13** below.

Table 13: Baseline Demographics - Subset Cohort (S-ROM and Summit Porocoat Stems)

Demographic Element		COM N=114	MOM N=112	COM vs. MOM p-values
Enrollment	Number of procedures	114	112	-
	Number of patients	114	112	-
Age in years	Mean Age	58.5	58.9	0.744
	Minimum Age	24	25	
	Maximum Age	75	75	
Gender	Females	55 (48%)	53 (47%)	0.895
	Males	59 (52%)	59 (53%)	
Body Mass Index [kg / m ²]	Mean BMI	29.9	30.8	0.274
	Minimum BMI	20.7	19.8	
	Maximum BMI	49.2	48.8	
Primary Diagnosis	Avascular Necrosis	12 (10.5%)	7 (6%)	0.338
	Developmental Dysplasia	3 (2.6%)	2 (2%)	1.000
	Epiphyseal Defect	2 (1.8%)	0 (0%)	0.498
	Osteoarthritis	93 (81.6%)	98 (88%)	0.271
	Post Traumatic Arthritis	4 (3.5%)	5 (4%)	0.747
Harris Hip Score	Mean Pre-Op HH Score	47.4	47.5	0.950
	Minimum Pre-Op HH Score	15	23	
	Maximum Pre-Op HH Score	69	66	
Harris Hip Pain Category (Range 0-44)	Mean Pre-op HH Pain	13.5	13.6	0.930
	Minimum Pre-op HH Pain	0	0	
	Maximum Pre-op HH Pain	20	20	
Harris Hip Function Score (Range 0-33)	Mean Pre-op HH Function	18.7	18.6	0.948
	Minimum Pre-op HH Function	2	2	
	Maximum Pre-op HH Function	30	33	
Harris Hip Activity Score (Range 0-14)	Mean Pre-op HH Activity	7.8	8.1	0.380
	Minimum Pre-op HH Activity	0	2	
	Maximum Pre-op HH Activity	12	14	
Harris Hip Deformity Score (Range 0-4)	Mean Pre-op HH Deformity	3.1	2.8	0.327
	Minimum Pre-op HH Deformity	0	0	
	Maximum Pre-op HH Deformity	4	4	
Harris Hip Range of Motion Score (Range 0-5)	Mean Pre-op HH ROM	4.3	4.4	0.654
	Minimum Pre-op HH ROM	1	2	
	Maximum Pre-op HH ROM	5	5	

The demographics of the bilateral cohort (subjects who received a contra-lateral hip during the study period) study population are typical for a total hip replacement study performed in the US.

Comparisons were conducted and means were compared with a t-test, and proportions were compared with Fisher's Exact test. Results of these analyses are provided in **Table 14** below.

Table 14: Baseline Demographics - Bilateral Cohort

Demographic Element		COM N=12	MOM N=16	COM vs. MOM p-values
Enrollment	Number of procedures	12	16	-
	Number of patients	12	16	-
Age in years	Mean Age	61.7	61.1	0.865
	Minimum Age	49	41	
	Maximum Age	72	74	
Gender	Females	4 (33%)	10 (63%)	0.252
	Males	8 (67%)	6 (37%)	
Body Mass Index [kg / m2]	Mean BMI	30.4	29.0	0.417
	Minimum BMI	23.2	23.4	
	Maximum BMI	38.4	39.5	
Primary Diagnosis	Avascular Necrosis	4 (33%)	0 (0%)	0.024
	Osteoarthritis	8 (67%)	16 (100%)	0.024
Harris Hip Score	Mean Pre-Op HH Score	47.1	48.7	0.704
	Minimum Pre-Op HH Score	34	28	
	Maximum Pre-Op HH Score	62	66	
Harris Hip Pain Category (Range 0-44)	Mean Pre-op HH Pain	13.3	13.8	0.828
	Minimum Pre-op HH Pain	10	10	
	Maximum Pre-op HH Pain	20	20	
Harris Hip Function Score (Range 0-33)	Mean Pre-op HH Function	17.9	18.6	0.719
	Minimum Pre-op HH Function	7	2	
	Maximum Pre-op HH Function	24	30	
Harris Hip Activity Score (Range 0-14)	Mean Pre-op HH Activity	8.2	8.4	0.812
	Minimum Pre-op HH Activity	5	2	
	Maximum Pre-op HH Activity	12	11	
Harris Hip Deformity Score (Range 0-4)	Mean Pre-op HH Deformity	3.3	3.5	0.766
	Minimum Pre-op HH Deformity	0	0	
	Maximum Pre-op HH Deformity	4	4	
Harris Hip Range of Motion Score (Range 0-5)	Mean Pre-op HH ROM	4.3	4.4	0.698
	Minimum Pre-op HH ROM	3	3	
	Maximum Pre-op HH ROM	5	5	

Component Distribution

The distribution of femoral stem and acetabular shell components of the system for each of the two treatment groups (investigational and control) is summarized below in **Table 15** for subjects in the All Enrolled Cohort. The applicant is only seeking approval for two

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of the femoral stems actually studied as part of the clinical study (i.e., Summit Porocoat (standard and high offset) and S-ROM femoral stems).

Table 15: Device Component Distribution – All Enrolled Cohort

		COM Group		MOM Group	
		N	%	N	%
Head Size	28mm	11	6%	13	7%
	36mm	183	94%	183	93%
Femoral Stems	AML	31	16%	32	16%
	Prodigy	15	8%	16	8%
	Summit Porocoat	67	35%	65	33%
	Standard Offset	25		22	
	High Offset	42		43	
	Summit Duofix	34	18%	36	18%
	Standard Offset	8		13	
High Offset	26		23		
S-ROM	47	24%	47	24%	
Acetabular Shells	100 series	107	55%	116	59%
	300 series	9	5%	7	4%
	Multihole	0	0%	0	0%
	Sector	78	40%	73	37%

The distribution of femoral stem and acetabular shell components of the system for each of the two treatment groups (investigational and control) is summarized below in **Table 16** for subjects in the Subset Cohort (subjects who received S-ROM and Summit Porocoat stems).

Table 16: Device Component Distribution – Subset Cohort (S-ROM, Summit Porocoat Stems)

		COM		MOM	
		N=114	%	N=112	%
Head Size	28mm	7	6%	6	5%
	36mm	107	94%	106	95%
Femoral Stems	Summit Porocoat	67	59%	65	58%
	Standard Offset	(25)	(22%)	(22)	(20%)
	High Offset	(42)	(37%)	(43)	(38%)
	S-ROM	47	41%	47	42%
Acetabular Shells	100 series	57	50%	64	57%
	300 series	9	8%	7	6%
	Sector	48	42%	41	37%

The distribution of femoral stem and acetabular shell components of the system for each of the two treatment groups (investigational and control) is summarized below in **Table 17** for subjects in the Bilateral Cohort (subjects who received a contra-lateral hip during the study period).

Table 17: Device Component Distribution – Bilateral Cohort

		COM		MOM	
		N=12	%	N=16	%
Head Size	28mm	1	8%	1	6%
	36mm	11	92%	15	94%
Femoral Stems	Summit Porocoat	5	42%	6	38%
	Standard Offset	(0)	(0%)	(2)	(13%)
	High Offset	(5)	(42%)	(4)	(25%)
	Summit Duofix	2	17%	2	13%
	S-ROM	2	17%	2	13%
	AML	3	25%	5	31%
	Prodigy	0	0%	1	6%
Acetabular Shells	100 series	4	33%	8	50%
	300 series	2	17%	0	0%
	Sector	6	50%	8	50%

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 390 enrolled subjects (194 investigational and 196 control cohorts) followed over the 24 month evaluation.

The key safety outcomes for this study are presented below in **Tables 18** through **39**.

Adverse events that occurred in the PMA clinical study:

The Safety Dataset was used to compare:

- 1) Revisions,
- 2) Adverse Events
- 3) Kaplan Meier Survivorship

1. Revisions

Revision was defined as a reoperation where any component (acetabular or femoral) was removed or replaced. There were a total of 2 revisions (1.0%) reported out of 194 procedures in the investigational cohort and 3 revisions

(1.5%) reported out of 196 procedures in the control cohort. **Table 18** provides a summary of the revision procedure, treatment group, age, gender, primary diagnosis, duration of implantation and reason for revision for each subject. None of the subjects in the Bilateral Cohort had a device revision. There appears to be no clinically meaningful difference in the rates of revision between the investigational and control cohorts.

