

IMPORTANT INFORMATION - Please Read Before Use
INFORMATIONS IMPORTANTES - À Lire avant utilisation
WICHTIGE INFORMATIONEN - Vor Gebrauch bitte lesen
INFORMACIÓN IMPORTANTE - Lea antes de usar el producto
INFORMAZIONI IMPORTANTI - Leggere prima dell'uso
INFORMAÇÕES IMPORTANTES - Por favor leia antes de utilizar
BELANGRIJKE INFORMATIE - Vóór gebruik doorlezen
VIGTIG INFORMATION - Læs dette før brug
VIKTIGT! - Läs detta innan produkten används
TÄRKEÄÄ TIETOA - Lue ennen käyttöä
ΣΗΜΑΝΤΙΚΕΣ ΠΛΗΡΟΦΟΡΙΕΣ - Παρακαλούμε διαβάστε πριν από τη χρήση
DŮLEŽITÉ INFORMACE - Před použitím si prosím přečtěte tento leták
FONTOS INFORMÁCIÓ - Kérjük, használat előtt olvassa elolvasandó
WAŻNE INFORMACJE - Przeczytać przed użyciem
DÔLEŽITÉ INFORMÁCIE - Prečítajte si ešte pred použitím


DePuy
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Rev. A

Pinnacle® CoMplete® Acetabular Hip System

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Implant package contents provided sterile. Unless marked as sterile, instrument set contents provided non-sterile.

DePuy Orthopaedics, Inc.
700 Orthopaedic Drive
Warsaw, IN 46582
Telephone 1-800-366-8143

CAUTION: FEDERAL LAW (USA) RESTRICTS THIS DEVICE TO SALE BY OR ON THE ORDER OF A PHYSICIAN

Information for Prescribers

Pinnacle® CoMplete® Acetabular Hip System

Description

Pinnacle® CoMplete® Acetabular Hip System

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) DePuy Pinnacle® acetabular shell/cup and which articulates with a compatible ceramic (BIOLOX *delta*® alumina) DePuy femoral bearing head as part of a total hip joint replacement. The components that are intended to be used with the Pinnacle® CoMplete® Acetabular Hip System are BIOLOX *delta*® ceramic heads, Pinnacle® Ultamet® metal liners, DePuy Summit® and SROM® femoral hip stems and Pinnacle® Acetabular Shells.

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.

Femoral Stem

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 F136 or ASTM F620 dependent on femoral stem size. The S-ROM® femoral sleeve is 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.

Pinnacle® Ultamet Metal Insert

The DePuy Pinnacle® (Ultamet®) metal insert/liner is designed to fit a compatible DePuy Pinnacle acetabular shell/cup and a compatible DePuy femoral bearing head as part of a total hip joint replacement. The Pinnacle® Ultamet® Metal Inserts consist of a metal acetabular bearing insert manufactured from high carbon CoCrMo (ASTM F1537). 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.

Pinnacle Acetabular Shells

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 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.

Do not mix inserts and shells from different systems. Pinnacle Acetabular Inserts can be used only with Pinnacle Acetabular Shells.

Pinnacle® CoMplete® Acetabular Hip System Sizing and System Compatibility

The correct selection of the prosthesis is extremely important. The following tables list the compatible components of the Pinnacle® CoMplete Acetabular Hip System:

TABLE 1 – DePuy Acetabular Component Compatibility:

| |
|---|
| Pinnacle 100 Acetabular Porocoat Cups 48mm - 66mm |
| Pinnacle 300 Acetabular Porocoat Cups 48mm - 66mm |
| Pinnacle Sector II Acetabular Porocoat Cups 48mm - 66mm |

TABLE 2 – DePuy Femoral Head Component Compatibility:

| |
|--|
| BIOLOX <i>delta</i> Ceramic Head 11/13 28mm and 36mm (+0, +3, +6 heads only) |
| BIOLOX <i>delta</i> Ceramic Head 12/14 28mm and 36mm (+1.5, +5, +8.5 and 36mm +12 heads only) |

