SUMMARY OF SAFETY AND EFFECTIVENESS

I. GENERAL INFORMATION

Device Generic Name:	Prosthesis, Hip, Semi-constrained, Resurfacing Metal/Metal hybrid fixation
Device Trade Name:	Cormet Hip Resurfacing System
Applicant Name and Address:	Corin USA 10500 University Center Drive, Suite 190 Tampa, FL 33612
Premarket Approval Number:	P050016
Date of Panel Recommendation:	February 22, 2007
Date of Notice of Approval to Applicant:	July 3, 2007

II. INDICATIONS FOR USE

The Cormet Hip Resurfacing System is a single use device intended for hybrid fixation: cemented femoral head and cementless acetabular component. The Cormet Hip Resurfacing System is intended for use in resurfacing hip arthroplasty for reduction or relief of pain and/or improved hip function in skeletally mature patients having the following conditions:

1. non-inflammatory degenerative arthritis such as osteoarthritis and avascular necrosis;
2. inflammatory arthritis such as rheumatoid arthritis.

The Cormet Hip Resurfacing System is intended for patients who, due to their relatively younger age or increased activity level, may not be suitable for traditional total hip arthroplasty due to an increased possibility of requiring ipsilateral hip joint revision.

III. CONTRAINDICATIONS

1. Patients with active or suspected infection in or around the hip joint;
2. Patients who are skeletally immature;
3. Patients with bone stock inadequate to support the device including:
   - Patients with severe osteopenia should not receive the Cormet Hip Resurfacing System procedure. Patients with a family history of severe osteoporosis or severe osteopenia.
   - Patients with osteonecrosis or avascular necrosis (AVN) with >50% involvement of the femoral head (regardless of Ficat Grade) should not receive a Cormet Hip Resurfacing device.
   - Patients with multiple cysts of the femoral head (>1cm) should not receive a Cormet Hip Resurfacing device.
   - Note – In cases of questionable bone stock, a Dual Energy X-Ray Absorptiometry (DEXA) scan may be necessary to assess inadequate bone stock.

4. Patients with any vascular insufficiency, muscular atrophy, or neuromuscular disease severe enough to compromise implant stability or postoperative recovery.
5. Females of child bearing age due to unknown effects on the fetus of metal ion release.
6. Patients with known moderate or severe renal insufficiency.
7. Patients who are immunosuppressed with diseases such as AIDS or persons receiving high doses of corticosteroids.
8. Patients who are severely overweight.
9. Patients with known or suspected metal sensitivity (e.g., jewelry).

IV. WARNINGS AND PRECAUTIONS

1. Patients on medications (such as high-dose or chronic amino glycoside treatment) or with co-morbidities (such as diabetes) that increase the risk of future, significant renal impairment should be advised of the possibility of increase in systemic metal ion concentration. Preoperative and postoperative monitoring of renal function (such as creatinine, Glomerular Filtration Rate (GFR), Blood Urea Nitrogen (BUN)) will be necessary.
2. Currently, Corin does not have a commercially available modular femoral head for use with the Cormet resurfacing shell. If the Cormet resurfacing head must be revised to a total hip arthroplasty, the acetabular shell should also be revised even if it is well fixed.
3. Based on the analysis of a multicenter prospective study of 1030 patients in 14 centers the following were identified as risk factors for revision: Patients who are female, who receive a smaller component size (i.e. 40 or 44mm), who have a diagnosis other than osteoarthritis (i.e. avascular necrosis, rheumatoid arthritis), a leg length discrepancy greater than or equal to 1 cm, or low baseline Harris Hip Score (HHS) have a greater risk of revision than other patients. The more risk factors a patient has, the greater the risk of procedure failure requiring a revision to the hip. Please see Tables 21 and 23 for revision rates for each risk factor group.

Please see the complete list of *Warnings and Precautions* in the Instructions for Use for the Cormet Hip Resurfacing System.

V. DEVICE DESCRIPTION

General Overview

The Cormet Hip Resurfacing System is a metal-on-metal hip resurfacing system. The system consists of a stemmed resurfacing femoral head component designed for cemented fixation and an acetabular component designed for cementless fixation. The acetabular component has a bi-coating™ of plasma sprayed titanium and hydroxyapatite (HA).

Materials

Table 1: Materials

Component	Material	Standard
Femoral Resurfacing Head	Cobalt Chromium Alloy	ASTM F75[1]
Acetabular Component	Cobalt Chromium Alloy Unalloyed Pure Titanium (coating) Hydroxyapatite powder (coating)	ASTM F75 ISO 5832 Part 2[2] ASTM F1185[3]

Sizing and System Compatibility

Each femoral head component is compatible with two acetabular components with the exception of the 56mm diameter head, which is only compatible with the 62mm nominal outside diameter (OD) acetabular cup.

Table 2: Description of Components

Femoral Head (Nominal Outside Diameter)	**Acetabular Component** (Nominal Inside Diameter of cup x Nominal Outside Diameter of cup)
40mm	40 x 46mm, 40 x 48mm
44mm	44 x 50mm, 44 x 52mm
48mm	48 x 54mm, 48 x 56mm
52mm	52 x 58mm, 52 x 60mm
56mm	56 x 62mm

VI. ALTERNATE PRACTICES AND PROCEDURES

1. Non-surgical treatment (e.g., reduced activity, medications, physical therapy) or no treatment at all;
2. Other commercially available total hip replacement devices. Commonly used implant bearing materials for total hip arthroplasty include metal on ultra-high molecular weight polyethylene (UHMWPE), ceramic on UHMWPE, metal on metal, and ceramic on ceramic.
3. Rotational osteotomy;
4. Hip fusion.

VII. MARKETING HISTORY

The Cormet Hip Resurfacing System was launched in Europe in 1997. It has been distributed in the countries listed in Table 3. The Cormet Hip Resurfacing System has not been withdrawn from marketing for any reason relating to the safety and effectiveness of the device.

[1] Standard Specification for Cobalt-28 Chromium-6 Molybdenum Alloy Castings and Casting Alloy for Surgical Implants

[2] Implants for Surgery. Metallic Materials. Part 2: Unalloyed Titanium

[3] Standard Specification for Composition of Hydroxylapatite for Surgical Implants

Table 3: Worldwide Marketing History

Argentina	Ecuador	Italy	Spain
Australia	Egypt	Japan	Sri Lanka
Belgium	Finland	Lebanon	Sweden
Brazil	France	Malta	Switzerland
Canada	Germany	Mexico	Syria
Chile	Greece	Pakistan	Taiwan
China	Holland	Portugal	Turkey
Colombia	India	Qatar	U.A.E.
Croatia	Iran	Saudi Arabia	U.K.
Cyprus	Israel	South Africa	Venezuela

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Reported Device Related Adverse Effects

The most commonly reported Cormet Hip Resurfacing device related adverse events are:

- femoral neck fracture
- femoral component migration/loosening
- acetabular component migration/loosening
- femoral subsidence
- dislocation
- greater trochanter fracture
- lesser trochanter fracture

A complete list of the frequency and rate of complications and adverse events identified in the clinical study are provided in the Summary of Clinical Studies, Tables 18-20.

Potential Adverse Effects

The following adverse effects may occur in association with hip replacement surgery including the Cormet Hip Resurfacing System:

1. Device failure because the components cannot be expected to indefinitely withstand the activity level and loads of normal healthy bone.
2. Dislocation of the hip resurfacing prosthesis can occur due to inappropriate patient activity, trauma or other biomechanical considerations.
3. Loosening of hip resurfacing components can occur. Early mechanical loosening may result from inadequate initial fixation, 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.
4. Fatigue fracture of the implants as a result of excessive loading, malalignment, or trauma.
5. Peripheral neuropathies, nerve damage, circulatory compromise and heterotopic bone formation may occur.
6. Surgical complications including, but not limited to: genitourinary disorders; gastrointestinal disorders; vascular disorders, including thrombus; bronchopulmonary disorders, including emboli; myocardial infarction or death.
7. A sudden, pronounced, intraoperative blood pressure decrease due to the use of bone cement.

8. Hematoma or damage to blood vessels resulting in large blood loss.
9. Delayed wound healing.
10. Superficial or deep infection. Infections may occur months to years after surgery and these infections are difficult to treat and may require reoperation with removal surgery and later replacement at another time.
11. Increased hip pain and/or reduced hip function.
12. Metal sensitivity reactions or allergic reactions or metallosis.
13. Adverse effects may necessitate reoperation, revision, arthrodesis of the involved joint, Girdlestone and/or amputation of the limb. Surgeons should advise patients of these potential adverse effects.
14. Bone perforation or fracture (occurring either intraoperatively or occurring postoperatively as a result of trauma, excessive loading, osteolysis or osteoporosis).
15. Wear deformation of the articular surface (as a result of excessive loading or implant malalignment).
16. Limb length discrepancy.
17. Osteolysis and/or other periprosthetic bone loss.

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

IX. SUMMARY OF PRECLINICAL STUDIES

General Overview

The following preclinical studies were carried out on the Cormet Hip Resurfacing System: wear, frictional torque, fatigue strength testing, surface coating characterization, range of motion (ROM), luxation wear, metal ion analysis and sterilization/shelf-life validation.

Wear Testing

Worst Case Design:
The applicant performed wear testing on both extremes of the range (40mm and 56mm) in order to explore the potential worst case scenarios.

Acceptance Criteria:
The amount of wear particles produced was compared to the wear generated by a 28mm bearing couple (control), which is the standard size for a total hip replacement.

Methods:
Three wear testing studies were completed.

1. Three variables were tested to investigate which parameters had the most effect on wear: Sphericity, Diametrical Clearance and Metallurgy. The test compared the 'heat-treated' (Hot Isostatically Pressed and Solution Annealed) Cormet device to the previously manufactured 'as-cast' type device. Two 48mm diameter Cormet devices and one 'as-cast' type device were run to two million cycles at 2.1kN maximum load (3x body weight) establishing steady-state conditions with diametrical bearing clearances of 81μm, 291μm and 300μm respectively.
2. Another wear study evaluated the effect of metallurgy ('as cast' vs. 'heat-treated' high carbon 40mm diameter Co-Cr-Mo bearings) on wear. Four 28mm and four 56mm diameter 'double heat-treated' metal-on-metal bearings were run to six million

cycles under normal gait conditions. Radial clearance of the bearings was controlled to 110μm, initial surface finish to 0.01μm and sphericity to between 4 to 8μm. The loading cycle was based on the 'Paul' cycle applying between 50N and 2450N at 1Hz.

3. The final study investigated the effects of heat treatment on wear rates in metal-on-metal bearings. Four 40mm diameter 'as-cast' and four 40mm diameter 'heat-treated' metal-on-metal bearings were tested under standard and 'severe' gait (fast-jogging) conditions up to six million cycles. Diametrical clearances were a mean of 214μm in the 'heat-treated' group and 258μm in the 'as cast' group and sphericity was controlled to <10μm in all the samples. All components were subject to three million cycles of 'normal walking' (standard gait) with a maximum load of 2450N at 1Hz.

Results:

1. There is no difference between the 'heat-treated' Cormet and 'as cast' devices. However, the Cormet devices, with improved sphericity, did show improved wear performance over versions of previously manufactured devices.
2. The 28mm diameter bearings indicated the highest steady-state wear rate with the largest running-in wear occurring in the 56mm bearings. The 40mm group had lower running-in and steady-state wear compared to the 28mm coupling. The 56mm bearings produced the lowest steady-state wear of all the groups.
3. The steady-state wear rates ($0.4mm^3/10^6$ cycles) found during 'normal walking' were similar to those for 36mm diameter metal-on-metal bearings reported in the literature. When 'normal walking' was resumed after the 'severe' wear, then the steady state wear rates returned to the level found prior to the 'severe' test regime.

Frictional Torque

Worst Case Design:

Size 56mm bearing samples were assumed 'worst-case' since torque is proportional to head diameter. These samples had the minimal diametrical clearances of 150μm, which provides the maximum initial contact area.

Acceptance Criteria:

Andersson *et al.*[1] suggested the torque required to remove a well cemented acetabular cup from a cadaveric socket is 100Nm.

Methods:

1. In December 2005, five 56mm heads were paired with five 62mm cups to give the specified diametrical clearance (150μm). The frictional torque of each bearing pair was recorded independently in flexion-extension and internal-external rotation under a joint load of 2.45kN and 4.5kN.
2. Two 48mm diameter Cormet heads were studied with diametrical clearances of 81 and 291 microns.
3. New and worn components from previous wear studies were tested (40mm and 56mm heads). Flexion-extension and rotational torques were measured. Tests were performed at normal walking loads (2.45kN) and at extreme load cycles (4.5kN).

Results:

1. The maximum absolute torque was recorded at an average of 11.9Nm and 22.4Nm under a test load of 2.45kN and 4.5kN, respectively. The maximum absolute torque for internal-

external rotation was found to be an average of 3.3Nm and 3.9Nm under a test load of 2.45kN and 4.5kN, respectively.

2. The 81μm and 291μm samples exhibited maximum torques (during the initial running-in period) of 18.5Nm and 8.5Nm, reducing to averages of 11Nm and 5.3Nm, respectively, during steady-state wear.
3. The maximum torque was found to occur during flexion-extension motion. The maximum absolute (modulus) torque was recorded in the 'as-new' condition for the 56mm bearings at an average of 7.40 and 10.65Nm for the loads of 2.45kN and 4.5kN, respectively.

Fatigue Strength Testing

Worst case:
The distance from the center of rotation of the spherical head to the point of contact between the stem and the pre-drilled hole is the maximum for the 56mm head. The force that is transmitted through the center of the resurfacing head, therefore, creates a maximum bending moment in the 56mm device.