Table 18: Revisions – All Enrolled Cohort

Procedure(s)	Treatment Group	Age / Gender	Primary Diagnosis	Duration of Implantation	Reason for Revision / Removal
Femoral ceramic head and metal insert removed and replaced	Investigational (COM)	67/M	Osteoarthritis	23.3 mo	Deep infection
Femoral ceramic head and metal insert removed and replaced	Investigational (COM)	75/F	Osteoarthritis	0.6 mo	Incision and Drainage procedure
Femoral metal head, insert, shell, and stem removed and replaced	Control (MOM)	70/F	Osteoarthritis	19.5 mo	Loose prosthesis and occult infection
Femoral metal head removed and replaced	Control (MOM)	50/M	Avascular necrosis	4.2 mo	Chronic dislocations
Femoral metal head was exchanged	Control (MOM)	61/M	Osteoarthritis	1 wk	Irrigation and debridement of a hematoma and evaluation of leg length stability intra-operatively

2. Adverse Events

Adverse events reported from the clinical study of 390 hip procedures are listed in **Tables 19** through **36** below.

a. Adverse Events by Subject

In **Tables 19** through **27** 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. Fisher's Exact Test was used to compare proportions across the two treatment groups.

1. Intraoperative Complications

The most common intraoperative complication for the all enrolled cohort was femoral bone fracture, which was observed in 3.1% of all subjects (12/390). There was no difference in the proportions of observed intraoperative adverse events across treatment groups (see **Table 19** below). Fisher's Exact Test was used to compare proportions across the two treatment groups

Table 19: Comparison of Frequency of Intraoperative Adverse Events for the All Enrolled Cohort

Adverse Events	COM		MOM		p-value
	AEs / Subjects (%)	95% Confidence Interval	AEs / Subjects (%)	95% Confidence Interval	
Fracture of femur	4 / 194 (2.1%)	0.6 - 5.2	8 / 196 (4.1%)	1.8 - 7.9	0.380
Seating acetabular prosthesis	0 / 194 (0.0%)	-	2 / 196 (1.0%)	0.1 - 3.6	0.499
Seating femoral prosthesis	1 / 194 (0.5%)	0.0 - 2.8	1 / 196 (0.5%)	0.0 - 2.8	1.000
Other complication	2 / 194 (1.0%)	0.1 - 3.7	3 / 196 (1.5%)	0.3 - 4.4	1.000

Other intraoperative adverse events denoted as other complication above consisted of:

- COM: one (1) arterial bleed occurring during surgical approach, one (1) inadequate spinal anesthesia, and
- MOM: one (1) volatile blood pressure resolved with medical management, one (1) high spinal anesthesia level resulting in stoppage of case and repeat surgery without complication, and one (1) excessive blood loss and metal liner did not engage correctly resulting in a new shell and liner placement.

The intraoperative adverse events for the Subset Cohort (S-ROM, Summit Porocoat Stems) are provided below (**Table 20**). There were no clinically significant differences in the frequency of intraoperative adverse events between treatment groups.

Table 20: Comparison of Frequency of Intraoperative Adverse Events Subset Cohort (S-ROM, Summit Porocoat Stems)

Adverse Events	COM		MOM	
	AEs / Subjects (%)	95% Confidence Levels	AEs / Subjects (%)	95% Confidence Levels
Fracture of femur	2 / 114 (1.8%)	0.2 - 6.2	6 / 112 (5.4%)	2.0 - 11.3
Other complication	2 / 114 (1.8%)	0.2 - 6.7	3 / 112 (2.7%)	0.6 - 7.6

The intraoperative adverse events for the Bilateral Cohort (subjects that received a contra-lateral hip during the study period) are provided below (Table 21).

Table 21: Comparison of Frequency of Intraoperative Adverse Events Bilateral Cohort

Adverse Events	COM		MOM	
	AEs / Subjects (%)	95% Confidence Levels	AEs / Subjects (%)	95% Confidence Levels
Fracture of femur	0 / 12 (0.0%)	0.0 - 0.0	1 / 16 (6.3%)	0.2 - 30.2

2. 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, constitutional symptoms, gastrointestinal, respiratory, and dermatological.

There was no statistically or clinically meaningful difference in the proportion of postoperative systemic adverse events (see Table 22 below).

Table 22: Comparison of Frequency of Postoperative Systemic Adverse Events – All Enrolled Cohort

Adverse Events at the 24 month Endpoint	COM			MOM			p-value*
	AEs / Subjects	%	95% Confidence Interval	AEs / Subjects	%	95% Confidence Interval	
Allergy	0 / 194	0.0	0.0 - 0.0	1 / 196	0.5	0.0 - 2.8	1.000
Cancer	3 / 194	1.5	0.3 - 4.5	3 / 196	1.5	0.3 - 4.4	1.000
Cardiovascular	27 / 194	13.9	9.4 - 19.6	22 / 196	11.2	7.2 - 16.5	0.448
Central nervous system	16 / 194	8.2	4.8 - 13.1	16 / 196	8.2	4.7 - 12.9	1.000
Constitutional symptom	24 / 194	12.4	8.1 - 17.9	20 / 196	10.2	6.4 - 15.3	0.526
Dermatological	20 / 194	10.3	6.4 - 15.5	19 / 196	9.7	5.9 - 14.7	0.867
Endocrine/metabolic	5 / 194	2.6	0.8 - 5.9	5 / 196	2.6	0.8 - 5.9	1.000
Gastrointestinal	21 / 194	10.8	6.8 - 16.1	21 / 196	10.7	6.8 - 15.9	1.000
Genitourinary	17 / 194	8.8	5.2 - 13.7	20 / 196	10.2	6.4 - 15.3	0.730
Head, eyes, ears, nose and throat	11 / 194	5.7	2.9 - 9.9	11 / 196	5.6	2.8 - 9.8	1.000
Hematological	15 / 194	7.7	4.4 - 12.4	18 / 196	9.2	5.5 - 14.1	0.717
Infection	1 / 194	0.5	0.0 - 2.8	0 / 196	0.0	0.0 - 0.0	0.497
Lymphatics	2 / 194	1.0	0.1 - 3.7	0 / 196	0.0	0.0 - 0.0	0.247
Metabolic/laboratory	2 / 194	1.0	0.1 - 3.7	2 / 196	1.0	0.1 - 3.6	1.000
Musculoskeletal	107 / 194	55.2	47.9 - 62.3	101 / 196	51.5	44.3 - 58.7	0.479
Neurological	1 / 194	0.5	0.0 - 2.8	0 / 196	0.0	0.0 - 0.0	0.497
Other - accident	6 / 194	3.1	1.1 - 6.6	5 / 196	2.6	0.8 - 5.9	0.770
Other - edema	4 / 194	2.1	0.6 - 5.2	2 / 196	1.0	0.1 - 3.6	0.448
Pain	0 / 194	0.0	0.0 - 0.0	1 / 196	0.5	0.0 - 2.8	1.000
Peripheral nervous system	7 / 194	3.6	1.5 - 7.3	8 / 196	4.1	1.8 - 7.9	1.000
Pulmonary embolism	2 / 194	1.0	0.1 - 3.7	1 / 196	0.5	0.0 - 2.8	0.622
Respiratory system	18 / 194	9.3	5.6 - 14.3	20 / 196	10.2	6.4 - 15.3	0.865
Thrombosis/thrombophlebitis	1 / 194	0.5	0.0 - 2.8	1 / 196	0.5	0.0 - 2.8	1.000
Wound problem	0 / 194	0.0	0.0 - 0.0	1 / 196	0.5	0.0 - 2.8	1.000

* *p*-values calculated using Fisher's exact test for independent proportions (two-sided)

For both the investigational and control treatments the most commonly reported postoperative systemic complication was musculoskeletal. Frequently reported adverse events for the subset cohort included: cardiovascular and gastrointestinal.

There was no clinically meaningful difference in the frequency of postoperative systemic adverse events (see **Table 23** below).