TABLE 3 – DePuy Femoral Stem Component Compatibility:

| |
|--|
| Summit Porous standard offset |
| Summit Porous high offset |
| S-ROM stems and porous sleeves standard offset |
| S-ROM stems and porous sleeves high offset |

TABLE 4 – DePuy Acetabular Bone Screw Compatibility:

| |
|---|
| 6.5mm Pinnacle cancellous bone screws (15 – 70mm) |
|---|

Indications and Usage

The Pinnacle® CoMplete® Acetabular Hip system is a single use device intended for uncemented fixation. The 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.

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.

Information for Use

The DePuy instrumentation system, as well as DePuy's system of trial components, must be used to assure proper fit and alignment of the prosthesis. Correct fit and alignment will reduce stresses at interface surfaces to enhance implant fixation. The surgeon should refer to the appropriate surgical technique manual on use of the instrument system and implantation of the prosthesis. A special instrument is provided to enable the surgeon to remove the insert once it has been fitted in place.

Warnings and Precautions

Warnings:

Only physicians who are familiar with the implant components, instruments, procedure, clinical applications, adverse events, and risks associated with the Pinnacle® CoMplete® Acetabular Hip System should use this device.

Improper prosthesis selection or alignment, inadequate fixation, use where contraindicated or in patients whose medical, physical, mental or occupational conditions will likely result in extreme stresses to the implant may result in premature failure due to loosening, fracture or wear. Postoperative care is extremely important. The patient should be instructed on the limitations of the device and should be cautioned regarding load bearing, ranges of motion and activity levels permissible. Early motion and load bearing should be carefully monitored.

The Pinnacle (Ultamet) metal inserts are intended for use only with BIOLOX *delta* ceramic femoral heads in corresponding diameter sizes. The inner diameter of the insert must correspond to the hip head size. Use of an insert with a non-matching hip head size will result in higher stresses, accelerated wear and early failure.

This implant should not be used with other manufacturers' components or instruments. Use of components or instruments other than those recommended could lead to loosening, wear, fracture and premature failure.

Do not mix inserts and shells from different systems. Pinnacle metal inserts can be used only with Pinnacle acetabular shells/cups.

Implants are for single use only. Do not reuse an implant in order to ensure there has been no damage to the implants.

When used with multiple components of a total replacement system, the MR compatibility and safety of the entire system of implants has not been evaluated and the entire system of implants has not been tested together for heating or migration in the MR environment.

Precautions:

Pre-operative

- The patient should be informed of all potential risks and adverse effects contained in this insert. The patient should be warned that the implants can break or become damaged as a result of strenuous activity or trauma.
- Preoperative planning provides essential information regarding the appropriate prosthesis and likely combinations of components. If, during preoperative planning, an appropriately sized component is not available, the procedure should not take place. An appropriate range of implant sizes should be available prior to performing the surgical procedure.
- To prevent contamination of this prosthesis, keep free of lint and powders. Do not open the package until surgery.
- Diabetes, at present, has not been established as a contraindication. However, because of increased risk for complications such as infection, slow healing, slow wound healing, etc. the physician should fully consider the advisability of hip arthroplasty in the severely diabetic patient.

Intra-operative

- Use the recommended trial components for size determination, trial reduction and range of motion evaluation. To prevent contamination of this prosthesis, keep free of lint and powders. Do not place the implant in contact with prepared bone surface before the final decision to implant has been made; thus preserving the integrity of the actual implants and their sterile packaging.
- The trial prostheses should not be implanted.
- Examine instruments for wear or damage before use. Instruments that have experienced excessive use or force may be susceptible to breakage.