Acceptance Criteria:
ISO 7206-8 "Implants for Surgery - Partial and Total Hip Joint Prostheses - Part 8: Endurance Performance of Stemmed Femoral Components with Application of Torsion" for total hip replacements.

Methods:
The test method was configured to simulate the fault condition of the resurfacing head similar to ISO 7206-4 "Implants for Surgery - Partial and Total Hip Joint Prostheses - Part 4: Determination of Endurance Properties of Stemmed Femoral Components." The short stem was fixed 25mm below the underside of the head. Five static tests were performed. The failure point was identified as the point on the load/extension graphs where the elastic region ended (became non-linear).

Five samples were then dynamically tested at 3kN (approximately 50% of the mean static failure load) at 30Hz to five million cycles.

Results:
The mean static failure load was 6.28 ± 0.55 kN. All samples went on to survive higher loads without catastrophic failure, but with permanent deformation of the femoral stem. Five samples were then dynamically tested at 3kN at 30Hz to five million cycles without failure in the same test configuration.

Surface Coating Characterization

The acetabular component is coated with a plasma sprayed unalloyed titanium and hydroxyapatite (HA) coating.

Plasma Spray

Acceptance Criteria:

The static shear strength of surface/substrate interface should exceed 20 MPa for porous surface coatings as tested per ASTM F1044 "Standard Test Method for Shear Testing of Calcium Phosphate Coatings and Metallic Coatings." The static tensile strength of the surface/substrate shall exceed 20 MPa for porous surface coatings. Shear fatigue strength testing per ASTM F1160 "Standard Test Method for Shear and Bending, Fatigue of Calcium Phosphate and Metallic Medical and Composite Calcium Phosphate/Metallic Coatings" should exceed 10 million cycles at a stress of 10MPa.

Methods:

The static shear strength of surface/substrate was tested per ASTM F1044. The static tensile strength of the surface/substrate was evaluated per ASTM F1147 "Standard Test Method for Tension Testing of Calcium Phosphate and Metal Coatings" and the shear fatigue strength was evaluated per ASTM F1160.

Results:

Table 4 summarizes the results of the plasma spray coating testing.

Table 4: Plasma Spray Coating Test Results

Test	N	Results	S.D.
Static Shear (ASTM F1044)	5	20.9 MPa	4.1
Static Tension (ASTM F1147)	3	35.9 MPa	2.8
Abrasion Strength	6	54.1mg weight loss	6.4
Surface Roughness	6	Ra 25.7 microns	7.2

Shear fatigue strength testing per ASTM F1160 was completed on six samples for 10 million cycles at a stress of 10MPa with no failures.

Hydroxyapatite (HA) Coating

Acceptance Criteria:

The acceptance criteria are described in FDA's "510(k) Information needed for Hydroxyapatite Coated Orthopaedic Implants dated March 10, 1995 (revised 2/20/97)."

Methods:

The HA coating was characterized with regard to density, particle size, porosity thickness, Ca/P ratio, solubility/dissolution, bonding strength and crystallinity.

Results:

Table 5 summarizes the results of the HA characterization.

Table 5: HA Coating Characterization

Chemical Composition	$2(Ca_5(PO_4)_3OH)$
Trace Elements	As <1 ppm Cd <1 ppm Hg <1 ppm Pb <1 ppm Total Heavy Metals <50
Ca/P ratio	Powder 1.697 (1.667± 0.03) Coating 1.655 (1.667± 0.02)
Crystallinity	Coating: 62%
Crystalline Phases	%HAP Powder: >97% Coating: >70%
	% Alpha Tricalcium Phosphate (TCP) Powder: 0 Coating: <4%
	% Beta TCP Powder: 0 Coating: <6%
	%TCPM Powder: 0 Coating: <7%
	%CaO Powder: 0.7% Coating: <1%

Density	3.096 g/cm^3
Grain Size	10% <17 μm 90% <83 μm
Porosity	Global porosity: 27% Pore medium size: 38.92 μm Standard deviation: 31.71 μm
Thickness	119 μm
Solubility	$2x10^{-56}$
Tensile Strength	33.31 MPa (S.D. 6.5 MPa)
Adhesive Strength	14.9 MPa

Range of Motion

Worst Case Design:

A cylindrical "femoral neck" results in the smallest angles of articulation. Therefore, a cylindrical "femoral neck" was utilized to detect impingement between the acetabular cup and femoral neck. The 56mm diameter Cormet resurfacing head bearing surface subtends the smallest angle in the size range. The 62mm and 64mm acetabular cups' bearing surfaces subtend the largest angle in the size range (64mm not available in US). Therefore, the 56mm diameter head paired with the 62/64mm cup coupling produced the smallest articular angle before impingement.

Acceptance Criteria:

As outlined in ISO 21535:2002 "Specific requirements for hip-joint replacement implants" the minimum allowable angle of flexion/extension is 80°, abduction/adduction is 60° and internal/external rotation is 90°.

Methods:

Range of motion was evaluated per ISO 21535, which is intended for stemmed total hip replacements with diaphyseal fixation. The test protocol was modified to consider the proximal bone preserving nature of hip resurfacing, by molding a cylindrical femoral neck around the stemmed component. Flexion/extension, abduction/adduction and internal/external rotation were measured by identifying the angle at which impingement occurs.

Results:
The flexion/extension angle at which impingement occurred with the worst case components was 83°, the abduction/adduction angle at which impingement occurred was 70° and the internal/external degree of rotation at which impingement occurred was 111°.

Luxation Wear

Worst Case Design:
Five 40mm and five 56mm bearings were tested. Bearing clearances were controlled to 400μm, the maximum specified in the manufacturing tolerances.

Acceptance Criteria:
Komistek *et al.*[2] used fluoroscopy to demonstrate that small diameter total hip replacement devices (metal-on-polyethylene) subluxed several millimeters during each gait cycle. With metal-on-metal bearings they were not able to detect any subluxation up to the resolution of the fluoroscope, which is 750 microns.

Methods:
Five 40mm and five 56mm bearings were tested in Ringers solution at 37° according to the procedure 'Determination of Resistance to Luxations and Repositions of Total Hip Joint Prostheses' by Kaddick *et al.*[3] A horizontal preload of 1kN was used. The forces required to cause luxation of the bearings during the first cycle were then recorded and the displacement noted. The cups were examined and then repeated luxations were performed (a further 999 cycles per bearing couple). A displacement of 10mm was pre-set since this was greater than the displacement required to cause luxation in the 40mm and 56mm diameter bearings found during the first luxation.

Results:
After the first luxation cycle, a small decrease in luxation force occurred for all bearing couples, which was thought to be due to rounding of the cup rim. Thereafter, a steady increase in maximum luxation force was noted until steady-state was achieved. This increase was consistent with increased surface roughening of both the head and cup bearing surfaces. Forces to cause luxation were in excess of 2kN for both the 40mm and 56mm bearings.

Metal Ion Analysis

Description of Study Population
A metal ion study was conducted at Coventry & Warwickshire Hospital, United Kingdom outside of the applicant's US IDE study. A series of 29 patients who underwent a unilateral metal-on-metal hip resurfacing procedure were prospectively followed over a seven-year period. Seven of the 29 patients underwent a metal-on-metal hip resurfacing procedure on the contralateral hip during the course of the study. These seven patients along with four other patients who had a previous hip resurfacing on the other hip had their metal ion levels assessed over time to determine the effect of bilateral hip resurfacing on metal ion levels.

Implant Identification
Both the Corin-McMinn device and the Cormet device (the subject device) used in this study have cups with a HA coated back on a plasma sprayed titanium layer over the CoCr substrate with a supero-medial peg. Heads are similar in both devices, for use with cement and uncoated in the cement/implant contact areas. The significant differences between the Corin-McMinn and the Cormet are that the former has a splined supero-medial cup peg (Cormet is parallel and non-splined), two bearing surface integral introducer holes (Cormet has no holes) and two opposing stippled pads on the cup back (Cormet has low profile locating splines and no pads).

Measurement Techniques
Blood samples were taken from each patient. A plastic intravenous cannula was inserted, the metal needle removed and 5 mls of blood withdrawn and discarded. Samples were then taken and placed in 2 ml Heparin tubes, which had been tested for cobalt and chromium contamination. The blood was centrifuged and the plasma transferred into trace-metal free polycarbonate tubes. Cobalt and chromium levels were determined.

Metal Ion Levels
Metal ion levels are raised and remain elevated following metal-on-metal hip resurfacing; however, it is unclear if the levels to which they are raised are of any clinical significance.

Summary of Data
For patients with one resurfacing device, results of the study indicate that metal ion levels for cobalt and chromium initially increased following a metal-on-metal hip resurfacing but plateaued and started to decrease between one and two years post-implantation. The levels remained below their peak, but did not return to preoperative levels throughout the seven-year follow-up reported in this study. Implantation of a contralateral metal-on-metal resurfacing system further raised the metal ion levels, more notably cobalt ions compared to chromium ions. The cobalt levels did not return to normal following bilateral hip resurfacing and remained higher than patients with unilateral hip resurfacing over four years. Chromium levels following bilateral surgery do not return to normal, but are only slightly higher when compared to levels of a unilateral resurfacing. Appropriate Contraindications and Warnings have been added to the labeling due to increased metal ion levels.

Sterilization and Shelf Life Validation

Femoral head and acetabular components of the Cormet Hip Resurfacing System are sterilized by gamma irradiation delivered from a $cobalt_{60}$ source. The sterilization process has been validated to achieve a sterility assurance level of 10^{-6} at a minimum dose of 25kGy in compliance with the requirements of EN 556-1:2001 Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices and AAMI TIR 27, 2001, *Sterilization of Health Care Products - Radiation Sterilization - Substantiation Of 25 kGy As a Sterilization Dose - Method Vd Max.* The irradiation process is carried out by a subcontractor, Isotron PLC, Reading, UK. The product is not labeled "pyrogen free". The Cormet Head devices are packaged in double-peel pouch packages and the Cormet Cup devices are packaged in double-blister packages to maintain sterility. Shelf life testing on both package configurations was performed to verify package integrity equivalent to five years.

X. SUMMARY OF CLINICAL STUDIES

Purpose of the Investigation

The purpose of this investigation was to test the hypothesis that the Cormet Hip Resurfacing System is as effective as conventional total hip arthroplasty. The Cormet Hip Resurfacing System was the investigational treatment and a conventional total hip arthroplasty system served as the control group. Effectiveness was measured via a composite endpoint described below. Safety was determined by collection of the incidence of perioperative and postoperative complications.

Study Design

A prospective, multi-center, IDE study was conducted utilizing components of the Cormet Hip Resurfacing System in the United States.

Control Group

The control group was comprised of total hip arthroplasty patients from an alumina ceramic total hip prosthesis. These ceramic total hip prostheses were approved via PMA. Table 6 compares the investigational and study parameters.

Table 6: Protocol Comparisons

Protocol Element	Cormet IDE Study	Ceramic Total Hip (Control)
Type of Study	IDE – Hip Resurfacing	IDE – Total Hip Arthroplasty
Bearing Type	Metal-on-Metal	Ceramic-on-Ceramic
Study Design	Prospective, non-randomized, historical control	Prospective, randomized
Number of centers	14	16
Dates of enrollment	5/17/2001- 8/5/2003 (pivotal) Continued access through July 2006 (ongoing)	10/29/1996 – 10/20/1998
Number of procedures	1148	349
Follow-Up Intervals	Preoperative, 6 weeks, 6, 12, 24 and 24+ months*	Preoperative, 6 weeks, 6, 12, 24 and 24+ months*
Outcome Measures	Harris Hip Score Adverse Events Radiographs Questionnaire	Harris Hip Score Adverse Events Radiographs Questionnaire

* 24+ month evaluations include all 24 month evaluations completed, as well as data from a later visit, if the 24 month evaluation was not available.

The core data collected from these studies was the same. In addition, the follow-up time-points and the intervals around these time-points were very similar as illustrated in Table 7.

Table 7: Follow-up Intervals Comparison

	Cormet Approved protocol	Cormet PMA submission	Ceramic Total Hip Control
6 weeks	±2 weeks	±2 weeks/+expanded	±3 weeks
6 months	±1 month	±1 month + expanded	±1 month
1 year	±2 months	±2months/+expanded	±2 months
2 years	±2 months	±2 months/+ expanded	±2 months
2+ years		Any evaluation 22+ months=24+ months	

The patient populations recruited into both studies were similar. A side-by-side comparison of the inclusion/exclusion criteria between the studies is presented in Table 8.

Table 8: Inclusion/Exclusion Criteria Comparison

Inclusion/Exclusion	Cormet Approved Protocol	Control Group Study
Is skeletally mature	X	X
Is mentally capable of follow-up	X	X
Will be available for 2 yr follow-up	X	X
Deemed candidate by diagnosis of investigator	X	X
No active infection	X*	X
No severe osteoporosis	X*	X
Not a prisoner	X	X
Is not pregnant	X	X
Is not morbidly obese	X*	X*
No ipsilateral previous surgery	X	X
No extensive deformity of femoral head	X*	Not applicable
No known allergies to implants	X	None included in study
No neoplastic disease	X*	None included in study
No above the knee amputation either extremity	X	None included in study
No previous Girdlestone procedure	X	Information Not Available to Applicant
No previous hip fusion	X	Information Not Available to Applicant
No above the knee amputation (AKA) of either extremity	X	Information Not Available to Applicant
Does not require structural bone graft	X	Information Not Available to Applicant
No previous ipsilateral hemi-resurfacing, total resurfacing, total bipolar, total unipolar, or total hip replacement	X	Information Not Available
No nonunion or malunion of the femur	X	Information Not Available
Has preoperative Harris Hip Score (HHS) < 70 points	X	No limits
No Congenital Dysplasia of the Hip (CDH)	X	Included in study
Age	No specified limits	21-75
Inflammatory Arthritis	Included in study	None included in study

*Primary Investigator (PI) discretion

The majority of the eligibility criteria were consistent for both studies. Comparisons of the populations enrolled found the groups to be similar on age, diagnosis and preoperative Harris Hip Score (HHS).