Table 23: Comparison of Frequency of Postoperative Systemic Adverse Events – Subset Cohort (S-ROM, Summit Porocoat Stems)

Adverse Events at the 24 month Endpoint	COM			MOM		
	AEs / Subjects	%	95% Confidence Levels	AEs / Subjects	%	95% Confidence Levels
Cancer	1 / 114	0.9	0.0 - 4.8	2 / 112	1.8	0.2 - 6.3
Cardiovascular	16 / 114	14.0	8.2 - 21.8	13 / 112	11.6	6.3 - 19.0
Central nervous system	11 / 114	9.6	4.9 - 16.6	8 / 112	7.1	3.1 - 13.6
Constitutional symptom	17 / 114	14.9	8.9 - 22.8	11 / 112	9.8	5.0 - 16.9
Dermatological	7 / 114	6.1	2.5 - 12.2	9 / 112	8.0	3.7 - 14.7
Endocrine/metabolic	3 / 114	2.6	0.6 - 7.5	3 / 112	2.7	0.6 - 7.6
Gastrointestinal	14 / 114	12.3	6.9 - 19.8	12 / 112	10.7	5.7 - 18.0
Genitourinary	9 / 114	7.9	3.7 - 14.5	11 / 112	9.8	5.0 - 16.9
Head, eyes, ears, nose and throat	4 / 114	3.5	1.0 - 8.7	5 / 112	4.5	1.5 - 10.1
Hematological	10 / 114	8.8	4.3 - 15.5	8 / 112	7.1	3.1 - 13.6
Musculoskeletal	56 / 114	49.1	39.6 - 58.7	56 / 112	50.0	40.4 - 59.6
Other - accident	4 / 114	3.5	1.0 - 8.7	3 / 112	2.7	0.6 - 7.6
Other - edema	3 / 114	2.6	0.6 - 7.5	2 / 112	1.8	0.2 - 6.3
Pain	0 / 114	0.0	0.0 - 0.0	1 / 112	0.9	0.0 - 4.9
Peripheral nervous system	5 / 114	4.4	1.4 - 9.9	4 / 112	3.6	1.0 - 8.9
Pulmonary embolism	1 / 114	0.9	0.0 - 4.8	1 / 112	0.9	0.0 - 4.9
Respiratory system	10 / 114	8.8	4.3 - 15.5	12 / 112	10.7	5.7 - 18.0
Thrombosis/thrombophlebitis	0 / 114	0.0	0.0 - 0.0	1 / 112	0.9	0.0 - 4.9
Wound problem	0 / 114	0.0	0.0 - 0.0	1 / 112	0.9	0.0 - 4.9

For both the investigational and control treatments the most commonly reported postoperative systemic complication was musculoskeletal. Frequently reported adverse events for the bilateral cohort included: cardiovascular, gastrointestinal, hematological and dermatological.

There was no clinically meaningful difference in the frequency of postoperative systemic adverse events (see **Table 24** below).

Table 24: Comparison of Frequency of Postoperative Systemic Adverse Events – Bilateral Cohort

Adverse Events at the 24 month Endpoint	COM			MOM		
	AEs / Subjects	%	95% Confidence Levels	AEs / Subjects	%	95% Confidence Levels
Cancer	1 / 12	8.3	0.2 - 38.5	0 / 16	0.0	0.0 - 0.0
Cardiovascular	4 / 12	33.3	9.9 - 65.1	6 / 16	37.5	15.2 - 64.6
Central nervous system	2 / 12	16.7	2.1 - 48.4	1 / 16	6.3	0.2 - 30.2
Constitutional symptom	1 / 12	8.3	0.2 - 38.5	2 / 16	12.5	1.6 - 38.4
Dermatological	4 / 12	33.3	9.9 - 65.1	4 / 16	25.0	7.3 - 52.4
Endocrine/metabolic	1 / 12	8.3	0.2 - 38.5	2 / 16	12.5	1.6 - 38.4
Gastrointestinal	3 / 12	25.0	5.5 - 57.2	2 / 16	12.5	1.6 - 38.4
Genitourinary	3 / 12	25.0	5.5 - 57.2	2 / 16	12.5	1.6 - 38.4
Head, eyes, ears, nose and throat	0 / 12	0.0	0.0 - 0.0	2 / 16	12.5	1.6 - 38.4
Hematological	2 / 12	16.7	2.1 - 48.4	5 / 16	31.3	11.0 - 58.7
Infection	1 / 12	8.3	0.2 - 38.5	0 / 16	0.0	0.0 - 0.0
Metabolic/laboratory	1 / 12	8.3	0.2 - 38.5	1 / 16	6.3	0.2 - 30.2
Musculoskeletal	12 / 12	100	73.5 - 100.0	16 / 16	100	79.4 - 100.0
Other - accident	1 / 12	8.3	0.2 - 38.5	0 / 16	0.0	0.0 - 0.0
Peripheral nervous system	0 / 12	0.0	0.0 - 0.0	1 / 16	6.3	0.2 - 30.2
Pulmonary embolism	2 / 12	16.7	2.1 - 48.4	0 / 16	0.0	0.0 - 0.0
Respiratory system	4 / 12	33.3	9.9 - 65.1	2 / 16	12.5	1.6 - 38.4
Thrombosis/thrombophlebitis	1 / 12	8.3	0.2 - 38.5	0 / 16	0.0	0.0 - 0.0

3. Postoperative Operative Site Adverse Events

The most commonly reported postoperative operative site complication for investigational and control subjects was trochanteric bursitis. Other complications included wound problems, dermatological, musculoskeletal, pain, and thigh pain.

There were no statistical differences in the proportions of postoperative operative site adverse events (see **Table 25** below) for the All Enrolled Cohort, with the exception of 'Other – Accident', which showed a significantly higher proportion in the investigational COM group

compared to the control MOM group (these consisted of hip pain, bruised hip, glass in foot, fall, and muscle strain).

Table 25: Comparison of Frequency of Postoperative Operative Site Adverse Events – All Enrolled Cohort

Adverse Events at the 24m Endpoint	COM			MOM			p-value*
	AEs / Subjects	%	95% Confidence Interval	AEs / Subjects	%	95% Confidence Interval	
Bone fracture	2 / 194	1.0	0.1 - 3.7	4 / 196	2.0	0.6 - 5.1	0.685
Deep infection	1 / 194	0.5	0.0 - 2.8	0 / 196	0.0	0.0 - 0.0	0.497
Dermatological	13 / 194	6.7	3.6 - 11.2	7 / 196	3.6	1.5 - 7.2	0.176
Dislocation	2 / 194	1.0	0.1 - 3.7	2 / 196	1.0	0.1 - 3.6	1.000
Hematoma	3 / 194	1.5	0.3 - 4.5	2 / 196	1.0	0.1 - 3.6	0.684
Hematoma requiring drainage	1 / 194	0.5	0.0 - 2.8	1 / 196	0.5	0.0 - 2.8	1.000
Infection	0 / 194	0.0	0.0 - 0.0	1 / 196	0.5	0.0 - 2.8	1.000
Musculoskeletal	8 / 194	4.1	1.8 - 8.0	7 / 196	3.6	1.5 - 7.2	0.799
Other - accident	5 / 194	2.6	0.8 - 5.9	0 / 196	0.0	0.0 - 0.0	0.030
Other - edema	0 / 194	0.0	0.0 - 0.0	4 / 196	2.0	0.6 - 5.1	0.123
Pain	9 / 194	4.6	2.1 - 8.6	8 / 196	4.1	1.8 - 7.9	0.810
Pain: thigh	8 / 194	4.1	1.8 - 8.0	4 / 196	2.0	0.6 - 5.1	0.258
Subluxation	0 / 194	0.0	0.0 - 0.0	1 / 196	0.5	0.0 - 2.8	1.000
Trochanteric bursitis	15 / 194	7.7	4.4 - 12.4	10 / 196	5.1	2.5 - 9.2	0.309
Wound problem	12 / 194	6.2	3.2 - 10.6	10 / 196	5.1	2.5 - 9.2	0.667

* *p*-values calculated using Fisher's exact test for independent proportions (two-sided)

The most commonly reported postoperative operative site complication for investigational and control subjects was trochanteric bursitis and wound problems for the Subset Cohort (S-ROM and Summit Porocoat Stems). Other complications included musculoskeletal, pain, and thigh pain.

There was no clinically meaningful difference in the frequency of postoperative operative site adverse events reported for the Subset Cohort (S-Rom, Summit Porocoat Stems) as seen in **Table 26** below.

Table 26: Comparison of Frequency of Postoperative Operative Site Adverse Events – Subset Cohort (S-ROM, Summit Porocoat Stems)

Adverse Events at the 24 month Endpoint	COM			MOM		
	AEs / Subjects	%	95% Confidence Levels	AEs / Subjects	%	95% Confidence Levels
Bone fracture	0 / 114	0.0	0.0 - 0.0	1 / 112	0.9	0.0 - 4.9
Deep infection	1 / 114	0.9	0.0 - 4.8	0 / 112	0.0	0.0 - 0.0
Dermatological	2 / 114	1.8	0.2 - 6.2	3 / 112	2.7	0.6 - 7.6
Dislocation	1 / 114	0.9	0.0 - 4.8	1 / 112	0.9	0.0 - 4.9
Hematoma	1 / 114	0.9	0.0 - 4.8	2 / 112	1.8	0.2 - 6.3
Hematoma requiring drainage	1 / 114	0.9	0.0 - 4.8	1 / 112	0.9	0.0 - 4.9
Infection	0 / 114	0.0	0.0 - 0.0	1 / 112	0.9	0.0 - 4.9
Musculoskeletal	5 / 114	4.4	1.4 - 9.9	5 / 112	4.5	1.5 - 10.1
Other - accident	4 / 114	3.5	1.0 - 8.7	0 / 112	0.0	0.0 - 0.0
Other - edema	0 / 114	0.0	0.0 - 0.0	3 / 112	2.7	0.6 - 7.6
Pain	7 / 114	6.1	2.5 - 12.2	5 / 112	4.5	1.5 - 10.1
Pain: thigh	4 / 114	3.5	1.0 - 8.7	4 / 112	3.6	1.0 - 8.9
Trochanteric bursitis	8 / 114	7.0	3.1 - 13.4	6 / 112	5.4	2.0 - 11.3
Wound problem	9 / 114	7.9	3.7 - 14.5	4 / 112	3.6	1.0 - 8.9

The most commonly reported postoperative operative site complications for investigational and control subjects in the Bilateral Cohort were dermatological, thigh pain, and trochanteric bursitis.