- Carefully examine each component and its packaging for any signs of damage that may have occurred during shipping or handling. Do not implant components if the packaging is damaged or if the implant shows signs of damage. Due to the brittle nature of the material, ceramic components are particularly susceptible to premature failure when scratched, cracked or otherwise damaged. Likewise, a new implant should be handled carefully to avoid damage that could compromise the mechanical integrity of the device and cause early failure or loosening.
- Implants should be accepted by the hospital or surgeon only if received with the factory packaging and labeling intact. If the sterile barrier has been broken, return the component to DePuy Orthopaedics, Inc.
- An implant should never be re-used. Any implant, once used, should be discarded. Even though it appears undamaged, it may have small defects and internal stress patterns that may lead to failure. DePuy's Single Use devices have not been designed to undergo or withstand any form of alteration, such as disassembly, cleaning or re-sterilization, after a single patient use. Reuse can potentially compromise device performance and patient safety.
- The highly polished bore of the insert should not come into contact with abrasive surfaces, as this may damage the bore and affect performance. In addition, all mating surfaces should be clean before assembly to ensure proper seating. If the insert is not properly seated into the shell it may become loose.
- Do not scratch acetabular shells and femoral components to prevent damage to the articulation surfaces. Replace any component that has been scratched or otherwise damaged during the implant procedure.
- Ensure that the inner diameter of the acetabular shell/cup matches the outer diameter of the insert. Ensure that the outer diameter of the femoral head matches the inner diameter of the insert.
- Always ensure proper alignment and seating of the acetabular and femoral components. Malalignment of the components and/or soft tissue imbalance may cause excessive wear and early implant failure.
- Care should be taken to remove bone chips and metallic debris from the implant site to reduce the risk of debris induced accelerated wear of the articular surfaces of the implant.
- Care should be taken to avoid damage to the soft tissue and blood supply during dissection of the capsular tissue.

In order to prevent sepsis, the physician is advised to follow the following recommendations:

- Consistent use of prophylactic antibiotics.
- Utilizing a laminar flow clean air system.
- Having all operating room personnel, including observers, properly attired.
- Protecting instruments from airborne contamination.
- Impermeable draping.

Post-operative

- Excessive physical activity levels and trauma to the joint replacement may cause early failure of the implant
- Loosening of the components may increase production of wear particles and accelerate damage to the bone
- Periodic, long-term follow-up is recommended to monitor the position and state of the prosthetic components, as well as the condition of the adjoining bone.

Patient Education

- Warn the patient of the surgical risks, possible adverse effects, and possible operative complications that may occur with joint arthroplasty.
- Warn the patient of the limitations of artificial joint replacement devices.
- Caution the patient to protect the joint replacement from unreasonable stresses and to follow the treating physician's instructions. In particular, warn the patient to strictly avoid high impact activities, such as running and jumping, during the first post-operative year while the bone is healing.
- Warn the patient that artificial joint replacement devices can wear out over time and may require replacement.
- All patients should be instructed on the limitation of the prosthesis and the possibility of subsequent surgery. The patient should be cautioned to monitor activities and protect the replaced joint from unreasonable stresses and follow the written instructions of the physician with respect to follow-up care and treatment. Patients should be informed that their weight and activity level may affect the longevity of the implant. Patients should be advised to report any pain, decrease in range of motion, swelling, fever, etc. as this may indicate positional changes in the implant that could lead to premature failure.

Potential Adverse Effects

Reported Device Related Adverse Effects

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

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

A complete list of the frequency and rate of complications and adverse events identified in the clinical study are provided in Tables below within the Summary of Clinical Study section.

Potential Adverse Effects Associated with Any Total Hip Arthroplasty

The following adverse effects may occur 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 necessitate 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.

Summary of Clinical Investigations

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.