Both groups have a hard-on-hard bearing surface without the risk of issues associated with polyethylene debris.

Composite Clinical Success Endpoints

A patient is defined as a Composite Clinical Success (CCS) if at 24 months all of the following criteria outlined in Table 9 are met.

Table 9: Summary of the Composite Clinical Success

Composite Clinical Success Criteria
Harris Hip Score ≥80 at Month 24+
No revisions/pending revisions
Radiographic Success Criteria
Acetabular Migration (vertical/horizontal): <5mm
Acetabular Migration (varus/valgus): <5°
Acetabular Radiolucencies: not in all zones
Femoral Subsidence (axis femoral canal) < 5mm or Femoral Tilt varus/valgus <1°
Femoral Radiolucencies: not in all zones
Absence of device related Adverse Events

The primary efficacy objective of this study was to demonstrate clinical non-inferiority with regard to the likelihood of clinical success at Month 24 relative to the control. To achieve this goal, it was necessary to determine clinical success status in as large a percentage of procedures as possible. This was necessary to insure that bias arising from losses to follow-up was small enough to permit valid inference. For procedures in the Pivotal Study Unilateral Cohort for which Month 24 Harris Hip Total score was missing, a later Harris Hip Total score was used. The analysis demonstrated that these later scores were an accurate predictor of Month 24 score, and as such minimized bias by imputing missing Month 24 values with these later values. Additional statistical analyses were performed in order to demonstrate that the rollback imputation as well as the out of window procedures had no effect on the overall results.

Month 24+ CCS Actual[B] Pivotal Study Unilateral Patients (see Table 16) was defined to be the primary comparison.

Study Modifications

The data presented is from a study designed to be a prospective, non-randomized (yet concurrently controlled) clinical study used to evaluate the Cormet Hip Resurfacing System. However, multiple modifications were made to the study design throughout the course of the study and subsequent data analyses. These changes were discussed by the Orthopaedic and Rehabilitation Devices Panel (the Panel) on Thursday, February 22, 2007.

1. ***Control Group History***
   The original study compared the investigational device group, Group I, and two non-concurrent control groups, Group II and Group III. Group I was the investigational group treated with the Cormet Hip Resurfacing System. Patients were to be sequentially enrolled. Group II was the control group treated with a marketed metal-on-metal total hip replacement. Group III was the control group treated with any marketed metal-on-polyethylene total hip replacement. Each investigational site was to generate data for Groups I and II, or data for Groups I and III. However, as enrollment into the study progressed, no control patients were actually enrolled for utilization in the analysis of data for this study. To address the absence of a control group, the applicant proposed and explored multiple historical control alternatives (metal-on-metal then ceramic-on-ceramic) as they began to analyze their data. The ceramic total hip approved via PMA was finally selected as the control.

2. ***Data Analysis***
   The composite clinical success analysis included all of the originally approved and proposed study endpoints; however, the radiographic endpoint success criterion was different and appeared to be less stringent.

a. *Changes to data collection (radiographic) techniques*
The IDE approved protocol included a radiographic measurement technique as outlined in Table 10.

Table 10: Comparison of Measurement Techniques

Radiographic Analysis	**Original IDE Protocol dated March 20, 2003**	**Original PMA Submission March 30, 2005**	**Actual Technique PMA Amendments 8 and 13**
Acetabular Migration vertical/ horizontal	Reference inferior teardrops	Reference bottom of pelvis	Same as Original Protocol
Acetabular Migration varus/valgus	Angle between a line joining edges of the cup and a line joining tear drops	Angle between a line joining edges of the cup and a line joining bottom of pelvis	Same as Original Protocol
Acetabular Radiolucencies	Serial	Same as Original Protocol	Same as Original Protocol
Femoral Subsidence Axis Femoral Canal	Line to lateral femoral cortex	Same as Original Protocol	Line from head center to top of greater trochanter
Femoral Tilt Varus/Valgus	Lines through femur midpoint and stem	Same as Original Protocol	Same as Original Protocol
Femoral Radiolucencies	Serial	Same as Original Protocol	Same as Original Protocol

b. *Changes to radiographic analyses*
The final data analysis used a revised measurement technique and then applied revised success criteria to evaluate radiographic success. Please see Table 11 for a summary of the radiographic success criteria. The sponsor has combined the femoral subsidence and femoral tilt endpoint into one. Therefore, the femoral component need only meet one of its endpoints to be a success. In addition, the original criteria indicated a radiolucency in any zone was considered a failure, as is common in hip prosthesis studies. However, the final proposed analysis indicated radiolucencies not in all zones to be a success.

Table 11: Comparison of Radiographic Success Criteria

Radiographic Success Criteria	Original IDE Protocol	Original PMA Submission	Actual Criteria Used
Acetabular Migration vertical/ horizontal	< 5mm	Same as Original Protocol	Same as Original Protocol
Acetabular migration varus/valgus	< 5 degrees	Same as Original Protocol	Same as Original Protocol
Acetabular Radiolucencies	None in any zone	Not Evaluated	Not in all zones
Femoral subsidence axis femoral canal	< 5mm	Same as Original Protocol	Combined < 5mm and < 1 degree (must have both for failure)
Femoral tilt varus/valgus	< 1 degree	Same as Original Protocol	
Femoral Radiolucencies	None in any zone	Not Evaluated	Not in all zones

Metal-on-metal hip resurfacing devices are relatively new to the US orthopaedic community and the radiographic evaluation criteria of these devices have not been uniformly accepted.

c. *Proposed primary effectiveness and safety endpoints definitions*
This section outlines the composite clinical success outcomes used in the approved IDE Protocol, which differ from the endpoints described in the previous section.

Approved IDE Protocol
The original IDE success definition was outlined as "...at 24 months a patient is defined as a success, if all four of the following are met:

1. Harris Hip Score (HHS) ≥ 20 point improvement
2. Has not had and is not planning a revision surgery.
3. Radiographic Success:
    a. Acetabular component
        - Migration <5mm vertical or horizontal
        - Migration <5°in varus/valgus
        - No new or progressive radiolucencies >1mm in **any** zones
    b. Femoral component
        - Subsidence <5mm
        - Tilting <1° in varus/valgus
        - No new or progressive radiolucencies >2mm in **any** zones
4. No device related complications—an AE due to the design and/or material composition of the implant and/or implant instrumentation; the relationship to the device will be determined by the investigator.

Any patient who does not meet all of the above criteria during any evaluation time point out to two years will be considered a failure."

This summary outlines the changes in study design and analysis that have been implemented throughout the course of the study and PMA review. Please see Section XII Panel Recommendation for additional information.

Study Objectives and Assessments

Study Population

Corin collected US IDE clinical trial data on 1154 cases implanted with the Cormet Hip Resurfacing System. Six procedures involved use of a pegged acetabular component, not part of the IDE. These cases were analyzed separately. Study data were therefore presented on 1148 study cases. There were no major protocol deviations reported during a comparable timeframe in the control group, however, there was one approved deviation for inflammatory arthritis. These data are not included in this submission. Eight investigational procedures involved enrollment under the compassionate use provisions. The study populations are identified in Table 12.

Table 12: Study Cohort Definitions

Cohort Name	Definition	Procedures/patients
All Enrolled	All patients enrolled in either the pivotal study or continued access.	1148/1030
Pivotal Study Unilateral	Unilateral patients enrolled in the pivotal study. Includes patients who had second side replaced after two years of follow-up (730 days).	337/337
Pivotal Study Bilateral	Patients with first implant in the pivotal study who had their second hip replaced within 730 days of the index procedure. Four incidences where second hip was not included in this study group because of use of pegged cups.	105/55
Continued Access	Patients implanted after the pivotal study close (Aug 6, 2003) under continued access provision. Note: seven of these patients are also included in the pivotal study bilateral patient population above.	698/640
Compassionate Use	Implanted with investigational device under compassionate use between end of pivotal IDE study and beginning of continued access approval.	8/7

Baseline Characteristics of Investigational and Control Groups

The demographics for the pivotal unilateral study as compared to the control are identified in Table 13.

Table 13: Comparison of Pivotal Study to Control

Population	Investigational Pivotal Study Unilateral Patients	Ceramic Total Hip Control Pivotal Study Unilateral Patients	Wilcoxon (continuous) or Chi-squared (discrete) P values
Number of procedures	337	266	
Number of patients	337	266	
Mean Age	50.1	53.3	<0.01
Gender M/F	67.7%/32.3%	62%/38%	0.150
Mean weight (lbs)	190.4	188.7	0.692
Diagnosis	85.8% OA, 1.2% RA, 13.1% AVN	83.7% OA, 16.3% AVN	For Diagnosis=OA p=0.135
Preoperative HHS mean total score	50.1, SD=11.6	49.7, SD=11.3	0.233

Baseline demographic and clinical characteristics between Cormet Hip Resurfacing System patients in Pivotal Study Unilateral group and Ceramic-on-Ceramic Unilateral Control group patients were compared. There was no statistically significant difference in patient gender. Approximately two-thirds of both cohorts were male (67.7% versus 62.0%). There were no statistically significant differences in the distributions of diagnoses with approximately 85% of both cohorts presenting with a primary diagnosis of osteoarthritis, (85.8% versus 83.7%). Mean weights were similar between these two groups (190.4, SD=40.7 lbs versus 188.7 lbs; SD=39.7). Height was not obtained during the Cormet Hip Resurfacing System study precluding comparisons involving BMI.

Baseline overall function as reflected in mean Harris Hip Total scores also was very similar between the Pivotal Study Unilateral investigational and control groups. In contrast, the difference in mean ages was statistically significant between groups (50.1, SD=9.6 versus 53.3, SD=11.1, Wilcoxon rank sum $p<0.01$). Although statistically significant, a difference in mean age of just three years is unlikely to be of clinical significance.

Propensity score analyses were performed to assess the magnitude of and to adjust for potential selection bias. The propensity model included age, weight, baseline HHS, gender, and pre surgery presence of marked pain. The mean propensity scores were very similar in the Cormet and ceramic total hip control groups, [0.589 (0.088 SD) and 0.550 (0.103 SD), respectively]. The values were very similar in magnitude suggesting that, taken as a set, these variables had relatively little impact on characterizing what kind of patients received the Cormet implant relative to what kind of patients received the ceramic total hip control device. This implies that any between group differences in patient populations for the covariates included in the model did not affect the conclusion of the non-inferiority for CCS.

The demographics for all other populations are identified in Table 14.

Table 14: Demographics for Other Populations

Population	Investigational Pivotal Study Bilateral	Continued Access	All Enrolled
Number of procedures	105	698	1148
Number of patients	55	640	1030
Mean Age	47.7	52.3	51.2
Gender M/F	71.4%/28.6%	74.2%/25.8%	71.9%/28.1%
Mean weight (lbs)	195.1	194.9	193.8
Diagnosis	81.0% OA, 1.9% RA, 17.1% AVN	92.1% OA, 0.3% RA 7.6% AVN	89.1% OA, 0.8% RA 10.1% AVN
Preoperative HHS mean total score	48.7, SD=11.8	50.1, SD=11.4	50.0, SD=11.5

Patient Accounting

Pivotal Study Unilateral Patient Accountability

Table 15 presents an overview of the data available for the pivotal study cohort.

Table 15: Pivotal Study Unilateral Patient Accountability

Status at Month 24+	Number of Subjects
Pivotal study group enrollment	337
Patients with complete CCS score	292
Patient died before month 24+	1
Patients not evaluated for CCS	44
Died after 24 month interval	2
Complete HHS data only	9
Complete radiographic data only	5
Patients with no Month 24+ data; Potential lost to follow-up	28

The availability of follow-up evaluation for the investigational and control Pivotal Study Unilateral group is provided in Table 16.