There was no clinically meaningful difference in the frequency of postoperative operative site adverse events for the Bilateral Cohort (see **Table 27** below).

Table 27: Comparison of Frequency of Postoperative Operative Site Adverse Events – Bilateral Cohort

Adverse Events at the 24 month Endpoint	COM			MOM		
	AEs / Subjects	%	95% Confidence Levels	AEs / Subjects	%	95% Confidence Levels
Dermatological	2 / 12	16.7	2.1 - 48.4	0 / 16	0.0	0.0 - 0.0
Pain: thigh	0 / 12	0.0	0.0 - 0.0	1 / 16	6.3	0.2 - 30.2
Trochanteric bursitis	0 / 12	0.0	0.0 - 0.0	1 / 16	6.3	0.2 - 30.2

b. Comparison of Subjects with Any Adverse Event

There were no statistically or clinically significant differences in the proportions of adverse events grouped by type of AE (intraoperative, postoperative operative site, or systemic) or overall, across investigational (COM) and control (MOM) treatment groups for the All Enrolled Cohort (see Table 28 below).

Table 28: Safety Dataset - Comparison of Subjects with any Adverse Event - All Enrolled Cohort

Adverse Events at 24m Endpoint	COM			MOM			P-value*
	AEs / Subjects	%	95% Confidence Interval	AEs / Subjects	%	95% Confidence Interval	
Any Complication	148 / 194	76.3	69.7 - 82.1	142 / 196	72.4	65.6 - 78.6	0.418
Intraoperative	7 / 194	3.6	1.5 - 7.3	13 / 196	6.6	3.6 - 11.1	0.251
Operative Site	60 / 194	30.9	24.5 - 38.0	46 / 196	23.5	17.7 - 30.0	0.111
Systemic	135 / 194	69.6	62.6 - 76.0	129 / 196	65.8	58.7 - 72.4	0.450

* p-values calculated using Fisher's exact test for independent proportions (two-sided)

There were no clinically significant differences in the frequency of adverse events grouped by type of AE (intraoperative, postoperative operative site, or systemic) across treatment groups for subjects in the Subset Cohort (S-ROM, Summit Porocoat Stems) (see Table 29 below).

Table 29: Safety Dataset - Comparison of Subjects with any Adverse Event – Subset Cohort (S-ROM, Summit Porocoat stems)

Adverse Events	COM			MOM		
	AEs / Subjects	%	95% Confidence Levels	AEs / Subjects	%	95% Confidence Levels
Any Complication	80 / 114	70.2	60.9 - 78.4	81 / 112	72.3	63.1 - 80.4
Intraoperative	4 / 114	3.5	1.0 - 8.7	9 / 112	8.0	3.7 - 14.7
Operative Site	33 / 114	28.9	20.8 - 38.2	28 / 112	25.0	17.3 - 34.1
Systemic	75 / 114	65.8	56.3 - 74.4	75 / 112	67.0	57.4 - 75.6

There were no clinically significant differences in the frequency of adverse events grouped by type of AE (intraoperative, postoperative operative site, or systemic) across treatment groups for the Bilateral Cohort (see **Table 30** below).

Table 30: Safety Dataset - Comparison of Subjects with any Adverse Event – Bilateral Cohort

Adverse Events	COM			MOM		
	AEs / Subjects	%	95% Confidence Levels	AEs / Subjects	%	95% Confidence Levels
Any Complication	12 / 12	100	73.5 - 100.0	16 / 16	100	79.4 - 100.0
Intraoperative	0 / 12	0.0	0.0 - 0.0	1 / 16	6.3	0.2 - 30.2
Operative Site	2 / 12	16.7	2.1 - 48.4	2 / 16	12.5	1.6 - 38.4
Systemic	12 / 12	100	73.5 - 100.0	16 / 16	100	79.4 - 100.0

c. Distribution of Adverse Events over Time

In **Tables 31 - 36**, a time course of the occurrence of post-operative systemic adverse events is displayed.

Below (**Table 31**) is the time course distribution of the occurrence of post-operative systemic adverse events for the all enrolled cohort. 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 31 - Time Course Occurrence of Post-Operative Systemic Adverse Events:
All Enrolled Cohort**

Complication	Interval														Total		
	Post-op		4 Week		3 Month		1 Year		2 Year		3 Year		Unknown Onset				
	I	C	I	C	I	C	I	C	I	C	I	C	I	C	I	C	
	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Allergy		1														1	
Cancer					1	2	2	1								3	3
Cardiovascular	24	15	2		3	4	10	8	1	2						40	29
Central Nervous System	13	11	1	1	3	4	3	2	2	1						22	19
Constitutional Symptom	23	22	2	1	1	2				2						26	27
Dermatological	15	12	2	2	4	1	3	5	1	1						25	21
Endocrine/Metabolic	3	2						3	1		1					5	5
Gastrointestinal	18	9	3		1	4	11	8	2	6						35	27
Genitourinary	14	9	2	1	6	4	6	8	1	2		1				29	25
Head, Eyes, Ears, Nose, and Throat	3	3	1	2	3	5	3	3	1	1						11	14
Hematological	14	15			3	2	1	1	2	2						20	20
Infection							1									1	
Lymphatics			1								1					2	
Metabolic/Laboratory	1	1					1	1								2	2
Musculoskeletal	16	22	23	29	57	52	70	49	26	41	2	2	1	1	195	196	
Neurological									1							1	
Other - Accident		1	1			3	3	1	1		1					6	5
Other - Edema	1		3					1	1							4	2
Pain				1													1
Peripheral Nervous System	2	2	1	1	2	3	2	1	1	1						8	8
Pulmonary Embolism				1	2											2	1
Respiratory System	4	9	5	4	4	6	4	3	2	4						19	26
Thrombosis/Thrombophlebitis	1	1														1	1
Wound Problem		1															1
Total	152	136	47	43	90	92	120	95	42	64	5	3	1	1	457	434	

* I = investigational group, C = control group, N = number of occurrences

Table 32 shows the time course distribution of the occurrence of post-operative systemic adverse events for the Subset Cohort (S-ROM and Summit Porocoat stems). 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 32: Time Course Occurrence of Post-Operative Systemic Adverse Events: Subset Cohort (S-ROM, Summit Porocoat stems)

Complication	Interval																Total	
	Post-op		4 Week		3 Month		1 Year		2 Year		3 Year		Unknown Onset		I	C		
	I	C	I	C	I	C	I	C	I	C	I	C	I	C				
	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N		
Cancer					1	1	1								1	2		
Cardiovascular	14	8	2		1	3	5	6		1					22	18		
Central Nervous System	8	4	1	1	3	2	1		1	1					14	8		
Constitutional Symptom	17	11	1			2				1					18	14		
Dermatological	6	5		1			1	3		1					7	10		
Endocrine/Metabolic	2	2						1	1						3	3		
Gastrointestinal	9	7	3		1	1	6	4	2	1					21	13		
Genitourinary	4	4	2		4	3	2	6		2					12	15		
Head, Eyes, Ears, Nose, and Throat	1	2			2	3	1	2							4	7		
Hematological	6	6			3	1	1		1	1					11	8		
Musculoskeletal	9	10	14	12	27	24	36	23	14	25		1		1	100	96		
Other - Accident		1	1			1	2	1	1						4	3		
Other - Edema			3					1		1					3	2		
Pain				1												1		
Peripheral Nervous System	1	1	1		2	2	2	1							6	4		
Pulmonary Embolism				1	1										1	1		
Respiratory System	2	7	3	3	2	3	2	1	2						11	14		
Thrombosis/Thrombophlebitis		1														1		
Wound Problem		1														1		
Total	79	70	31	19	46	46	60	50	22	34		1		1	238	221		

* I = investigational group, C = control group, N = number of occurrences

Table 33 shows the time course distribution of the occurrence of post-operative systemic adverse events for the Bilateral Cohort. 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 33: Time Course Occurrence of Post-Operative Systemic Adverse Events: Bilateral Cohort

Complication	Interval												Total		
	Post-op		4 Week		3 Month		1 Year		2 Year		3 Year				
	I	C	I	C	I	C	I	C	I	C	I	C	I	C	
	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Cancer							1							1	
Cardiovascular	7	3	1		1		2	3		1				11	7
Central Nervous System	2	1			1									3	1
Constitutional Symptom	1	2												1	2
Dermatological	3	2		1	1	1	2	1						6	5
Endocrine/Metabolic		1						1			1			1	2
Gastrointestinal	2						5	1		1				7	2
Genitourinary	2	1				1	4		1					7	2
Head, Eyes, Ears, Nose, and Throat		1				1									2
Hematological	1	4			1			1		1				2	6
Infection							1							1	
Metabolic/Laboratory		1					1							1	1
Musculoskeletal	2	3	4	3	8	13	8	10	2	11				24	40
Other - Accident							1							1	
Peripheral Nervous System						1									1
Pulmonary Embolism					2									2	
Respiratory System		1	1		1		2	1		2				4	4
Thrombosis/Thrombophlebitis	1													1	
Total	21	20	6	4	15	17	27	18	3	16	1			73	75

* I = investigational group, C = control group, N = number of occurrences

In **Tables 34**, a time course of the occurrence of post-operative operative site adverse events is displayed for the All Enrolled Cohort. An adverse event may be reported more than once per subject in the table if the adverse event occurred more than once across time.