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. The following subset of the components studied in the IDE are currently for use with the Pinnacle® CoMplete® Acetabular Hip System and are discussed below: 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

Among the 390 subjects enrolled in the IDE study, 226 received a S-ROM or Summit Porocoat femoral stem. Various analyses were carried out on this Subset Cohort since only these components are currently for use with the Pinnacle® CoMplete® Acetabular Hip System 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 contra-lateral 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> | | | | | | | | | | |

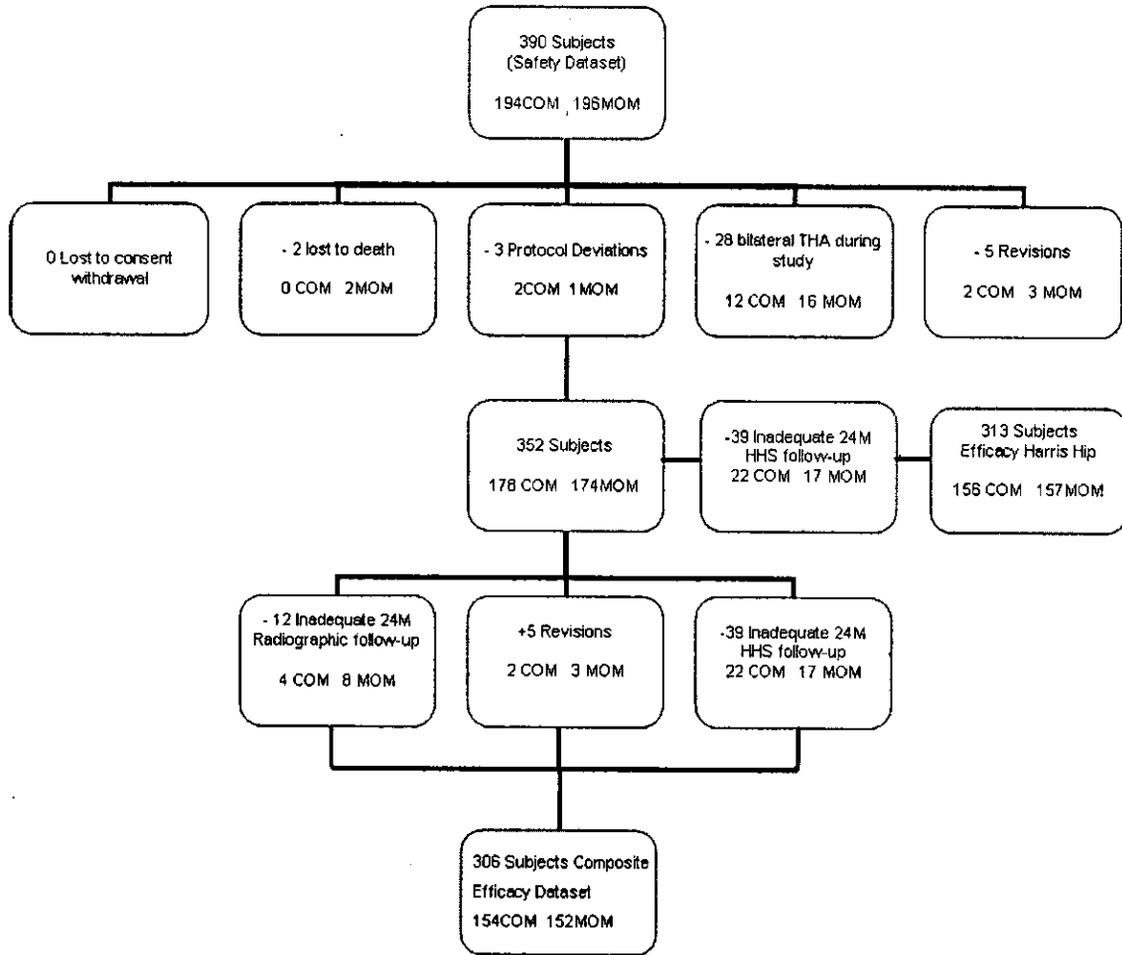
A total of 10 subjects were withdrawn from this investigation. Three of 10 were investigational and 7 of 10 were control devices. Of the 3 investigational devices, 2 were revised and 1 died. Of the 7 control devices, 3 were revised, 3 died, and 1 withdrew consent. The deaths were for reasons unrelated 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

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.