Table 16: Procedure Accounting and Follow-up Compliance Table Pivotal Study Unilateral Patients and Controls

As of Date of Database Closure	Pre-Op		Week 6		Month 6		Month 12		Month 24		Month 24+		Month 36	
	I	C	I	C	I	C	I	C	I	C	I	C	I	C
(1)Theoretical follow-up	337	266	337	266	337	266	337	266	337	266	337	266	314	266
(2) Cumulative deaths including non-theoretically due	0	0	0	0	0	0	0	1	1	2	1	2	4	2
(3) Cumulative revisions including non-theoretically due	0	0	2	1	5	1	7	3	16	3	16	3	24	3
(4) - Not Yet Overdue	0	0	0	0	0	0	0	0	0	0	0	0	32	0
(5) - Deaths+revisions among theoretical due	0	0	2	1	5	1	7	4	17	5	17	5	26	5
(6) = Expected due for clinic visit	337	266	335	265	332	265	330	262	320	261	320	261	256	261
(7) = Expected due+revisions among theoretical due	337	266	337	266	337	266	337	265	336	264	336	264	280	264
All Evaluated Accounting (Actual[B]) Among Expected Due Procedures[1]														
	I	C	I	C	I	C	I	C	I	C	I	C	I	C
(8) All Evaluated Visit Compliance (%)	100.0%	100.0%	99.1%	99.2%	90.4%	94.0%	89.7%	98.1%	85.6%	97.7%	91.3%	98.5%	39.8%	73.2%
(9) Harris Hip Total Score	337	252	328	245	288	238	285	245	263	246	283	252	77	186
(10) Radiographic evaluation			313		232		234		259		291		53	
(11) CCS at Mos. 24, 24+ or HHS+radio. Otherwise			332	245	297	238	294	245	243	250	292	256	97	186
(12) Actual[B] % Follow-up for CCS or HHS+radio.CCS			99.1%	92.5%	89.5%	89.8%	89.1%	93.5%	72.3%	94.7%	86.9%	97.0%	37.9%	71.3%
Within Window Accounting (Actual[A]) Among Expected Due[1]														
	I	C	I	C	I	C	I	C	I	C	I	C	I	C
(13) Harris Hip Total Score	337	252	277	221	161	183	192	215	200	206	281	251	22	156
(14) Radiographic evaluation			277		161		192		202		283		22	
(15) CCS at Mos. 24, 24+ or HHS+radio otherwise			277	221	161	183	192	215	202	209	285	254	22	156
(16) Actual[A] % Follow-up for CCS or HHS+radio.CCS			82.7%	83.4%	48.5%	69.1%	58.2%	82.1%	60.1%	79.2%	84.8%	96.2%	8.6%	59.8%

1 Actual A: Patients contributing all endpoint data that were evaluated within the protocol defined window.
Actual B: Patients contributing any data that were evaluated at a visit regardless of whether the visit was within the follow-up windows (not overlapping other protocol defined visit intervals)

Pivotal Study Unilateral
The follow-up rate at Month 24+ for patients with complete information to determine safety and effectiveness was 84.8% (285/336) for the investigational group and 96.2% (254/264) for the control group.

The following follow-up rates are also of interest:

Pivotal Study Bilateral
At Month 24+, the follow-up rate is 56.1% (55/98) in comparison to 95% (79/83) for the bilateral control cohort.

Continued Access
At Month 24+, 54.9% (134/244) of subjects due for evaluation have complete Harris Hip Scores and 6.1% (15/244) of subjects have complete radiographic data. Many subjects have not reached the Month 24 endpoint.

All Enrolled Patient Accountability
At Month 24+, the follow-up rate is 50.7% (348/686) in comparison to 96.5% (335/347) for the control "all enrolled" cohort. In addition, although there have been 1,148 procedures completed to date, many of the patients have not yet reached the Month 24+ endpoint in the continued access study.

Control
At Month 24+, the control follow-up rate was 96.2% (254/264).

Patient Discontinuation

Pivotal Study Unilateral Patients

Investigational Group (N=337)
All 337 patients in the Pivotal Study Unilateral group were theoretically due for Month 24+ follow-up evaluation. Of these 320 patients were expected due for the Month 24+ follow-up evaluation. One patient died prior to the Month 24+ follow-up and 16 patients had one or more of the components of the Cormet Hip Resurfacing System revised or removed prior to the Month 24+ visit. A total of 292 of the 336 patients (86.9%) who did not die prior to Month 24 were included in the CCS analysis. Of the 44 patients not included, two died after Month 24, nine had complete HHS (all success) only, and five had complete radiographs (all success) only. Twenty-eight patients did not return for Month 24+ follow-up.

Control Group (N=266)
Of the 266 patients in the control group, 261 patients were due for Month 24+ follow-up. One patient had one or more components of the ceramic total hip system revised, two patients died prior to the Month 24 follow-up visit. A total of 256 of a possible 264 patients (97.0%) were included in the CCS analysis. Of the nine patients not included, five had incomplete HHS scores and four patients were considered lost to follow-up.

Pivotal Study Bilateral Procedures

Investigational Group (N=105)
Of the 105 procedures (55 patients) in the bilateral group, 99 procedures were theoretically due for the Month 24+ follow-up evaluation including one (1) procedure not yet overdue. Three patients (three hips) had one or more of the components of the Cormet Hip Resurfacing System revised or removed prior to the Month 24 visit and one patient is not yet overdue for the Month

24+ visit. Of the 95 procedures expected to be seen, 73 procedures (76.8%) had at least some clinical follow-up at Month 24 follow-up. Patients representing 22 procedures did not complete Month 24 follow-up.

Control Group (N=83)
For the 52 patients (83 procedures) in the bilateral ceramic total hip control group, 82 hips were evaluated at Month 24+. No patients died or were revised. One patient was lost to follow-up. This patient was last seen at the Month 6 evaluation at which time a HHS of 97 points was reported.

Continued Access (N=698)
The 640 patients representing 698 hips continue to be followed in the Continued Access study. Two hundred thirty-six procedures are expected due for Month 24+ evaluation and 32 procedures are not yet overdue for the Month 24+ evaluation. The Sponsor continues to enroll and follow patients according to the study protocol. To date, 18 patients have discontinued in the study; two patients died and 16 patients had revision to one or more components of the Cormet Hip Resurfacing System.

Patient complaints

Investigational Group
There were no specific complaints related to the use of the Cormet Hip Resurfacing System from patients involved in the IDE. The Short Musculoskeletal Functional Assessment (SMFA) is a 46-item assessment of patient function and a subset of 12 questions, the "bother index," is an assessment of how patients are bothered by functional problems. Study patients completed the SMFA during the course of the investigation. Overall there were large improvements in scores over time, which may be an indicator of general satisfaction.

Eight Product Experience Reports were received by the Sponsor for product marketed outside the US from December 2003 through November 10, 2005. There were no complaints by patients reported in this series.

Control Group
Study results indicate that no patients were reported to specifically complain about their total hip replacement. However, this study asked the question: "Are you satisfied with the results of your surgery?" at each follow-up interval. Six patients (2.2%) answered "no" to this question at the Month 24 follow-up interval. Reasons included two incidences of patients involved in traumatic events, one post revision of femoral stem, one patient with multiple medical problems and two patients with pain at or near the operative site.

Safety

Operative Site Adverse Events

The safety of the Cormet Hip Resurfacing System was evaluated on the basis of adverse events (AEs) which were defined as any untoward medical occurrence during the course of the investigation including any unintended sign, symptom, or disease related to the device use. The All Enrolled cohort of 1148 procedures is used as the denominator for safety considerations of the investigational group and 349 for the control procedures even though 24 month follow-up data is not available on all patients.

Intraoperative Events

Thirty-one cases (2.7%) reported intraoperative adverse events in the Cormet IDE study compared to 52 cases (14.9%) reported for the control population.

Postoperative Events

Two hundred eight cases (18.1%) with postoperative hip related events were reported for the Cormet IDE population compared to 79 (22.6%) for the control population.

Fifty-eight cases (5.1%) with postoperative device related events were reported for the Cormet IDE population compared to 19 (5.4%) for the control population.

Table 17 provides a summary of intra-operative and postoperative site complications for the 1148 Cormet Hip Resurfacing System procedures and the ceramic total hip control.

Table 17: Summary of Complication Comparisons between All Enrolled Investigational and Control Devices

	Investigational			Control			Exact
	n[8]	N[9]	%	n[8]	N[9]	%	p-value
Any complication	427	1148	37.2%	229	349	65.6%	0.000
Any hip-related complication	219	1148	19.1%	97	349	27.8%	0.001
Any device-related complication	58	1148	5.1%	27	349	7.7%	0.064
Any operative complication[1]	31	1148	2.7%	52	349	14.9%	0.000
Any post operative complication[2]	412	1148	35.9%	212	349	60.7%	0.000
Any post operative hip-related complication[3]	208	1148	18.1%	79	349	22.6%	0.063
Any post operative device-related complication[4]	58	1148	5.1%	19	349	5.4%	0.782
Any post operative serious complication[5]	104	1148	9.1%				
Any post operative serious hip-related complication[6]	18	1148	1.6%				
Any post operative serious device-related complication[7]	49	1148	4.3%				
Deaths	6	1148	0.5%	5	349	1.4%	0.142

Notes:

[1] Complications occuring during implant procedure as reported on Complication Form.

[2] Complications occuring after implant procedure as reported on Complication Form.

[3] Includes any post operative hip-related complication.

[4] Includes any post operative complication.

[5] Includes any post operative complication meeting the criteria for a serious complication as assessed by the investigator.

[6] Includes any post operative complication hip-related complication assessed by the investigator as serious.

[7] Includes any post operative complication.

[8] Number of procedures with at least one of the specific types of complications.

[9] Total number of procedures in this cohort of patients.

Systemic Events

Systemic adverse events were those reported events that did not relate directly to the operation or the operative site/device. An analysis of the types of events reported and their time course showed expected rates of other body system complications for this type of population.

The control group's higher rates of systemic AEs were distributed over time. These trends may be attributable to the greater maturity of the control database. In the control database, all patients had greater than 24 months of experience reported whereas only a fraction of the investigational group has experience past Month 24.

Table 18 provides a summary of systemic complications for the 1148 Cormet Hip Resurfacing System procedures and the ceramic total hip control.

Table 18: Systemic Adverse Events for All Enrolled Investigational and Control Devices

	Investigational			Control			Exact
	n[1]	N[2]	%	n[1]	N[2]	%	p-value[3]
Arrhythmia (operative)	1	1148	0.1%	0	349	0.0%	1.000
Bronchopulmonary	2	1148	0.2%	12	349	3.4%	<0.001
Carcinoma	4	1148	0.3%	18	349	5.2%	<0.001
Cardiovascular	14	1148	1.2%	33	349	9.5%	<0.001
Death unrelated to device	6	1148	0.5%	5	349	1.4%	0.142
Deep Venous Thrombosis (DVT)	9	1148	0.8%	0	349	0.0%	0.128
Gastrointestinal	8	1148	0.7%	19	349	5.4%	<0.001
Genitourinary	8	1148	0.7%	20	349	5.7%	<0.001
Infection remote location	10	1148	0.9%	4	349	1.1%	0.750
Lack of nutrition	1	1148	0.1%	0	349	0.0%	1.000
Low hemoglobin/hematocrit	3	1148	0.3%	0	349	0.0%	1.000
Neuropathy	1	1148	0.1%	0	349	0.0%	1.000
Neurosensory	8	1148	0.7%	32	349	9.2%	<0.001
Nosebleed	1	1148	0.1%	0	349	0.0%	1.000
Pulmonary Embolism (PE)	4	1148	0.3%	1	349	0.3%	1.000
Rash	8	1148	0.7%	10	349	2.9%	0.003
Thrombophlebitis	0	1148	0.0%	3	349	0.9%	0.013
Trauma (non-hip related)	10	1148	0.9%	30	349	8.6%	<0.001
Varicose veins	1	1148	0.1%	0	349	0.0%	1.000
Other	218	1148	19.0%	102	349	29.2%	<0.001

[1] Number of procedures experiencing this type of complication
[2] Total population number, 24+ Month data only available on 532 procedures
[3] Two-sided Fisher's Exact tests. Comparisons were not performed for femoral neck notched (operative), greater trochanter notching (operative), ceramic insert chip (operative), and femoral neck fracture since both devices were not exposed to these types of events. Also, p-values are not reported when there were no events in either group.

Hip Related Events

Hip related events were the most reported postoperative complications concerning the hip or operative site. Table 19 gives a breakdown of the rates of hip related complications for the investigational group and the corresponding control group.

Reviewing these events as they occurred over time, the rates of hip related complications seem to be higher in the control group in the immediate postoperative (up to Week 6) timeframe. However, there were more hip related complications in the investigational group at Week 6 to Month 6. The majority of events seem to be related to postoperative hip pain (bursitis, tendonitis and muscle weakness) at the operative site.

Table 19: Hip Related Adverse Events by Time Occurrence All Enrolled Procedures

	Intra-operative		Post Surgery to Week 6		Week 6 To Month 6		Month 6 to Month 12		Month 12 to Month 24		Post Month 24		Total	
	I	C	I	C	I	C	I	C	I	C	I	C	I	C
Acetabular crack (operative)	0	1	0	0	0	0	0	0	0	0	0	0	0	1
Acetabular malpositioned (operative)	0	0	0	0	1	0	0	0	3	0	0	0	4	0
Broken drill bit	1	0	0	0	0	0	0	0	0	0	0	0	1	0
Bursitis	0	0	0	0	14	5	10	4	5	4	4	3	33	16
Deep Infection	0	0	0	0	0	0	0	1	2	0	1	0	3	1
Elevated metal ion level	0	0	0	0	1	0	0	0	0	0	0	0	1	0
Femoral Crack (operative)	0	12	0	0	0	0	0	0	0	0	0	0	0	12
Femoral neck notched (operative)	6	0	0	0	0	0	0	0	0	0	0	0	6	0
Femoral radiolucency	0	0	0	0	0	0	1	0	6	0	5	0	12	0
Greater Trochanter Notching (operative)	1	0	0	0	0	0	0	0	0	0	0	0	1	0
Hematoma	1	0	3	3	2	0	1	0	1	0	0	0	8	3
Heterotopic Bone Formation	0	0	2	6	4	5	0	0	7	1	0	1	13	13
Hip Pain (operative side)	0	1	15	2	17	3	10	1	12	1	7	1	61	9
Leg Length Discrepancy	1	0	7	0	8	0	1	0	3	0	2	0	22	0
Limp	0	0	7	0	5	0	1	0	0	0	0	0	13	0
Loose Body	1	0	0	0	0	0	0	0	0	0	0	0	1	0
Muscle Weakness	2	0	2	0	5	1	0	0	1	0	0	0	10	1
Myositis ossificans	0	0	1	0	3	0	1	0	1	0	0	0	6	0
Nerve palsy	1	2	1	3	2	0	0	0	0	0	0	0	4	5
Skin split	1	0	0	0	0	0	0	0	0	0	0	0	1	0
Soft tissue trauma	0	0	1	0	0	2	0	2	0	6	1	4	2	14
Squeaking implant/clicking	0	0	2	0	10	0	4	0	4	1	0	1	20	2
Subchondral cyst	0	0	0	0	0	0	0	0	1	0	0	0	1	0
Subluxation	0	0	1	0	1	0	1	0	0	0	3	0	6	0
Superficial infection	0	0	4	5	2	0	1	0	0	0	0	0	7	5
Tendonitis	0	0	1	1	7	1	3	3	6	1	3	0	20	6
Trochanteric Crack (operative)	0	7	0	0	0	0	0	0	0	0	0	0	0	7
Wound Related (non-infected)	0	0	17	16	1	0	2	1	2	0	0	0	22	17
Other	0	4	0	1	2	0	2	1	1	1	0	1	5	8

Device Related Events Among Patients

The protocol definition of device related adverse event was "an adverse event that occurs due to the design and/or material composition of the implant and/or implant instrumentation." From this definition, we have further refined the category to include:

- Bone breakage around the implanted components;
- Aseptic loosening of the components, including complete radiolucency around the stem or evidence of AVN under the femoral head;
- Breakage of the device components (stem fracture, acetabular liner fracture, etc.);
- Movement of the components in situ;
- Dislocation of the hip.