Table 34: Time Course Occurrence of Postoperative, Operative Site Adverse Events - All Enrolled Cohort

Complication	Interval										Total		
	Post-op		4 Week		3 Month		1 Year		2 Year		I	C	
	I	C	I	C	I	C	I	C	I	C			
	N	N	N	N	N	N	N	N	N	N	N	N	
Bone Fracture		2	1	1	2			1				3	4
Deep infection									1			1	
Dermatological	11	6	1			1	1					13	7
Dislocation	3	1		1		2						3	4
Hematoma	1	2	1						1			3	2
Hematoma Requiring Drainage	1	1										1	1
Infection								1					1
Musculoskeletal	1	4	3		3	4	1	1		1		8	10
Other - Accident	1				2		1		1			5	
Other - Edema		4											4
Pain	2	2	1	2	4	3	1	1	1			9	8
Pain: Thigh			2	1	3	1		1	3	1		8	4
Subluxation						1							1
Trochanteric Bursitis		2	1	1	7	6	4	2	5	1		17	12
Wound Problem	13	7		3								13	10
Total	33	31	10	9	21	18	8	7	12	3		84	68

* I = investigational group, C = control group, N = number of occurrences

In **Tables 35**, a time course of the occurrence of post-operative operative site adverse events is displayed for the Subset Cohort (S-ROM and Summit Porocoat Stems). An adverse event may be reported more than once per subject in the table if the adverse event occurred more than once across time.

Table 35: Time Course Occurrence of Postoperative, Operative Site Adverse Events- Subset Cohort (S-ROM, Summit Porocoat stems)

Complication	Interval										Total	
	Post-op		4 Week		3 Month		1 Year		2 Year			
	I	C	I	C	I	C	I	C	I	C	I	C
	N	N	N	N	N	N	N	N	N	N	N	N
Bone Fracture		1										1
Deep infection									1			1
Dermatological	2	2				1						2 3
Dislocation	2	1										2 1
Hematoma	1	2										1 2
Hematoma Requiring Drainage	1	1										1 1
Infection								1				1
Musculoskeletal	1	3	1		2	3	1	1		1		5 8
Other - Accident	1				1		1		1			4
Other - Edema		3										3
Pain	2	1		1	3	2	1	1	1			7 5
Pain: Thigh			1	1	2	1		1	1	1		4 4
Trochanteric Bursitis		1	1		3	4	4	2	2			10 7
Wound Problem	9	2		2								9 4
Total	19	17	3	4	11	11	7	6	6	2		46 40

* I = investigational group, C = control group, N = number of occurrences

In **Tables 36**, a time course of the occurrence of post-operative operative site adverse events is displayed for the bilateral cohort. An adverse event may be reported more than once per subject in the table if the adverse event occurred more than once across time.

Table 36: Time Course Occurrence of Postoperative, Operative Site Adverse Events - Bilateral Cohort

	Interval							
	Post-op		3 Month		1 Year		Total	
	I	C	I	C	I	C	I	C
	N	N	N	N	N	N	N	N
Complication								
Dematological	2						2	
Pain: Thigh						1		1
Trochanteric Bursitis				1		1		2
Total	2			1		2	2	3

* I = investigational group, C = control group, N = number of occurrences

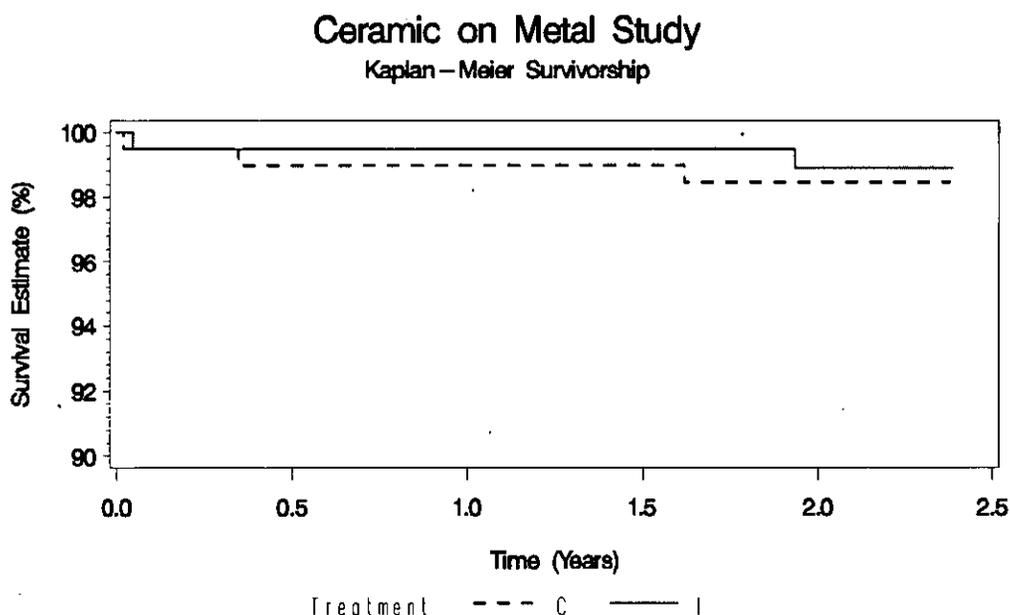
3. Kaplan-Meier Survivorship Analysis

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 37**. When revision was defined as the endpoint for survivorship, the results demonstrated a 98.9% survivorship (95% confidence interval: 95.6%-99.7%) for the investigational subjects at 2.4 years and a 98.4% survivorship (95% confidence interval: 95.2%-99.5%) for the control hips at 2.4 years. There was no clinically or statistically significant difference between investigational and control subjects (log-rank p-value =0.659).

These survivorship results are comparable to the results reported in national joint registries.

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



Event=Revision for any reason

Table 37: Safety Dataset - Survival Estimates Across Time: All Enrolled Cohort

Treatment	Years Post-op				
	0.0	0.5	1.0	1.5	2.0
I – Survival Estimate	100%	99.5%	99.5%	99.5%	98.9%
I - # Subjects Remaining	194	193	191	182	118
C – Survival Estimate	100%	99.0%	99.0%	99.0%	98.4%
C - # Subjects Remaining	196	191	190	185	114

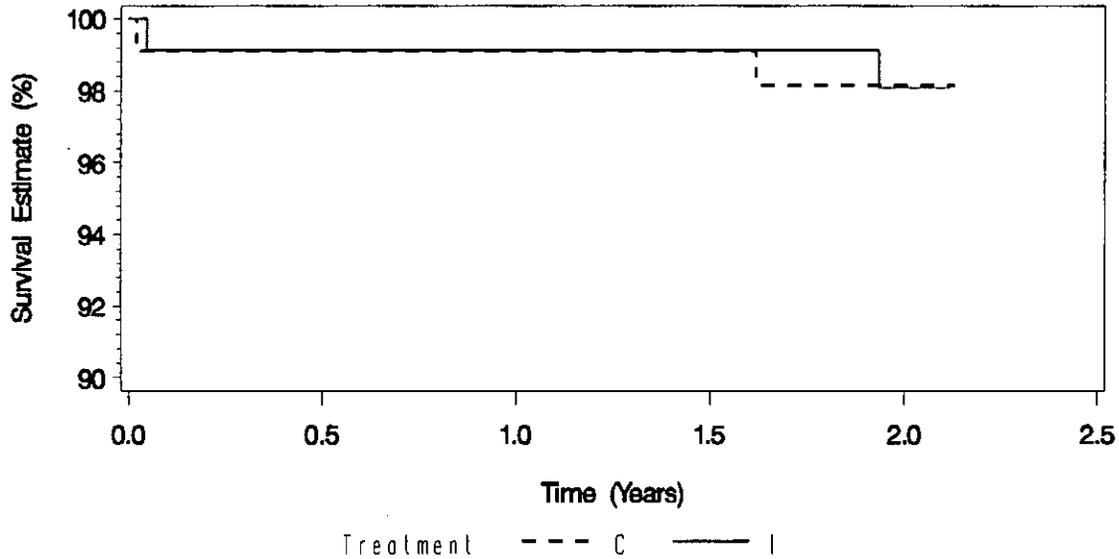
I: Investigational

C: Control

Survivorship analyses for the Subset Cohort (subjects who received S-ROM and Summit Porocoat stems only) are presented graphically in **Figure 4** and in tabular form across time in **Table 38**. Results for the Subset Cohort demonstrated a 98.1% survivorship (95% confidence interval: 92.5%-99.5%) for the investigational subjects at 2.1 years and a 98.2% survivorship (95% confidence interval: 92.9%-99.5%) for the control hips at 2.1 years. There was no statistically significant difference between investigational and control subjects (log-rank p-value =0.985).