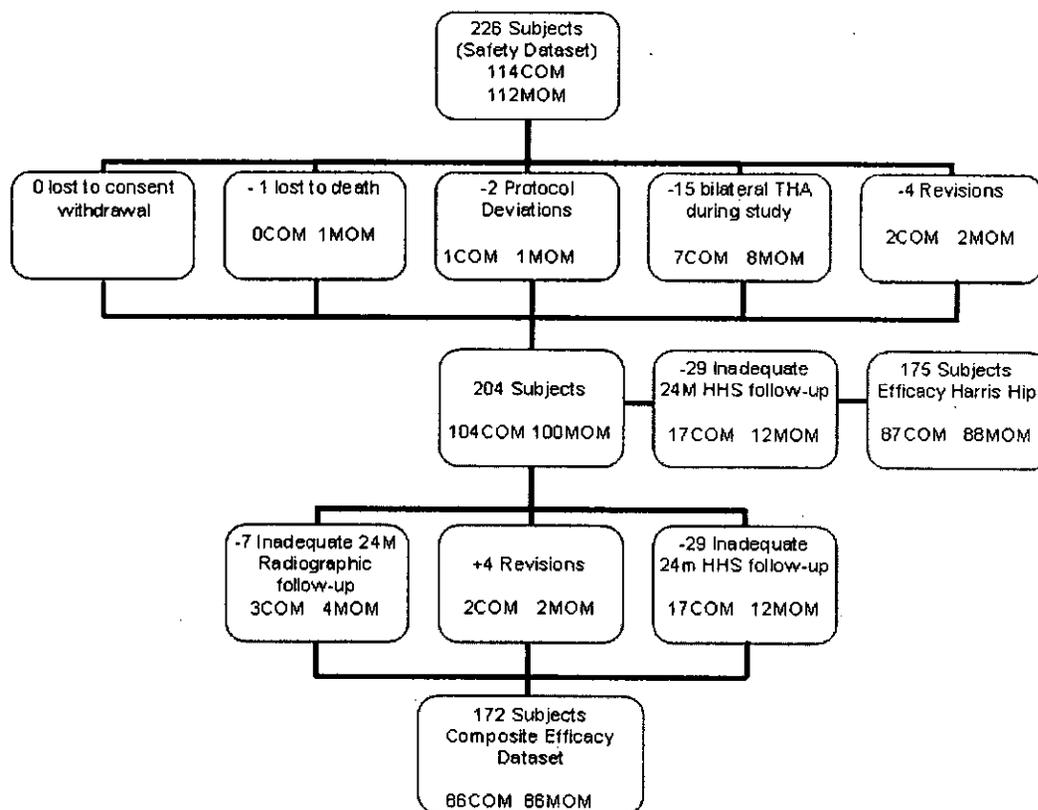
This is summarized in **Table 11** below.

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.

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 / m ²] | 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 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 | Standard Offset | 67 | 35% | 65 | 33% |
| | | High Offset | 25 | | 22 | |
| | | | 42 | | 43 | |
| | Summit Duofix | Standard Offset | 34 | 18% | 36 | 18% |
| | | High Offset | 8 | | 13 | |
| | | 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 | |
| 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 | | | | | | | | | | | |
|-----------------------------|-----------|-----------|-----------|----------|-----------|-----------|----------|----------|-----------|----------|-----------|-----------|
| | Post-op | | 4 Week | | 3 Month | | 1 Year | | 2 Year | | Total | |
| | 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

| Complication | Interval | | | | | | | |
|-----------------------|----------|---|---------|---|--------|---|-------|---|
| | Post-op | | 3 Month | | 1 Year | | Total | |
| | I | C | I | C | I | C | I | C |
| | N | N | N | N | N | N | N | N |
| 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