Table 20 gives a breakdown of the rates of device related AEs for the investigational group and the corresponding control group.

Table 20: Device Related Adverse Events by Time Occurrence All Enrolled Procedures

	Intra-Operative		Post Surgery to Week 6		Week 6 To Month 6		Month 6 to Month 12		Month 12 to Month 24		Post Month 24		Total	
	I	C	I	C	I	C	I	C	I	C	I	C	I	C
Acetabular fracture	0	1	0	0	0	0	0	0	0	0	0	0	0	1
Acetabular loosening	0	0	3	0	3	0	0	0	3	0	2	0	11	0
Avulsed lesser trochanter	0	0	0	1	0	0	1	0	0	0	0	0	1	1
Ceramic Insert Chip (operative)	0	8	0	0	0	0	0	0	0	0	0	0	0	8
Dislocation	0	0	1	8	0	2	0	0	1	0	0	0	2	10
Femoral fracture (operative)	0	1	0	0	0	0	0	0	0	0	0	0	0	1
Femoral fracture (post-op)	0	0	0	4	0	2	0	0	0	0	0	1	0	7
Femoral loosening	0	0	0	0	0	0	1	0	7	0	6	0	14	0
Femoral neck fracture	0	0	3	0	12	0	5	0	5	0	1	0	26	0
Femoral subsidence	0	0	0	0	1	0	1	1	1	1	1	0	4	2
Trochanter (greater) fracture	0	0	0	0	0	0	0	0	0	0	1	0	1	0

Pivotal Study Bilateral Patients

Six device related events (5.7%) were reported for the Pivotal Study Bilateral Procedures in the investigational group at Month 24+ follow-up. Reasons for device related events included: acetabular loosening (one patient, 1.0%), femoral loosening (one patient, 1.0%), femoral neck fracture (two patients, 1.9%), and femoral subsidence (two patients, 1.9%).

There were no events of acetabular fractures, avulsed lesser trochanter, dislocation, intraoperative or postoperative femoral fractures, or greater trochanter fracture in the bilateral investigational group.

There were six device related events (7.2%) during a comparable time frame for the Pivotal Study Bilateral Procedures in the control group. Reasons for device related events included two events of operative ceramic insert chip (2.4%), three events of dislocation (3.6%), and one event of postoperative femoral fracture (1.2%).

There were no events of acetabular fracture, acetabular loosening, avulsed lesser trochanter, operative femoral fracture, femoral loosening, femoral neck fracture, femoral subsidence, and greater trochanter fracture in the bilateral control group.

Continued Access Patients

Twenty device related events (2.9%) were reported for the Continued Access Cohort at Month 24+ follow-up. Reasons for device related events included: acetabular loosening (five procedures, 0.7%), dislocation (one procedure, 0.1%), femoral neck fracture (thirteen procedures, 1.9%), and femoral subsidence (one procedure, 0.1%).

There were no events of acetabular fracture, avulsed lesser trochanter, intraoperative femoral fracture, postoperative femoral fracture, femoral loosening or greater trochanter fracture in this cohort of procedures.

All Enrolled Patients

Fifty-nine device related events among 58 procedures were reported for the All Enrolled Cohort at Month 24+ follow-up. Reasons for device related events included: acetabular loosening (eleven procedures, 1.0%), avulsed lesser trochanter (one procedure, 0.1%), dislocation (two procedures, 0.2%), femoral loosening (14 procedures, 1.2%), femoral neck fracture (26

procedure, 2.3%s), femoral subsidence (four procedures, 0.3%), and trochanter (greater) fracture (one procedure, 0.1%).

There were no events of acetabular fracture, intraoperative femoral fracture, postoperative femoral fracture in this cohort of procedures.

Revisions

Investigational Group (N=1148)
A revision is defined as an adverse event necessitating removal or replacement of the original surgical device. A revision is considered to be the most severe adverse event as it indicates total failure of the surgical procedure or device.

Twenty-four (24) revisions were noted in the Pivotal Unilateral group and forty-four (44) revisions were observed in the entire investigational group. Tables 21 and 22 identify the study cohort and reason for revision and or removal of study components.

Table 21: Revisions in Pivotal Unilateral, Pivotal Bilateral, Continued Access, All Enrolled and Control Procedures

	Pivotal Unilateral (all procedures)	Pivotal Unilateral with Month 24+ Follow-up	Pivotal Bilateral (all procedures)	Continued Access (all procedures)*	Compassionate Use (all procedures)	All Enrolled (all procedures)	All Enrolled with Month 24+ Follow-up	Control All Enrolled with Month 24+ Follow-up
Revisions	24	24	4	16	0	44	44	5
N	337	302	105	698	8	1148	532	266
%	7.1%	7.9%	3.9%	2.3%	0.0%	3.8%	8.3%	1.9%

* Most continued access procedures have not been followed for 24+ Months.

Table 22: Reasons for Revision per Cohort

	Pivotal Study Unilateral	Pivotal Study Bilateral	Continued Access	Compassionate Use	Total
Number	337	105	698	8	1148
Femoral Neck Fracture	8	2	11	0	21
Acetabular Component Loosening	4	0	4	0	8
Femoral Component Loosening	11	0	0	0	11
Deep Joint Infection	0	1	1	0	2
Dislocation	1	0	0	0	1
Femoral Subsidence	0	1	0	0	1
Total	24	4	16	0	44

Considering the denominator of the entire pivotal group as 337 procedures, the revision rate is 7.1%. However, only 302 of the pivotal group procedures had Month 24+ follow-up available, making the revision rate for the pivotal unilateral group 7.9% (24/302).

Considering all enrolled procedures, the estimate of 3.8% based on 1148 enrolled procedures is a best case scenario because many of the continued access subjects were not yet due for their 2 year follow-up, yet they are considered revision free. Only 532 of the All Enrolled procedures had Month 24+ follow-up available, making the revision rate for the All Enrolled Group 8.3% (44/532).

Control Group (N=349)

Five patients (1.4%) were reported to have revision of one or more components of the ceramic total hip system. These patients were among the 266 unilateral patients. No patient in the bilateral group was revised; the reasons for revision are as follows:

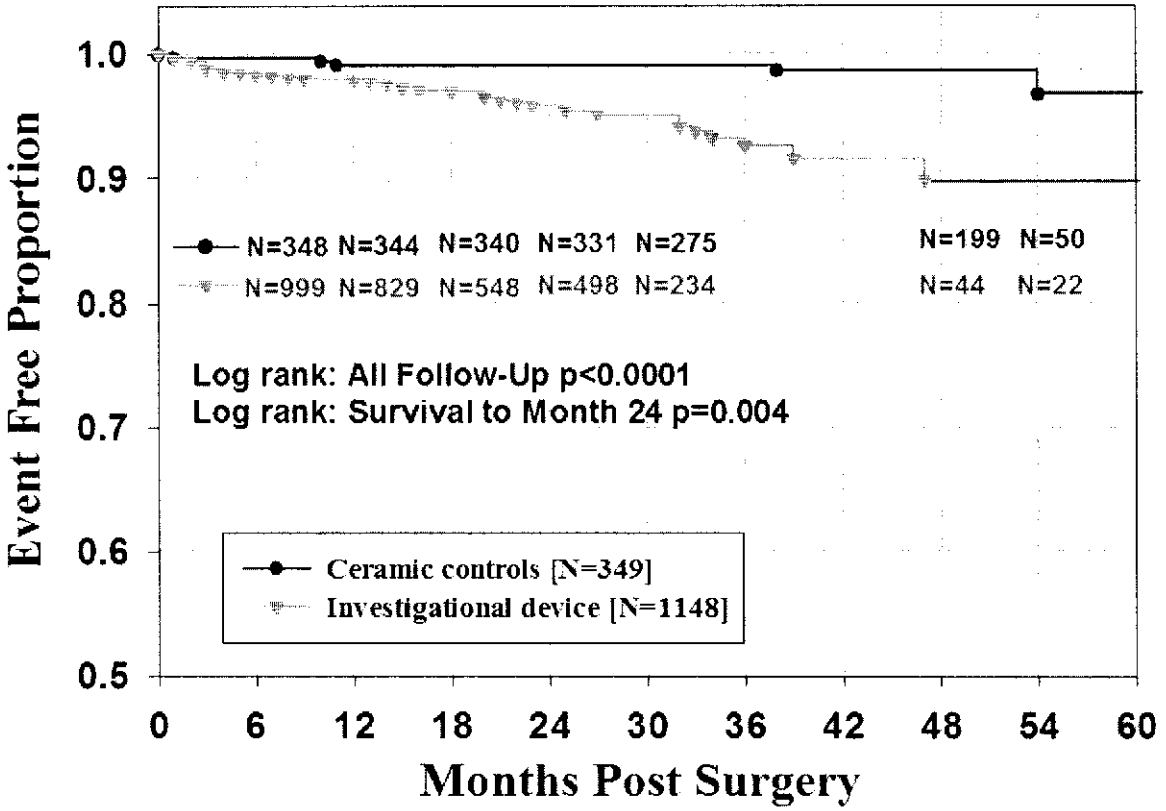
- For one patient, the femoral component and alumina head were revised. The patient fell approximately one month post surgery and sustained a periprosthetic fracture, which was treated with Open Reduction Internal Fixation (ORIF) and a cast. The patient went on to non-union and the femoral component and head were revised nine months post original surgery.
- For one patient, the acetabular component, insert and femoral head were revised due to recurrent anterior dislocation five days post original surgery.
- One patient had all components revised due to deep joint infection approximately 10 months post implantation. The patient was reported to have a girdlestone procedure performed after the components were removed.
- One patient had all components removed due to hip pain approximately three years postoperatively. Sepsis was suspected, but not confirmed.
- One patient had femoral stem and head revised 4.5 years postoperative due to stem loosening post a traumatic event that took place 15 months after the index procedure.

Survival Analysis

The primary study cohort for safety is considered the All Enrolled Procedures group. The distribution of study device failure over time was summarized by constructing a life-table that indicated the number of failures and the number of at-risk procedures over time. The distribution of failures over time was further assessed using Kaplan-Meier survival curves in order to provide graphical representations of survivorship over time.

The primary survival analysis defined device failure as any revision, no matter the model of failure, censoring only at death. The groups exhibit a Month 24 device survivorship of 99% and 96% for the control and investigational groups respectively. This was statistically significant in favor of the control ($p<0.01$). A survival curve on the 337 subjects in the Pivotal Study unilateral cohort showed that the survival at 24 months was 95%, virtually identical to that of the All Enrolled cohort.

FIGURE 1
KAPLAN-MEIER SURVIVAL CURVE:
ALL ENROLLED INVESTIGATIONAL AND CONTROL DEVICES



Risk Factor Analysis

The revision rate is 8.3% (44/532) if only procedures with Month 24+ follow-up are taken into consideration. A post-hoc subgroup analysis (Table 23) showed that within this patient cohort certain patients were at greater risk of experiencing a revision than other patients. Males had a lower revision rate than females (6.5% vs. 12.9%). Further, patients in whom a smaller component was implanted (40 or 44mm), patients with a diagnosis other than Osteoarthritis (OA, i.e., Avascular Necrosis, Rheumatoid Arthritis), patients with significant leg length discrepancy (≥ 1cm) and baseline HHS in the lowest quartile of function all had revision rates greater than the overall average of 7.9% for the Pivotal Unilateral group or 8.3% for the All Enrolled group with a Month 24+ follow-up.

Table 23 provides the risk of revision in the Pivotal Unilateral group and for the All Enrolled patients who received an investigational device.