Figure 4: Kaplan-Meier Survivorship Estimates

Ceramic on Metal Study: Subset Cohort (SROM, Summit Porocoat Stems Only)
Kaplan–Meier Survivorship



Event=Revision for any reason

**Table 38: Safety Dataset - Survival Estimates Across Time:
 Subset Cohort (S-ROM, Summit Porocoat Stems Only)**

Treatment	Years Post-op				
	0.0	0.5	1.0	1.5	2.0
I – Survival Estimate	100%	99.1%	99.1%	99.1%	98.1%
I - # Subjects Remaining	114	113	111	105	58
C – Survival Estimate	100%	99.1%	99.1%	99.1%	98.2%
C - # Subjects Remaining	112	109	108	105	60

Summary of analysis of adverse events – FDA has reviewed the differences found intra-operatively or post-operatively, and for individual adverse events, for the COM and the MOM and did not find any that raised major clinical concerns due to the COM device under study.

Metal Ion Analysis

A supplemental investigation was conducted at two (2) investigational centers. A total of 72 of the 390 study subjects, 36 MOM and 36 COM, were enrolled into this metal ion substudy. Chromium, cobalt, and titanium ions were measured preoperatively, and at 3 months, 12 months and 24 months postoperatively. Blood samples were taken at these intervals, and separated into serum and erythrocytes. Each of these sample types was tested for chromium, cobalt, and titanium ion levels. In addition, urine was tested for chromium and cobalt ion

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levels, but not for titanium. Results were reported in parts per billion (ppb), equivalent to µg/L. Data were right skewed, so medians were compared across treatment groups. **Table 39** below provides the sample size, median and range ion levels at each time interval for COM and MOM treatment groups for each of the 8 measurements.

Table 39: Median Ion Levels (µg/L)

		Preoperatively		3 Months		12 Months		24 Months	
		COM	MOM	COM	MOM	COM	MOM	COM	MOM
Urine Cobalt	N	29	32	28	29	35	32	27	28
	Median	0.22	0.24	1.82	2.05	2.52	1.98	2.99	2.64
	Range	0.09-2.24	0.04-3.14	0.19-5.25	0.15-6.70	0.31-28.25	0.60-17.14	0.38-16.05	0.40-40.90
Urine Chromium	N	29	32	27	29	35	32	27	27
	Median	0.14	0.15	0.63	0.86	0.99	0.88	1.26	1.2
	Range	0.06-1.90	0.04-0.89	0.09-1.38	0.12-2.56	0.10-7.05	0.27-3.64	0.20-6.89	0.20-4.22
Serum Cobalt	N	36	34	30	30	36	34	27	27
	Median	0.12	0.11	0.46	0.52	0.82	0.65	1	0.66
	Range	0.05-0.87	0.05-0.50	0.17-0.97	0.20-1.62	0.23-3.07	0.31-2.03	0.28-2.73	0.23-5.58
Serum Chromium	N	36	34	30	30	36	34	27	27
	Median	0.16	0.14	0.6	0.72	0.96	0.83	1.24	0.86
	Range	0.07-0.59	0.06-0.68	0.15-2.73	0.33-2.73	0.18-4.34	0.38-2.33	0.26-4.85	0.30-6.88
Serum Titanium	N	36	34	30	30	36	34	27	27
	Median	0.53	0.57	1.71	2.14	1.28	1.49	0.96	1.32
	Range	0.19-1.69	0.29-1.80	0.87-3.18	1.34-3.98	0.59-2.80	0.90-3.39	0.42-3.00	0.63-3.09
Erythrocyte Cobalt	N	36	34	30	30	36	33	30	30
	Median	0.08	0.08	0.25	0.26	0.43	0.33	0.5	0.33
	Range	0.04-0.42	0.05-0.83	0.09-0.40	0.14-0.64	0.14-1.31	0.15-1.18	0.24-1.69	0.14-6.23
Erythrocyte Chromium	N	35	33	27	28	36	33	30	30
	Median	0.98	0.8	0.9	0.89	1.25	1.6	1	0.89
	Range	0.20-6.60	0.25-3.00	0.30-3.95	0.35-3.05	0.30-6.87	0.20-52.52	0.30-4.65	0.45-8.77
Erythrocyte Titanium	N	36	34	30	30	36	33	30	30
	Median	0.88	0.86	0.85	1.03	0.93	0.9	0.65	0.83
	Range	0.50-7.45	0.60-3.03	0.65-2.83	0.55-2.40	0.55-1.35	0.50-1.63	0.05-1.55	0.40-2.15

Median values were compared across treatment groups at each time interval with a 2-sided Mann-Whitney U test because of anticipated skewness in data. There were no significant differences in medians across treatment groups at any time period, with the exception of serum titanium at 3 months ($p = 0.016$) and erythrocyte

titanium at 3 months ($p = 0.034$) (both instances indicated slightly lower titanium medians in the COM group).

While the metal ion levels associated with the Pinnacle[®] CoMplete[®] Acetabular Hip System were not statistically different than the metal-on-metal control group, the subsequent revision rates for the metal-on-metal control group as reported in national joint registries are acceptable.

The metal ion levels will continue to be monitored in subjects with the Pinnacle[®] CoMplete[®] Acetabular Hip System through a post approval study (see section **XIII – CDRH Decision**).

2. Effectiveness Results

Composite success or failure was determined at 24 months based upon a combination of clinical, radiographic, and revision criteria (see section **X.A.3. - Clinical Endpoints**). The primary analysis was a non-inferiority test of the proportion successful for the investigational group compared to the control group.

The primary composite success analysis was based on subjects with all five femoral stem types used in the IDE clinical study; however, the applicant is only currently seeking marketing approval for the Summit Porocoat femoral stem (standard and high offset) and the S-ROM femoral stem as components for the Pinnacle[®] CoMplete[®] Acetabular Hip System. Therefore, information is presented for the All Unilateral Enrolled Cohort as well as the Subset Unilateral Cohort (subjects who received S-ROM and Summit Porocoat stems).

Harris Hip Score (HHS)

Harris Hip Score was a component in determining composite success. Mean Harris Hip Scores were compared across treatment groups for all subjects as well as for the Subset Cohort of subjects with S-ROM and Summit Porocoat stems.

1. All Unilateral Enrolled: Preoperative Harris Hip score means were 48.5 (I) and 49.2 (C). There were 313 subjects in the Safety Dataset with an evaluable 24 month Harris Hip score (excluding subjects who had bilateral THA during the study period); treatment group means were 94.8 (I) and 95.8 (C) as shown in **Table 40**. The difference in 24 month Harris Hip score means across treatment groups was not significant.

Table 40: 24-Month Harris Hip Score Means, All Unilateral Subjects

Treatment	N	24 Month Harris Hip Score Mean	t-test p-value
COM	156	94.8	0.303
MOM	157	95.8	

A tally of subjects in Harris Hip Score ranges across time is presented in **Table 41** below. Not all subjects were seen at each interval and the following percentages were calculated using a denominator based on the number of available assessments in each interval.