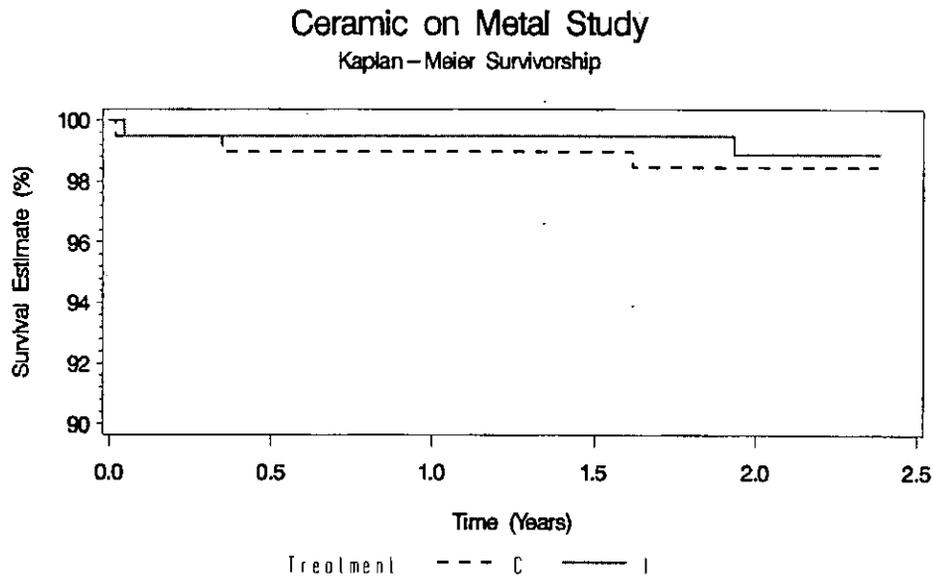
3. Kaplan-Meier Survivorship Analysis

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 |

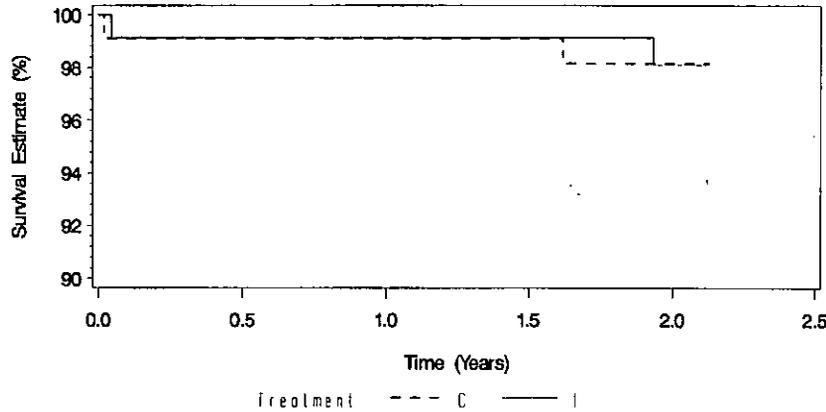
I: Investigational

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 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 ($\mu\text{g/L}$)

| | | 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.

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. Information is presented for the All Enrolled Unilateral 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 Enrolled Unilateral: 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 Enrolled Unilateral Cohort

| 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 Enrolled Unilateral Cohort

| 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 S-ROM 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 Enrolled Unilateral Cohort

| 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 ≥ 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 ≤ 2 mm | 151 / 151 (100.0%) | 148 / 148 (100.0%) | No Failures |
| Acetabular Migration ≤ 2 mm | 151 / 151 (100.0%) | 148 / 148 (100.0%) | No Failures |
| Cup Inclination ≤ 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 |
| * 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. | | | |
| ** 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. | | | |

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.

Conclusions Drawn from the Study Data

In conclusion, the results of this IDE clinical study have demonstrated safety and efficacy of the Pinnacle® CoMplete® Acetabular Hip System. Efficacy was demonstrated by showing that the investigational devices were non-inferior to the control devices with respect to the proportion of successes under a non-inferiority margin of 8%. Safety was demonstrated by showing that there were no significant differences in the proportions of adverse events across treatment groups and that survivorship was not significantly different across treatment groups. Long-term clinical performance of ceramic-on-metal devices continues to be studied.