Table 23: Risk of Revision in Pivotal Unilateral Cohort and All Enrolled Procedures

		Pivotal Unilateral (all procedures)	Pivotal Unilateral with Month 24+ Follow-up	All Enrolled (all procedures	All Enrolled with Month 24+ Follow-up
Gender	Female	11.9% (13/109)	12.8% (13/102)	6.5% (21/323)	12.4% (21/170)
	Male	4.8% (11/228)	5.5% (11/200)	2.8% (28/825)	6.4% (23/362)
Small Component Size	40/44 mm	16.7% (13/178)	17.3% (13/75)	7.4% (22/296)	15.2% (22/145)
	>40/44 mm	4.3% (11/259)	4.9% (11/227)	2.6% (22/843)	5.7% (22/387)
Non Osteoarthritis Diagnosis	AVN	13.6%(6/44)	15.8% (6/38)	6.9% (8/116)	12.7% (8/63)
	RA	25.0% (1/4)	25.0% (1/4)	11.1% (1/9)	14.4% (1/7)
	Osteoarthritis	5.9% (17/289)	6.5% (17/260)	3.4% (35/1023)	7.6% (35/462)
Leg Length Discrepancy greater than or equal to 1 cm	≥ 1 cm	13.0% (12/92)	14.5% (12/83)	6.1% (18/296)	14.0% (18/129)
	<1 cm	4.9% (12/245)	5.5% (12/219)	3.1% (26/849)	6.5% (26/403)
Baseline lowest quartile of function (HHS)	< 42.58	17.7% (15/85)	20.3% (15/74)	6.4% (18/283)	13.1% (18/137)
	≥ 42.58	3.6% (9/252)	4.0% (9/228)	3.1% (26/846)	6.7% (26/391)
Among 1st 25 procedures within a specific site	First 25	8.2% (12/147)	8.9% (12/135)	6.8% (16/234)	8.3% (16/192)
	After 1st 25	6.3% (12/190)	7.2% (12/167)	3.1% (28/914)	8.2% (28/340)

Twenty-one revisions occurred among the 323 procedures for female patients (6.5%) compared to 23 revisions for the 825 procedures for male patients (2.8%; p=0.015). Crude (single predictor variable) survival analyses were performed in order to account for unequal follow-up. Analyses revealed a hazard ratio for risk of revision equal to 2.1 (95% CI 1.2 to 3.9; p=0.01) comparing females to males. There were 22 revisions of patients with size 40mm or 44mm femoral components (296 procedures; 7.4%) compared to 22 revisions for patients implanted with sizes 48mm, 52mm or 56mm (843 procedures; 2.6%) [Note: implant size was unavailable for nine patients]. The hazard ratio for risk of revision was equal to 2.8 (95% CI 1.6 to 5.1; p=0.0006) comparing size 40mm or 44mm to larger sizes. When the effects of gender and size of component are simultaneously estimated, component size (p=0.02) but not gender (p=0.81) retains statistical significance. Reduced baseline function was associated with increased revision risk. The hazard ratio comparing patients in the lowest quartile of HHS scores (<43) to those with higher scores was 2.0 (95% CI 1.1 to 3.6; p=0.03). Having a preoperative leg length discrepancy ≥ 1cm was also associated with increased risk of revision. The crude hazard ratio was 2.2 (95% CI 1.2 to 3.9; p=0.01).

As an additional post-hoc analysis, the initial twenty-five (25) procedures at each center were evaluated to determine whether a learning curve could explain the number of revisions noted in the study. However, evaluation of the procedures with adequate follow-up data did not reveal revision rates to be significantly affected by a learning curve.

Two investigative sites (site 5 and site 10) had higher revision rates. These sites accounted for 17 of the 44 (38.6%) revisions in the study but only 250 of 1148 total procedures (21.8%). There were 27 revisions among the remaining 930 procedures (2.9% revision rate). When site 5 and site 10 were excluded, the small component size and female gender hazard ratios were 3.3 (95% CI 1.6 to 7.0, p=0.002) and 2.5 (95% CI = 1.2 to 5.4; p=0.02), respectively. Therefore, removing these two sites from the analysis did not affect the clinical or statistical significance of these two risk factors.

Patient age, diagnosis and preoperative weight were associated with increased risk for revision when all sites were included in the analysis. However, when site 5 (15 of the 44 revisions) was removed from the analysis, diagnosis other than osteoarthritis, emerged as a statistically significant risk factor in both the pivotal study unilateral patients and all enrolled procedures. The hazard ratio was 2.8 (95% CI 1.3 to 6.2) comparing procedures with diagnoses other than osteoarthritis (i.e., AVN and rheumatoid arthritis) to those with osteoarthritis after excluding site 5. A diagnosis other than osteoarthritis was a significant risk factor in the Pivotal Study Unilateral cohort (hazard ratio=2.5, 95% CI = 1.0 to 5.9). All of the other risk factors noted above were also statistically significant in the Pivotal Study Unilateral cohort. Table 24 provides the prevalence of risk factors for the Pivotal Unilateral group and for the All Enrolled patients with and without Site 5.

Table 24: Prevalence of Risk Factors for Pivotal Unilateral and All Enrolled Patients with and without excluding Site 5

		Pivotal Unilateral	Pivotal Unilateral Excluding Site 5	Pivotal Unilateral Site 5 Only	All Enrolled	All Enrolled Excluding Site 5	All Enrolled Site 5 Only
Small Component Size (40 or 44mm)	%	23.1%	22.7%	26.3%	26.0%	24.0%	35.6%
	n	78	68	10	296	227	69
	N	337	299	38	1139	945	194
Non Osteoarthritis Diagnosis	%	14.2%	15.7%	2.6%	10.9%	12.2%	4.6%
	n	48	47	1	125	116	9
	N	337	299	38	1148	954	194
Leg Length discrepancy ≥ 1cm	%	27.3%	19.7%	86.8%	25.9%	13.8%	85.1%
	n	92	59	33	296	131	165
	N	337	299	38	1145	951	194
Baseline lowest quartile of function (HHS)	%	25.2%	21.4%	55.3%	25.1%	24.8%	26.3%
	n	85	64	21	283	233	50
	N	337	299	38	1129	939	190
Among 1st 25 procedures within a specific site	%	43.6%	41.8%	57.9%	20.4%	21.9%	12.9%
	n	147	125	22	234	209	25
	N	337	299	38	1148	954	194

However, two factors, small component size and diagnosis other than osteoarthritis emerged as consistently statistically significant for both pivotal study unilateral patients and all enrolled procedures. The following table emphasizes the combined effect of these factors when analyzing revisions among patients with minimum 24+ month follow-up. Risk is smallest when neither risk factor is present, intermediate if either risk factor is present and maximum when both risk factors are present.

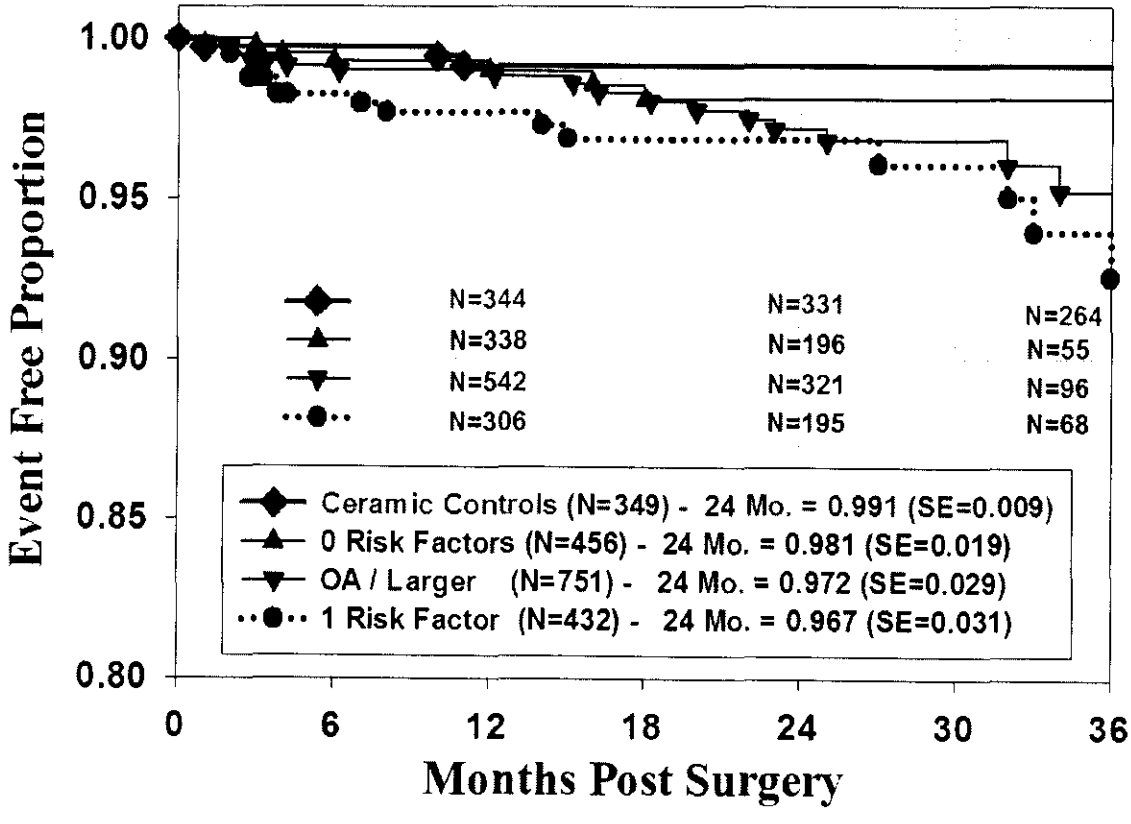
Table 25: Additive Effect of Risk Factors on Revision Rates

Diagnosis	Component Size (Correlated with Gender)	All-enrolled 24+month follow-up[1]	All enrolled minus Site 5 with 24+ month follow-up[1]	Pivotal Unilaterals follow-up to 24 months[1]	Pivotal Unilaterals minus Site 5 follow-up to 24 months[1]
OA	Larger	17/335=5.1%	8/296=2.7%	7/195=3.6%	1/169=0.6%
OA	Smaller	18/127=14.2%	12/104=11.5%	10/65=15.4%	6/55=10.9%
Non OA	Larger	5/52=9.6%	5/49=10.2%	4/32=12.5%	4/32=12.5%
Non OA	Smaller	4/18=22.2%	4/18=22.2%	3/10=30%	3/10=30%

Note: [1] In order to provide meaningful comparisons of revision rates that accounted for varying follow-up times among subgroups, analyses were restricted to the subgroup of patients who required revision no matter when the revision occurred plus all patients who had at least 24 months of follow-up. Since this includes revisions among procedures not expected due for 24 month follow-up, revision rates in this subset are conservatively estimated.

A Kaplan-Meier survival analysis (Figure 2) was performed comparing the Cormet subjects with 0 and 1 risk factors to the ceramic total hip control. At 24 months the implant survival was 98.1% for Cormet subjects with 0 risk factors and 96.7% for those with 1 risk factor. For Cormet subjects with a diagnosis of osteoarthritis and having a larger implant size, implant survival was 97.2%.

FIGURE 2
KAPLAN-MEIER SURVIVAL CURVE:
CORMET SUBJECTS (ALL ENROLLED) WITH 0 AND 1 RISK FACTORS,
NO RISK FACTORS AND CERAMIC TOTAL HIP CONTROL



Survival among Pivotal Unilateral Study devices depended upon the number of risk factors present. The same was true in the All Enrolled Procedures cohort. Among all enrolled procedures, when 0, 1, 2, or 3 of these risk factors were present, risk of revision was 6 of 456 (1.3%), 16 of 432 (3.7%), 15 of 213 (7.0%), and 7 of 46 (15.2%), respectively. There was one procedure that had four risk factors but has not been revised.

To account for unequal follow-up, these analyses are repeated restricting attention to patients with at least 24 months follow-up (including all revisions). Revision risks for patients with 0, 1, 2, and 3 risk factors are 6 of 202 (3.0%), 16 of 206 (7.8%), 15 of 98 (15.3%), and 7 of 25 (28.0%), respectively, among procedures with at least 24 months of follow-up. There was one procedure with 4 risk factors. This patient has not been revised. The linear trend in percentages is statistically significant ($p<0.0001$).

Deaths:

Six Cormet Hip Resurfacing System patients died during the course of the investigation. One patient died five days postoperatively, possibly due to a pulmonary embolism. Two patients died due to cardiac disease, both greater than 24 months postoperatively. Two patients died of lung cancer, one 16 months postoperatively and one 25 months postoperatively. One patient died 22 months postoperatively of unknown causes.

Two ceramic total hip control patients died prior to the two-year anniversary during the course of the investigation. One patient died of a massive myocardial infarction approximately 10 months post surgery. Another patient died approximately 18 months post surgery due to carcinoma.

Summary of Adverse Events

The control group data is more mature as all patients have passed their 2-year visit. In order to avoid extrapolating beyond the follow-up experience in the investigational group, the control follow-up was truncated at the maximum number of days encountered in the investigational group (1803 days).

Among comparable AE types there were more incidences of dislocation ($p< 0.01$) among control patients. There was no difference in the incidence of device related AEs ($p=0.064$) between the investigational (58 procedures; 5.1%) and the control (27 procedures; 7.7%). There were more revisions (44 of 1148; 3.8%) in the investigational group than the control group (5 of 349; 1.9%). Of the 44 revisions in the 1148 procedures in the investigational group, 48% (21/44) were for femoral neck fracture.

Composite Clinical Success (CCS)

The following four criteria were required to be simultaneously achieved in order for a procedure to be defined as a composite clinical success:

- HHS ≥80;
- Radiographic Success;
- Absence of Device Related Adverse Events;
- Absence of Revision/Removal or pending Revision/Removal.

The determination of safety and efficacy of the Cormet Hip Resurfacing System was based on the evaluation of these parameters. Safety and effectiveness data (CCS) for the Pivotal Study Unilateral group is reported for the Month 24+ timeframe.

Harris Hip Score Success

Individual patient composite HHS results at Month 24 postoperatively were compared to the preoperative status.

Pivotal Study Unilateral Patients

In Tables 26-28 the distribution of total HHS scores collected over time is shown for the unilateral procedures in the investigational group and the control group using time windows.