Table 41: Harris Hip Total Score – All Unilateral Enrolled

Harris Hip Total Score								
	Pre-Op		3 Month		12 Month		24 Month	
	COM	MOM	COM	MOM	COM	MOM	COM	MOM
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Excellent (91-100)	0 (0%)	0 (0%)	84 (58.7%)	87 (63.0%)	124 (83.8%)	135 (88.8%)	130 (83.3%)	133 (84.7%)
Good (81-90)	0 (0%)	0 (0%)	35 (24.5%)	26 (18.8%)	13 (8.8%)	9 (5.9%)	17 (10.9%)	15 (9.6%)
Fair (71-80)	1 (0.6%)	0 (0%)	13 (9.1%)	15 (10.9%)	4 (2.7%)	6 (3.9%)	1 (0.6%)	8 (5.1%)
Poor (<71)	155 (99.4%)	157 (100%)	10 (7.0%)	10 (7.2%)	6 (4.1%)	2 (1.3%)	8 (5.1%)	1 (0.6%)
Missing	0 (0%)	0 (0%)	1 (0.7%)	0 (0%)	1 (0.7%)	0 (0%)	0 (0%)	0 (0%)
Total	156	157	143	138	148	152	156	157

- Subset Cohort (subjects with S-ROM and Summit Porocoat Stems):
Preoperative Harris Hip score means for the Subset Cohort of subjects with S-ROM and Summit Porocoat stems only were 47.5 (I) and 48.6 (C). There were 175 subjects from the Subset Cohort in the Safety Dataset with an evaluable 24 month Harris Hip score (excluding subjects who had bilateral THA during the study period); treatment group means were 93.7 (I) and 97.0 (C) as shown in **Table 42**. The difference in 24 month Harris Hip score means across treatment groups for this subset analysis was significant.

Table 42: 24-Month Harris Hip Score Means, Subset Unilateral Cohort (subjects with SROM and Summit Porocoat Stems)

Treatment	N	24 Month Harris Hip Score Mean	t-test p-value
COM	87	93.7	0.019
MOM	88	97.0	

A tally of subjects in Harris Hip score ranges across time is presented in **Table 43** below for subjects in the subset cohort (S-ROM and Summit

Porocoat Stems). Not all subjects were seen at each interval and the following percentages were calculated using a denominator based on the number of available assessments in each interval.

Table 43: Harris Hip Total Score – Subset Unilateral Cohort (Summit Porocoat, S-ROM)

Harris Hip Total Score								
	Pre-Op		3 Month		12 Month		24 Month	
	COM	MOM	COM	MOM	COM	MOM	COM	MOM
Excellent (91-100)	0 (0.0%)	0 (0.0%)	40 (50.6%)	46 (56.8%)	69 (81.2%)	77 (87.5%)	69 (79.3)	78 (88.6%)
Good (81-90)	0 (0.0%)	0 (0.0%)	24 (30.4%)	15 (18.5%)	10 (11.8%)	6 (6.8%)	11 (12.6%)	9 (10.2%)
Fair (71-80)	0 (0.0%)	0 (0.0%)	8 (10.1%)	11 (13.6%)	0 (0.0%)	3 (3.4%)	1 (1.1%)	1 (1.1%)
Poor (<71)	87 (100%)	88 (100%)	6 (7.6%)	9 (11.1%)	5 (5.9%)	2 (2.3%)	6 (6.9%)	0 (0.0%)
Missing	0 (0.0%)	0 (0.0%)	1 (1.3%)	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Total	87	88	79	81	85	88	87	88

Radiographic Outcomes

All Subjects: Radiographic and all other components of composite success were compared across treatment groups at 24 months for the 306 subjects in the Efficacy Dataset (see the subject accounting dataset flowchart in **Figure 1**). The proportions of successes for investigational and control treatments were compared for each criteria. (See section **X.A.3. - Clinical Endpoints**) Results are presented in **Table 45** demonstrate no statistically significant differences between investigational and control hips for any of the criteria, or for overall composite success.

Subset Cohort (subjects with S-ROM and Summit Porocoat Stems): Radiographic successes and all components of composite success were compared across treatment groups at 24 months for the Subset Cohort (S-ROM, Summit Porocoat). Results are presented in **Table 47** below, and are consistent with the results on all subjects (**Table 45**).

Composite Success

The proportion successful for the investigational COM group was 92.2% while the proportion successful for the control MOM group was 92.8%. The non-inferiority p-value was 0.007 and the associated 95% lower 1-sided confidence limit for the investigational minus control difference in proportions successful was -5.51%. These results are summarized in **Table 44** below.

Table 44: Efficacy Success/Failure Dataset - Primary Endpoint Analysis, All Enrolled

Treatment	N	Proportion Successful (N)	Lower 1-Sided 95% CL for $X_I - X_C$	Non-inferiority P-value
COM	154	92.2% (142)	-5.51%	0.007
MOM	152	92.8% (141)		

CL = confidence limit

The primary analysis null hypothesis was rejected and it was concluded that the investigational device (COM) proportion successful is non-inferior to the control device (MOM) proportion successful using a non-inferiority margin of 8%.

Table 45: Comparison of Success Rates for Efficacy Dataset, All Unilateral Subjects

Subject Success Criteria	(Investigational) 154 Subjects Successes/ Evaluable Subjects	(Control) 152 Subjects Successes/ Evaluable Subjects	Fishers Exact p-value
Clinical Success*	144 / 152 (94.7%)	142 / 149 (95.3%)	1.000
Total Harris Hip Score \geq 80	144 / 152 (94.7%)	142 / 149 (95.3%)	1.000
Mild - Slight - No Pain	148 / 152 (97.4%)	145 / 149 (97.3%)	1.000
Radiographic Success**	149 / 151 (98.7%)	147 / 148 (99.3%)	1.000
Femoral Subsidence \leq 2mm	151 / 151 (100.0%)	148 / 148 (100.0%)	No Failures
Acetabular Migration \leq 2mm	151 / 151 (100.0%)	148 / 148 (100.0%)	No Failures
Cup Inclination \leq 4 Degrees	150 / 151 (99.3%)	147 / 148 (99.3%)	1.000
No Acetabular Osteolysis	151 / 151 (100.0%)	148 / 148 (100.0%)	No Failures
No Femoral Osteolysis	151 / 151 (100.0%)	148 / 148 (100.0%)	No Failures
Acetabular Lucencies $<$ 50%	150 / 151 (99.3%)	148 / 148 (100.0%)	1.000
Femoral Lucencies $<$ 50%	151 / 151 (100.0%)	148 / 148 (100.0%)	No Failures
Absence of Revision	152 / 154 (98.7%)	149 / 152 (98.0%)	0.683
Overall Subject Success Rate	142 / 154 (92.2%)	141 / 152 (92.8%)	1.000
<p>* There were 5 revisions (2I,3C) that did not meet the minimum 24 month follow-up criteria and these 5 were added to the Success/Failure Dataset. These 5 revisions were only counted in the proportion of subjects having an 'Absence of Revision' and in the 'Overall Subject Success Rate'. These 5 revisions are not counted in the 'Clinical Success' comparisons as noted by the denominators of 152 I and 149 C.</p> <p>** The 'Radiographic Success' denominators of 151 I and 148 C result from 2 additional subjects (1I, 1C) that have excluded success/failure (S/F) radiographic outcomes. These 2 subjects are included in the overall S/F dataset because they failed 'Clinical Success' criteria.</p>			

2. Subset Cohort (subjects with S-ROM and Summit Porocoat Stems):
 The post hoc primary analysis on the Subset Cohort of subjects who received S-ROM and Summit Porocoat stems did not yield a conclusion of non-inferiority. In addition, the sensitivity analysis demonstrated a more pronounced sensitivity to the potential effect of missing data for the Subset Cohort. Both of these results were anticipated, given the smaller sample size of the Subset Cohort. The amount of missing data for the Subset Cohort appears to be roughly similar across the

different stem types as shown in **Table 46** below (subjects with 'Missing' composite success/failure endpoint data are those missing from the efficacy dataset because of inadequate 24 month Harris Hip score follow-up or with inadequate 24 month radiographic follow-up (20 I, 16 C), as displayed in the subject accounting dataset flowchart in **Figure 2**.)