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 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.

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.

Overall Conclusions

The clinical data in this application support the reasonable assurance of safety and effectiveness of the Pinnacle® CoMplete® Acetabular System when used in accordance with the indications for use and indicated population. Therefore, it is reasonable to conclude that the benefits of the Pinnacle® CoMplete® Acetabular System for the target population, outweighs the risk of surgery when used in accordance with the direction of use.

Sterility and Handling

- The implants described in this package insert are provided sterile as indicated on the individual product's label.
- **DO NOT RESTERILIZE**
- Implants are for single use only. Components may not be resterilized by the hospital because of the possibility of damaging the articulating and interfacing surfaces of the implant
- The implants should be opened using aseptic OR techniques. The package should be opened only after the correct size has been determined, as opened packages may not be returned for credit.
- Implants in sterile packaging should be inspected to ensure that the packaging has not been damaged or previously opened. **DO NOT USE if the package is damaged or broken as sterility may be compromised.**

Further information is available from your DePuy representative on request.

An electronic version of the IFU might be available at www.eIFU.com

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INTERPRETATION OF SYMBOLS

SIGNIFICATION DES SYMBOLES

BEDEUTUNG DER SYMBOLE

INTERPRETACION DE SIMBOLOS

INTERPRETAZIONE DEI SIMBOLI

INTERPRETAÇÃO DE SÍMBOLOS

BETEKENIS VAN DE SYMBOLEN

BETYDNING AF SYMBOLER

FÖRKLARNING AV OLIKA SYMBOLERS BETYDELSE

SYMBOLIEN SELITYKSET

ΕΡΜΗΝΕΙΑ ΣΥΜΒΟΛΩΝ

VYSVĚTLIVKY VÝRAZŮ A SYMBOLŮ

**MAGYARÁZAT A HASZNÁLT JELEKHEZ
ÉS KIFEJEZÉSEKHEZ**

ZNACZENIE SYMBOLI I TERMINÓW

VYSVETLENIE TERMÍNOV A SYMBOLOV

| Symbol to be Included in IFU | Interpretation | Symbol(s) |
|------------------------------|--|--|
| X | DEPUY, INC. | D/DP |
| X | QUANTITY | QTY |
| X | MATERIAL | MATL |
| X | MANUFACTURED BY: | MFG and MFG/MANUFACTURED BY: |
| X | MANUFACTURER |  |
| X | MADE IN | MADE IN |
| X | DISTRIBUTED BY | DIST |
| X | SIZE | SIZE and SZ |
| X | CAUTION: FEDERAL (USA) LAW RESTRICTS THIS DEVICE TO SALE BY OR ON THE ORDER OF A PHYSICIAN | R_x Only |
| X | DO NOT USE IF PACKAGE IS DAMAGED |  |
| X | AUTHORISED REPRESENTATIVE IN THE EUROPEAN COMMUNITY | EC REP |
| X | OUTER DIAMETER / INNER DIAMETER | O.D. / I.D. |
| X | COBALT CHROME | C or CoCr |
| X | For recognized manufacturer and model designation, refer to product label. | For recognized manufacturer and model designation, refer to product label. |



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DePuy (Ireland)
Loughbeg, Ringaskiddy
Co. Cork
Ireland
Tel: +353 214914278
Fax: +353 214914199



*

DePuy Orthopaedics, Inc
700 Orthopaedic Drive
Warsaw, IN 46582
USA
Tel: 1+(800) 366 8143



*

DePuy International Ltd.
St. Anthony's Road
Leeds LS11 8DT
England
Tel: +44 (113) 270 0461
Fax: +44 (113) 272 4101

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700 Orthopaedic Drive
Warsaw, IN 46582
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Tel: 1+(800) 366 8143



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