Table 26: Pivotal Study Unilateral Patients and Unilateral Controls: Mean Harris Hip Total and ROM Scores: All Evaluated (Actual[B])

	Investigational Total Score					Controls Total Score					
	N	Mean	SD	Min	Max	N	Mean	SD	Min	Max	p-value[1]
Pre-0p	337	50.1	11.6	12.2	72.0	252	49.7	11.3	24.5	90.1	0.233
Week 6	329	77.4	12.4	26.4	100.0	246	79.0	11.7	40.6	100.0	0.021
Month 6	288	95.7	7.9	49.7	100.0	239	93.7	9.0	36.4	100.0	0.002
Month 12	285	96.2	7.9	41.9	100.0	246	95.0	8.0	52.3	100.0	0.002
Month 24	263	96.7	7.5	43.8	100.0	247	96.2	7.6	48.0	100.0	0.810
Month 24+	283	96.7	7.5	43.8	100.0	253	96.2	7.7	48.0	100.0	0.519
Month 36	80	96.2	7.6	66.9	100.0	187	96.0	7.7	48.6	100.0	0.619

	Investigational ROM Score					Controls ROM Score					
	N	Mean	SD	Min	Max	N	Mean	SD	Min	Max	p-value[1]
Pre-0p	337	4.37	0.57	0.83	5.00	262	4.33	0.50	2.08	5.00	0.133
Week 6	330	4.65	0.29	3.20	5.00	252	4.67	0.22	3.73	5.00	0.931
Month 6	289	4.83	0.17	4.25	5.00	243	4.86	0.16	3.40	5.00	0.242
Month 12	286	4.86	0.15	4.38	5.00	251	4.90	0.13	4.13	5.00	0.016
Month 24	263	4.86	0.17	3.85	5.00	251	4.91	0.13	3.90	5.00	0.000
Month 24+	283	4.86	0.16	3.85	5.00	254	4.91	0.13	3.90	5.00	0.000
Month 36	83	4.82	0.41	1.68	5.00	189	4.93	0.08	4.63	5.00	0.005

Notes: [1] Wilcoxon Rank Sum Test

Table 27: Pivotal Study Unilateral Patients vs. Unilateral Controls: Harris Hip Pain Category All Evaluated (Actual[B])

	Preoperative				Week 6				Month 6				Month 12			
	I		C		I		C		I		C		I		C	
Hip Pain	**n**	**%**		**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
None	0	0.0%	0	0.0%	131	39.6%	145	55.1%	206	70.5%	166	66.4%	216	75.3%	185	71.4%
Slight	0	0.0%	2	0.8%	149	45.0%	61	23.2%	68	23.3%	53	21.2%	51	17.8%	48	18.5%
Mild	2	0.6%	7	2.6%	30	9.1%	41	15.6%	9	3.1%	24	9.6%	7	2.4%	18	6.9%
Moderate	154	45.7%	94	35.3%	18	5.4%	15	5.7%	9	3.1%	7	2.8%	10	3.5%	8	3.1%
Marked	173	51.3%	160	60.2%	3	0.9%	1	0.4%	0	0.0%	0	0.0%	3	1.0%	0	0.0%
Disabled	8	2.4%	3	1.1%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%

	Month 24				Month 24+				Month 36				Wilcoxon Rank Sum p-values	
	I		C		I		C		I		C			
Hip Pain	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**Interval**	**p-value**
None	212	80.6%	196	76.3%	229	80.9%	197	76.1%	68	80.0%	150	78.1%	Preoperative	0.194
Slight	39	14.8%	45	17.5%	41	14.5%	45	17.4%	12	14.1%	27	14.1%	Week 6	0.026
Mild	5	1.9%	8	3.1%	6	2.1%	9	3.5%	2	2.4%	8	4.2%	Month 6	0.174
Moderate	4	1.5%	7	2.7%	4	1.4%	7	2.7%	3	3.5%	6	3.1%	Month 12	0.290
Marked	3	1.1%	1	0.4%	3	1.1%	1	0.4%	0	0.0%	1	0.5%	Month 24	0.223
Disabled	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	Month 24+	0.162
													Month 36	0.695

Table 28: Pivotal Study Unilateral Patients and Unilateral Controls: Harris Hip Function Score Category All Evaluated (Actual[B])

	Preoperative				Week 6				Month 6				Month 12			
	I		C		I		C		I		C		I		C	
Category	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Normal (40-47)	7	2.1%	9	3.6%	58	17.7%	41	16.7%	260	91.9%	201	85.2%	263	93.3%	215	88.5%
Mild Dysfunction (40-<40)	141	41.8%	96	38.1%	88	26.8%	92	37.4%	15	5.3%	28	11.9%	14	5.0%	25	10.3%
Moderate Dysfunction (20-<30)	138	40.9%	114	45.2%	141	43.0%	97	39.4%	8	2.8%	6	2.5%	5	1.8%	3	1.2%
Severe Dysfunction (10-<20)	42	12.5%	30	11.9%	40	12.2%	16	6.5%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Disabled (0-<10)	9	2.7%	3	1.2%	1	0.3%	0	0.0%	0	0.0%	1	0.4%	0	0.0%	0	0.0%

	Month 24				Month 24+				Month 36			
	I		C		I		C		I		C	
Category	n	%	n	%	n	%	n	%	n	%	n	%
Normal (40-47)	246	93.5%	229	93.9%	264	93.3%	237	93.7%	70	88.6%	174	93.0%
Mild Dysfunction (40-<40)	13	4.9%	12	4.9%	14	4.9%	12	4.7%	5	6.3%	10	5.3%
Moderate Dysfunction (20-<30)	4	1.5%	3	1.2%	5	1.8%	4	1.6%	4	5.1%	3	1.6%
Severe Dysfunction (10-<20)	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Disabled (0-<10)	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%

Wilcoxon Rank Sum p-values	
Interval	p-value
Preoperative	0.981
Week 6	0.038
Month 6	0.019
Month 12	0.062
Month 24	0.879
Month 24+	0.853
Month 36	0.214

Investigational Group

Eleven patients (3.9%) of 283 evaluable Pivotal Study Unilateral patients had a HHS <80 points at the Month 24+ follow-up interval. Two of these patients were subsequently revised, one patient for acetabular component loosening and the other for femoral component loosening. Another subsequently reported with acetabular loosening. One patient was reported to have knee pain that contributed to the low HHS. Investigators did not report specific concerns for the other five patients that would contribute to the low scores. Two patients, not evaluated at Month 24, had a HHS <80 points at the Month 36 interval. One patient reported a low HHS following a motor vehicle accident and the other patient stated that the limitations were due to the contralateral hip. There were no patients in the Pivotal Study Bilateral group with a HHS <80 points at Month 24 or Month 24+.

Control Group

Twelve patients in the Unilateral Control group (4.8%) had a HHS <80 points at the Month 24+ follow-up interval. Two patients had hip pain associated with the device, six patients had pain associated with other joint or medical issues, and two patients had mild or occasional pain limiting the HHS. One patient in the bilateral group had a HHS <80 points at Month 24 postoperatively due to back pain. One patient did not have a complete score at Month 24 but had a score <80 at Month 36 due to contralateral hip disease and compensatory strain on the ipsilateral side.

There was no statistical difference in mean HHS or number of patients with HHS ≥80 points in the Month 24 and Month 24+ between investigational Cormet Hip Resurfacing System and control ceramic total hip groups. The mean HHS at Month 24+ was 96.7 and 96.2 (p=0.52) and percentage of patients with ≥80 points was 96.1% and 95.3% (p=0.67) for the Pivotal Study Unilateral and Unilateral Control groups, respectively.

Pivotal Study Bilateral Group

There were no patients with a HHS < 80 in the bilateral Cormet group at Month 24 or Month 24+. Similarly, there were no bilateral procedures in the ceramic total hip control group with a HHS <80 at Month 24 or Month 24+. There was no statistical difference in HHS >80 points at Month 24 (two sided Fisher's exact test; p=0.213) or Month 24+ (two sided Fisher's exact test; p=0.130) comparing the Cormet Pivotal Study Unilateral with the Cormet Pivotal Study Bilateral groups.

There were no differences in scores at any postoperative time frame (Week 6 – Month 24+) when comparing the bilateral procedures with no more than slight hip pain to the pivotal study unilateral patient group. Both groups demonstrated no or slight pain in over 95 % of the patients at minimum Month 24.

Continued Access Group

There were two patients with HHS of < 80 points at minimum Month 24 postoperative in the Continued Access group. Overall HHS results for the continued access group are included in the all enrolled group.

All Enrolled Cohort

The total HHS at Month 24 and Month 24+ were in the excellent range for both all enrolled Cormet and control groups. There was no significant difference between the groups at Month 24 in the distribution of Harris Hip Pain Score category and Harris Hip Function Score category (p=0.456 and p=0.922 respectively). In addition, there were no differences between the Cormet and control All Enrolled Procedures groups based on HHS ≥80 at the Month 24 or Month 24+ follow-up time points.

Radiographic Success

Individual patient radiographic results at Months 24 and 24+ were compared to the baseline in order to detect radiolucencies in the femoral and acetabular zones, acetabular migration, femoral subsidence and femoral tilt. There were no radiographic failures in the control group at Month 24. Table 29 summarizes the findings for the Pivotal Unilateral group at Month 24 and Month 24+.

Table 29: Radiographic Findings for Pivotal Unilateral Group at Month 24 and Month 24+

	Month 24		Month 24+	
	N		N	
Total radiographs (Actual[B]) in Table 11[1]	259		291	
Not available to the reviewer for evaluation[2]	30		10	
Evaluable for radiographic success	229		281	
	n/N	%	n/N	%
Radiolucency Acetabular Component				
I	0 /228	0.0%	0 /279	0.0%
II	0 /228	0.0%	0 /279	0.0%
III	2 /228	0.9%	2 /279	0.7%
All[3]	0 /228	0.0%	0 /279	0.0%
Radiolucency Femoral Component				
Superior	0 /229	0.0%	1 /279	0.4%
Tip	1 /229	0.4%	2 /279	0.7%
Inferior	0 /229	0.0%	1 /279	0.4%
All[3]	0 /229	0.0%	1 /279	0.4%
Cup migration and tilt[4]				
Superior/Inferior migration >= 5 mm[3]	0 /228	0.0%	0 /278	0.0%
Medial/Lateral migration >= 5 mm[3]	0 /228	0.0%	0 /278	0.0%
Varus/Valgus Tilt >= 5 degrees[3]	0 /228	0.0%	0 /278	0.0%
Stem migration and tilt[4]				
Subsidence of the femoral component >= 5 mm	7 /224	3.1%	10 /274	3.6%
Stem Tilting >= 1 degree	172 /226	76.1%	205 /276	74.3%
Subsidence of the femoral component >= 5 mm and Stem tilting>= 1 degree[3]	7 /226	3.1%	10 /276	3.6%
Other assessments				
Anteroversion of the head >= 5 mm	49 /223	22.0%	55 /267	20.6%
Retroversion of the head >= 5 mm	69 /223	30.9%	89 /267	33.3%
Hypertrophy in any zone	0 /229	0.0%	0 /279	0.0%
Resorption in any zone	0 /229	0.0%	0 /279	0.0%
Lysis in any zone	10 /229	4.4%	12 /279	4.3%
Composite radiographic failure	**7 /228**	**3.1%**	**10 /279**	**3.6%**

Notes:

[1] Total radiographic evaluations performed for Month 24 or Month 24+ among procedures expected due. The procedures in this table were used in comparisons with control devices.

[2] Not available to the independent medical reviewer for evaluation.

[3] Required for composite radiographic endpoint used in constructing the Composite Clinical Success.

[4] Complete component migration and tilt could not be measured for 5 cases. However, in the absence of any other indicators of failure for the component and absence of qualitative indicators of failure of the component in a serial review, these cases were not considered failure.

Investigational Group

There were ten patients with radiographic evidence of femoral component instability at ≥Month 24 in the Pivotal Study Unilateral group. Instability was evidenced by femoral subsidence of >5mm and tilt of >1°. One patient also exhibited three-zone radiolucency around the femoral component. One of these patients had a HHS of 63 points at Month 24, considered a study failure. Another patient with femoral subsidence of >5mm had device related AEs of femoral neck fracture and subsequent femoral subsidence at Month 3 postoperatively. At Month 6, the

fracture healed and the component did not move further. The patient remains asymptomatic at Month 36 postoperatively. Two patients had revision of the femoral components due to femoral component loosening. The remaining patients do not have clinical symptoms associated with the femoral component instability as evidenced by HHS in the excellent range at minimum Month 24 postoperatively.

Pivotal Study Bilateral Group

A total of 55 radiographs were evaluated (58 available) for the pivotal study bilateral group at Month 24+. There were no components with a radiolucency in all zones at Month 24 or Month 24+. There was one (2.4%) cup failure based on migration and tilt criteria at Month 24 and an additional cup failure (4.1%) at Month 24+ based on these same criteria. There was one (2.3%) stem failure at Month 24 defined by both subsidence of $\geq$ 5mm and tilt of $\geq$ 1 degree and one (3.8%) additional stem failure at Month 24+. Based on composite radiographic endpoints used in constructing the CCS, there were a total of two (4.5%) radiographic failures at Month 24 in the bilateral investigational groups and a total of three (5.7%) radiographic failures at Month 24+ in this same group

Control Group

One patient in the unilateral control group was determined to be radiographically unstable at Month 24 postoperatively. The patient, status post a traumatic fall, exhibited radiolucency around the femoral device, 10mm of femoral subsidence and component tilt at the Month 24 postoperative interval. The patient was subsequently revised for femoral component loosening. No patient in the bilateral control group was determined to be radiographically unstable.