Table 46: S-ROM/Summit Porocoat Success/Failure/Missing Data

	COM			MOM		
	Success	Failure	Missing	Success	Failure	Missing
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
S-ROM	37 (84.1%)	4 (9.1%)	3 (6.8%)	37 (84.1%)	0 (0%)	7 (15.9%)
Summit Porocoat	39 (62.9%)	6 (9.7%)	17 (27.4%)	45 (77.6%)	4 (6.9%)	9 (15.5%)
Total	76 (71.7%)	10 (9.4%)	20 (18.9%)	82 (80.4%)	4 (3.9%)	16 (15.7%)

Table 47: Comparison of Success Rates for Efficacy Dataset, Subset Unilateral Cohort (S-ROM and Summit Porocoat Stems Only)

Subject Success Criteria	(Investigational) 86 Subjects Successes/ Evaluable Subjects	(Control) 86 Subjects Successes/ Evaluable Subjects	Fisher's Exact p-value
Clinical Success*	78/84 (92.9%)	83/84 (98.8%)	0.117
Total Harris Hip Score >= 80	78/84 (92.9%)	83/84 (98.8%)	0.117
Mild - Slight - No Pain	81/84 (96.4%)	84/84 (100%)	0.246
Radiographic Success**	81/83 (97.6%)	82/83 (98.8%)	1.000
Femoral Subsidence <= 2mm	83/83 (100%)	83/83 (100%)	No failures
Acetabular Migration <= 2mm	83/83 (100%)	83/83 (100%)	No failures
Cup Inclination <= 4 Degrees	82/83 (98.8%)	82/83 (98.8%)	1.000
No Acetabular Osteolysis	83/83 (100%)	83/83 (100%)	No failures
No Femoral Osteolysis	83/83 (100%)	83/83 (100%)	No failures
Acetabular Lucencies < 50%	82/83 (98.8%)	83/83 (100%)	1.000
Femoral Lucencies < 50%	83/83 (100%)	83/83 (100%)	No failures
Absence of Revision	84/86 (97.7%)	84/86 (97.7%)	1.000
Overall Subject Success Rate	76/86 (88.4%)	82/86 (95.3%)	0.161
<p>* There were 4 revisions (2I, 2C) that did not meet the minimum 24 month follow-up criteria and these 4 were added to the Success/Failure Dataset. These 4 revisions were only counted in the proportion of subjects having an 'Absence of Revision' and in the 'Overall Subject Success Rate'. These 4 revisions are not counted in the 'Clinical Success' comparisons as noted by the denominators of 84 I and 84 C.</p> <p>** The 'Radiographic Success' denominators of 83 I and 83 C result from 2 additional subjects (1I, 1C) that have excluded success/failure (S/F) radiographic outcomes. These 2 subjects are included in the overall S/F dataset because they failed 'Clinical Success' criteria.</p>			

Secondary Outcomes

Subjects reported their pain on a VAS pain scale, and also reported their satisfaction and function. Results for these secondary outcomes are given below for both treatment groups.

1. VAS Pain Score: 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 by treatment group over time is given in **Table 48**. The difference in means at 24 months was not significant ($p = 0.230$).

Table 48: VAS Pain Scale Means

Treatment Group	Pre-op	3 Month	12 Month	24 Month
COM	70.8 (n=156)	10.4 (n=142)	6.2 (n=146)	6.7 (n=155)
MOM	66.8 (n=157)	8.8 (n=139)	5.5 (n=152)	5.0 (n=156)

2. Subject Self-Reported Satisfaction and Function: Results of subject responses regarding satisfaction and function demonstrated that the subjects felt:
 - Their total hip increased their function in 98.2% (166/169) of the investigational cases and 97.1% (166/171) of the control cases at 24 months postoperatively.
 - Their total hip decreased their pain in 98.2% (166/169) of the investigational cases and 98.2% (168/171) of the control cases at 24 months postoperatively.
 - Their total hip decreased their need for pain medication in 95.9% (162/169) of investigational cases and 96.5% (165/171) of control cases at 24 months postoperatively.
 - They were satisfied with their total hip in 97.6% (165/169) of the investigational cases and 99.4% (170/171) of the control groups at 24 months postoperatively.

XI. PANEL MEETING RECOMMENDATION AND FDA’S POST-PANEL ACTION

A. Panel Meeting Recommendation

At an advisory meeting held on August 18, 2009, the Orthopaedic and Rehabilitation Devices Panel recommended that DePuy Orthopaedic’s Inc. PMA application for the

Pinnacle[®] CoMplete[®] Acetabular Hip System be “Approvable with Conditions”. The recommended conditions of approval are summarized as follows:

1. The labeling should be modified to reflect equivalency with metal-on-metal hip system labeling
2. A post-approval study, to include metal ion analysis and 10-year follow-up data, with a loosely defined control group
3. Improving the readability of the patient literature provided with the device.

B. FDA’s Post-Panel Action

CDRH concurred with the Panel recommendation on August 18, 2009. Below is a discussion of CDRH action on each of the Panel’s recommendations:

- A post-approval study that enrolls patients from the IDE study as well as new patients will clinically and radiographically follow patients out to 10 years.
- The physician and patient labeling has been modified to include contraindications, warnings and precautions consistent with legally marketed metal-on-metal total hip systems with respect to risks of metal ion release.
- The patient labeling has been modified to the appropriate reading level of patients to adequately assist the patient in understand the information presented.

As part of the development of the final conditions of approval for this PMA, CDRH considered not only the Panel input but also the available data that should be further evaluated, and our experience with post approval studies for hip implants.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Safety Conclusions

The adverse effects of the 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 Pinnacle[®] CoMplete[®] Acetabular Hip System were trochanteric bursitis, wound problems, musculoskeletal problems, dermatological problems, and pain. There were a total of 5 revisions (2I and 3C), 1.25%, reported out of 390 subjects. The Kaplan-Meier Survivorship Analysis for the all enrolled cohort demonstrated a 98.9% survivorship (95% confidence interval: 95.6% - 99.7%) for the investigational subjects at 2.4 years and a 98.4% survivorship (95% confidence interval: 95.2%- 99.5%) for control subjects at 2.4 years. The Kaplan-Meier Survivorship Analysis for the subset cohort of subjects receiving either the S-ROM or Summit femoral stem demonstrated a 98.1% survivorship (95% confidence interval: 92.5% - 99.5%) for the investigational subjects at 2.1 years and a 98.2% survivorship (95% confidence interval: 92.9% - 99.5%) for control subjects at 2.1 years. There was no clinical or statistical difference in the proportion of adverse events between the investigational and control cohorts.

Regarding metal ions, there have been literature reports of asymptomatic pseudotumors and delayed hypersensitivity reaction (ALVAL) in some patients with metal-on-metal hip systems, which may be associated with abnormal wear, metal hypersensitivity or toxic effects. While the concentration of metal ions may be higher in patients who receive metal on metal hip implants versus patients who receive other bearing surfaces (i.e. metal on polyethylene, ceramic on ceramic), there is no direct evidence demonstrating that elevated metal ions in subjects receiving a ceramic on metal device adversely effects health.

B. Effectiveness Conclusions

The primary effectiveness of the subject device was based on HHS, radiographic success and absence of revisions/removal. The secondary effectiveness results were based on the Visual Analog Scale (VAS) and Subject Self-Reported Satisfaction and Function Questionnaire. In accordance with 21 CFR 860.7, the results provide a reasonable assurance of effectiveness as described above. There were 313 all enrolled subjects in the Safety Dataset with an evaluable 24 month for Harris Hip Total score (excluding 28 subjects who had bilateral THA during the study period) demonstrating a means score of 94.8 (I) and 95.8 (C). There were 175 subjects from the Subset Cohort in the Safety Dataset with an evaluable 24 month Harris Hip Total score (excluding 15 subjects who had bilateral THA during the study period) demonstrating a mean score of 93.7 (I) and 97.0 (C). The differences in 24 month Harris Hip score means across treatment groups, for both analyses, were not significant. In addition, there were no statistical significant difference between the investigational and cohort hips, in either the all enrolled or subset cohort, for radiographic outcomes and the overall composite success.

C. Overall Conclusions

The clinical data in this application support the reasonable assurance of safety and effectiveness of the Pinnacle[®] CoMplete[®] Acetabular 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 Pinnacle[®] CoMplete[®] Acetabular Hip System for the target population outweighs the risk of surgery when used in accordance with the direction of use.

XIII. CDRH DECISION

CDRH issued an approval order on June 13, 2011. The final conditions of approval cited in the approval order are described below:

1. The applicant agreed to perform a 10 year post-approval study to evaluate the mid and long term safety and effectiveness of the Pinnacle[®] CoMplete[®] Acetabular Hip System. The study will enroll a total of 250 subjects; approximately 100 subjects recruited from the IDE clinical study and approximately 150 new subjects will be recruited. In addition, a subset of 44 metal ion subjects from the IDE clinical study will be recruited. Clinical assessments will be performed at the pre-op and operative visits. Clinical and radiographic assessments will be performed at the following intervals: 4-week, 3-month, 1-year, 2-years, 3-years (optional), 4-years (optional), 5-

years, 8 years, and 10 years post-operative. Postal survey assessments will be completed at the following intervals: 6-years, 7-years, and 9 years. Metal ion levels (cobalt and chromium) will be determined in a 44 patient subset group at years 5, 8, and 10 postoperatively. 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 has agreed to initiate this study within three months of the approval of this PMA.

2. The applicant agreed that all Post Approval Study Annual Reports and PMA Annual reports will include Post-Approval Study adverse event information reported to DePuy Orthopaedics Inc. or a designated party by practitioners and user facilities as described below.

- For adverse events that are deemed not MDR-reportable, summary information of the events and outcomes will be provided. These events would include all events of device malfunction, even if no adverse clinical event was associated with the malfunction.
- Summary analyses and summary interpretations of both anticipated and unanticipated adverse events will be provided.

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

XIV. 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.