Device Related Adverse Events

As identified previously, the following complications are considered to be device related adverse events for any hip resurfacing surgery:

- Component breakage;
- Femoral neck fracture;
- Collapse or AVN of the femoral head;
- Femoral loosening;
- Acetabular loosening;
- Dislocation.

Additional complications specific to total hip arthroplasty are included to compare the control ceramic total hip:

- Intraoperative chipping of the ceramic insert;
- Periprosthetic bone fractures.

Table 30 identifies the complications for the 1148 Cormet Hip Resurfacing System IDE patients compared to the ceramic total hip control.

Table 30: Relative Complications for the Cormet Hip Resurfacing IDE Patients Compared to the Ceramic Total Hip Control

	Pivotal Study Unilateral (N=337)	**Total Investigational Study (N=1148)**	**Ceramic Total Hip Pivotal Study Unilateral Control (N=266)**
Study Design	Multi-center IDE, Prospective, non-randomized	Multi-center IDE, Prospective, non-randomized	Multi-center IDE, Prospective, randomized
Femoral neck fracture	11	26	NA
Femoral loosening	13	14	0
Femoral subsidence	1	4	2
Acetabular loosening	5	11	0
Dislocation	1	2	7
Implant fracture	0	0	0
Intraoperative chipping	NA	NA	6
Periprosthetic fracture	2	2	9
AVN head/neck	0	0	NA
Femoral head collapse	0	0	NA
Total	33 events in 32 patients (9.5%)	59 events in 58 patients (5.1%)	24 events in 21 patients (7.9%)

There was no statistically significant difference in the rates of device related AEs between the investigational and control groups in either All Enrolled Procedures (p=0.064) or in the Pivotal Study Unilateral group (p=0.563).

Revision or Removal of Any Components/Pending Revision/Removal

Investigational Group

A total of 1148 Cormet Hip Resurfacing System procedures were performed during the course of the IDE and Continued Access. Forty-four procedures (3.8%) resulted in the revision or removal of one or more components. There were two pending revisions at the time of database lock for this report.

Twenty-four revisions were performed for patients in the Pivotal Study Unilateral group. Reasons for revision included: acetabular loosening (four patients), dislocation (one patient), femoral loosening (eleven patients), and femoral neck fracture (eight patients).

Four revisions were performed for patients in the IDE Pivotal Study Bilateral group: one deep infection, two femoral neck fractures, and one incidence of femoral component subsidence.

Sixteen revisions were performed for patients in the Continued Access portion of the study: eleven femoral neck fractures, four acetabular loosening, and one deep joint infection. A complication report for aseptic loosening of the acetabular component was submitted for one patient in the Continued Access portion of the study. This patient was considered pending

revision. Another patient with femoral neck fracture that has not healed is being monitored for potential revision surgery.

Statistical review of the revision population identified the following factors as significant for revision: female gender, a diagnosis other than Osteoarthritis, small component size, preoperative leg length discrepancy of ≥1 cm and preoperative HHS.

Kaplan Meier survivorship analysis results demonstrated a cumulative survival rate of 95.9% at a maximum of Month 24 postoperatively for the entire Cormet Hip Resurfacing System patient population. This was compared to 99.1% survivorship for the ceramic total hip control at the same time frame.

Control Group
There were five device failures (1.4%) during a comparable time frame in the control group. Reasons for revision included post-traumatic femoral component non-union, one dislocation in the perioperative time frame, one deep joint infection less than one year postoperative, one hip pain with suspected sepsis three years postoperative and one patient with post-traumatic subsidence of the femoral component. These patients were all in the Pivotal Study Unilateral group.

Final CCS Analysis

The following non-inferiority hypothesis was used in the primary efficacy analysis of CCS comparing the investigational group to the historical control group (HCG).

The null and alternative non-inferiority hypotheses were formulated to be consistent with the Blackwelder approach and are as follows:

H_o: $P_{Cormet} - P_{HCG} \leq -0.08$ (clinically inferior to control)
H_a: $P_{Cormet} - P_{HCG} > -0.08$ (not clinically inferior to control)

The study was designed to reject the null hypothesis that the investigational device is clinically inferior to the control. The non-inferiority delta was specified to be equal to 0.08. Thus, the study was designed to reject the null hypothesis that proportion of patients achieving composite clinical success with the investigational device is at least 0.08 less than the proportion of patients achieving composite clinical success with the control device.

A one-sided 95% non-inferiority confidence interval for the difference in proportions was determined. If the lower bound of this confidence interval exceeds -0.08 then the null hypothesis is rejected and we many conclude that in terms of composite clinical success, the investigational device is not clinically inferior to the control device.

Table 31 provides the results of Out-of-Window analyses which compare the results for Actual[A] (patients evaluated within protocol defined follow-up windows) and Actual[B] (patients contributing any data regardless of whether the visit was within the protocol defined follow-up windows). The first row of the table summarizes the results of the primary non-inferiority test for CCS (Month 24+ CCS (Actual[B])).

Table 31: Composite Clinical Success

	Investigational			Control			Non-Inferiority Test	
	n	N	Prop.	n	N	Prop.	Diff.	95% CI LB[3]
Month 24+[1] CCS (Actual[B])	251	292	0.860	224	256	0.875	-0.015	-0.063
Month 24+ CCS (Actual[A])[2]	246	285	0.863	223	254	0.878	-0.015	-0.062
Month 24 CCS (Actual[B])	207	243	0.852	219	250	0.876	-0.024	-0.075
Month 24 CCS (Actual[A])	171	202	0.847	187	209	0.895	-0.048	-0.103

Note:

1. Month 24+ outcomes are based on rollback imputations for missing Month 24 Harris Hip Scores. If the Month 24 Harris Hip Score is missing, the next available value is used (e.g., Month 36) to impute the missing value).
2. Actual[A] intervals: Analyses using Actual[A] intervals only include evaluations as follows: PreOp (on or before date of surgery); Immed. Interval 1-45 days; 6 Mo. Interval (6 ±1 mo); 1 Yr Interval (12 ± 2 mo); 2 Yr Interval (24 ± 2 mo.). Actual[A] Month 24+ outcomes use the rollback imputation for Harris Hip Scores and Radiographic Success. Actual[B] analyses include all evaluated assessments regardless of interval boundaries.
3. Lower bounds of 1sided 95% confidence intervals for differences between proportions with composite clinical success (Investigational minus Control). The study was designed to demonstrate clinical non-inferiority defined as a success rate no more than 0.08 smaller than control. The null hypothesis that the investigational device is inferior to the Control device is rejected if the lower bound of the confidence interval is larger than -0.08.

A procedure is defined as a composite clinical success if the Harris Hip Total score is at least 80 points at Month 24+, absence of revision of any of the components of the investigational device, absence of device related AEs, and absence of radiographic failure. Among Pivotal Study Unilateral patients, 251 of 292 (proportion=0.860) patients achieved Month 24+ composite clinical success. Similarly, 224 of 256 (proportion=0.875) Unilateral Control patients achieved composite clinical success. The difference in proportions is only -0.015. The lower bound of the one-sided 95% non-inferiority confidence interval is -0.063. Since -0.063 exceeds -0.08, the null hypothesis of inferiority is rejected with $p<0.05$ and it is concluded that the investigational device is not clinically inferior to the control device on the basis of this CCS.

Analysis demonstrates non-inferiority of the Cormet Hip Resurfacing System to the ceramic total hip control for the Month 24 evaluation or Month 24+ with expanded windows for patient follow-up.

XI. CONCLUSIONS DRAWN FROM THE STUDIES

CDRH believes that the sponsor has provided an adequate device description and preclinical testing information to support device safety. The clinical study evaluated safety and effectiveness based on HHS, radiographic success, absence of revision/removal and absence of device related adverse events. Although the specific endpoints and control were modified during the course of the study, the data provided is valid scientific evidence as defined per 21 CFR 860.7 and the results provide reasonable assurance of effectiveness. The percentage of patients requiring revision surgery within 2 years of the procedure 7.9% (24/302) of the unilateral cohort at 24+ Months and 8.3% (44/532) of the all enrolled cohort at 24+ Months is higher than the control revision rate of 1.9% (5/266). A post-hoc subgroup analysis identified patients who are female, who receive a smaller component size (i.e. 40 or 44mm), who have a diagnosis other than osteoarthritis (i.e. avascular necrosis, rheumatoid arthritis), a leg length discrepancy greater than or equal to 1 cm, or low baseline HHS have a greater risk of revision than other patients. The more risk factors a patient has, the greater the risk of procedure failure requiring a revision to the

hip. The sponsor has identified these risk factors to help surgeons with patient selection. The results of the clinical study provide a reasonable assurance that the Cormet Hip Resurfacing System is safe and effective for the indicated population. Therefore, CDRH believes that it is reasonable to conclude that the benefits of the use of the Cormet Hip Resurfacing System for the target population outweigh the risk of the illness or injury when used in accordance with the directions for use.

XII. PANEL RECOMMENTATION

The Orthopaedic and Rehabilitation Devices Panel (the Panel) met on Thursday, February 22, 2007 in Gaithersburg, Maryland. The Panel met in order to provide advice and a recommendation on the approvability of the Corin U.S.A. Cormet Hip Resurfacing System (P050016). CRDH solicited Panel input on the following issues:

1. There were multiple revisions to the proposed primary safety and effectiveness endpoints during the course of the IDE study and the review process of the PMA application.
2. The approved IDE study proposed to enroll concurrent control subjects. The PMA is based upon a proposed historical control, after multiple attempts to replace the concurrent control group. This historical control population allows the applicant access to individual patient data having similar clinical and radiographic evaluation data; and
3. The PMA reports differences in the percentage of subjects requiring revision surgery for this device, the control device and similar devices, and types of devices as presented in the literature and expected in common practice. To investigate the revision rates the sponsor did a post-hoc analysis to identify risk factors that may increase a patient's likelihood of having revision surgery.

The clinical data presented were collected in a non-randomized, multi-center study intended to assess the safety and effectiveness of the Cormet Hip Resurfacing System by demonstrating non-inferiority to the control treatment. Patient success was defined by the Composite Clinical Success endpoint of a Harris Hip Score greater than or equal to 80, no revision surgery, radiographic success, and no device-related adverse events. The results were found to be non-inferior to the historical control data for the ceramic total hip system.

The Panel voted (4-1) to recommend that the PMA application for the Cormet Hip Resurfacing System be found "Approvable with Conditions." The recommended conditions of approval are summarized as follows:

1. There should be a post approval clinical study that considers issues raised during the discussion, including: duration of the study, radiographic evaluation timepoints, metal ion serum levels and revision rates for a Kaplan-Meier survival analysis.
2. There should be mandatory surgical training associated with this device.
3. The labeling should reflect the risk factors identified by the sponsor for revision surgery (small component size, female gender, a non-osteoarthritis diagnosis, leg length discrepancies and a Harris Hip Score less than 42).

XIII. CDRH DECISION

CDRH concurred with the Panel recommendation of February 22, 2007 that there is a reasonable assurance of safety and effectiveness of the Cormet Hip Resurfacing System based on the results of the preclinical testing and the results of the clinical study.

Below is a discussion of CDRH action on each of the Panel's recommendations:

1. There should be a post approval clinical study that considers issues raised during the discussion, including: duration of the study, radiographic evaluation timepoints, metal ion serum levels and revision rates for a Kaplan-Meier survival analysis.

   CDRH agreed. See approval order.

2. There should be mandatory surgical training associated with this device.

   The sponsor has agreed to implement a training program, as outlined in the PMA. The training program begins with a web-based eSimulation Review followed by live surgery observation or review of a surgical video. The next stage will be hands on experience at a training center with interactive eSimulation, a sawbone workshop and tissue surgery practice. The final stage will be continued mentoring through the first surgery. See approval order.

3. The labeling should reflect the risk factors identified by the sponsor (small component size, female gender, a non-osteoarthritis diagnosis, leg length discrepancies and a Harris Hip Score less than 42).

   The instructions for use include the sponsor's detailed risk factor analysis and revision rates on each cohort. The sponsor has also added the following warning to their labeling.

   "Based on the analysis of a multicenter prospective study of 1030 patients in 14 centers the following were identified as risk factors for revision: Patients who are female, who receive a smaller component size (i.e. 40 or 44mm), who have a diagnosis other than osteoarthritis (i.e. avascular necrosis, rheumatoid arthritis), a leg length discrepancy greater than or equal to 1 cm, or low baseline HHS have a greater risk of revision than other patients. The more risk factors a patient has, the greater the risk of procedure failure requiring a revision to the hip. Please see Tables 21 and 23 for revision rates for each risk factor group."

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

The applicant's manufacturing facility was inspected and was found to be in compliance with the Quality System Regulation (21 CFR 820).

FDA issued an approval order on July 3, 2007.

XIV. APPROVAL SPECIFICATIONS

Directions for use: See the labeling.

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

Postapproval Requirements and Restrictions: See approval order.

XV. REFERENCES

[1] Anderson GBJ, Freeman, MAR, Swanson, SAV. Loosening of the cemented acetabular cup in total hip replacement. *Journal of Bone and Joint Surgery.* 1972; 54B: 590-599.

[2] Komistek RD,. In vivo comparison of the hip separation after metal-on-metal or metal-on-polyethylene total hip arthroplasty. *Journal of Bone and Joint Surgery.* 2002; 84-A: 1836-1841.

[3] Kaddick, Hallstrom B, Golladay GJ, Hoeffel D, Harris WH. Determination of resistance to luxations and repositions of total hip joint prostheses. In: Phuhl, W, editor. *Bioceramics in Orthopedics,* 1998.