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Orthopaedics

Tritanium® Primary Acetabular Shell Study

CLINICAL PROTOCOL

A prospective, post-market, multi-center study of the

Tritanium® Acetabular Shell

Sponsor: *Stryker Orthopaedics*
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Study Product: *Tritanium® Acetabular Shell*

Protocol Number: *69*

510(k) Clearance Number: *K081171*

Version 3.0

Date: 24 Aug 2020

CONFIDENTIAL

Protocol Change History

Version	Description	Changed By
1.0 9/30/2009	New	Kristin L. Given
1.1 1/26/2011	Data collection method changed from paper case report form to electronic data capture. All affected sections have been updated to reflect this change.	Kristin L. Given
2.0 6/1/2011	Removed PA-coated product and added MDM™ liner. Added background and device information for the MDM™ liner and X3® insert. Changed enrollment strategy from arms to treatment groups. Added EQ-5D and updated eCRF specifications to incorporate new device and questionnaire. Added Appendices G and H to comply with latest protocol template.	Kristin L. Given Michael A. Pelosi
3.0 8/24/2020	Removed EDC system, NetRegulus reference. Subject retention changed from a points accumulation program redeemable for a gift (Bennett Brothers), to a stipend system. Appendix F revised to now reference Product Labeling; Appendix H no longer needed.	Filesha Haniff

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List of Abbreviations

ADE	Adverse Device Effect
ADM	Anatomic Dual Mobility
AE	Adverse Event
AP	Anteroposterior
BMI	Body Mass Index
CP	Commercially Pure
eCRF	Electronic Case Report Form
CSA	Clinical Study Associate
CSM	Clinical Study Manager
DCF	Data Clarification Form
DCR	Data Clarification Request
EC	Ethics Committee
EQ-5D	EuroQol
ETA	Enhanced Tendon Anchor
GCP	Good Clinical Practice
HA	Hydroxyapatite
HHS	Harris Hip Score
HIPAA	Health Insurance Portability and Accountability Act
ICMJE	International Committee of Medical Journal Editors
ID	Inner Diameter
IRB	Institutional Review Board
LEAS	Lower Extremity Activity Scale
MDM	Modular Dual Mobility
NIDJD	Non-Inflammatory Degenerative Joint Disease
OD	Outer Diameter
PER	Product Experience Report
PI	Primary Investigator
PSF	Particle Sintered Foam
QOL	Quality of Life
ROM	Range of Motion
SAE	Serious Adverse Event
SC	Study Coordinator
SF-12	Short Form-12

List of Abbreviations

(continued)

THA	Total Hip Arthroplasty
THR	Total Hip Replacement
UADE	Unanticipated Adverse Device Effect
UHMWPE	Ultra High Molecular Weight Polyethylene

Study Synopsis

Title	A prospective, post-market, multi-center study of the Tritanium® Acetabular Shell
Short Title	Tritanium® Primary Acetabular Shell Study
Protocol Number	69
Phase	Post-market

Methodology	This study will be a prospective, non-randomized evaluation of the Tritanium® Acetabular Shell for primary total hip replacement (THR) with a cementless application in a consecutive series of patients who meet the eligibility criteria. Half of the cases will use the X3® polyethylene insert alone as the bearing surface; the other half will use the MDM™ liner coupled with a compatible ADM/MDM™ X3® insert as the bearing surface. Cases receiving the MDM™ liner may be coupled with Stryker 22.2 mm or 28 mm LFIT™ CoCr, BIOLOX *delta* or alumina ceramic heads. All cases will be implanted with a compatible Stryker femoral stem. Data from the Trident® X3® Polyethylene Insert Study will be used as a historical control for secondary objectives. This study was chosen for the following reasons: • Similar indication (primary THR) • The acetabular shell (Trident® HA Hemispherical Acetabular Shell) used in this study is a predicate for the Tritanium® Acetabular Shell, with similar design features. • The follow-up intervals and data collected in the Trident® X3® Study closely match the design of the current study. The survivorship value used for development of the statistical plan was calculated as a mean of the mid-term results published for three studies of similar acetabular shells. Articles presenting long-term results of additional acetabular shells of similar design will be used for comparison at the end of the study as available.
Study Duration	• Follow-up of each primary THR case to 10 years • Enrollment period of 18-24 months • Approximate 13-year total duration
Study Center(s)	7 – 12 centers

Hypothesis	The success rate, defined as freedom from acetabular revision, for hips implanted with the Tritanium® Acetabular Shell, is no worse than for hips implanted with similar technology as reported in the literature and Trident® X3® Study historical control at 5 years postoperative.
Objectives	Primary: To demonstrate, through absence of revision at 5 years postoperative, that acetabular replacement with the Tritanium® Acetabular Shell provides clinical results comparable to similar acetabular components. Secondary: • To study rates of screw fixation usage in Tritanium® Acetabular Shell (cluster hole) procedures and compare with those reported in the Trident® X3® Polyethylene Insert Study. • To compare pain, function and health related quality of life (QOL) between the Tritanium® Acetabular Shell combined group and the above-referenced historical control group. The following outcomes measures will be used for this comparison: o Harris Hip Score (HHS) o Short Form-12 (SF-12) o Lower Extremity Activity Scale (LEAS) o EQ-5D 1-year, 3-year, and 5-year HHS, SF-12 and LEAS data will be compared to the historical control with respect to improvement from preoperative scores. The EQ-5D data will be summarized and presented.

Objectives	• An additional Follow-Up Questionnaire will be administered annually in postoperative years 6-10 to assess patient satisfaction and pain, and to capture adverse events. This questionnaire will provide the survivorship information necessary to evaluate the primary objective of the study. • To review radiographic stability and complications between those hips implanted with the Tritanium® Acetabular Shell and those in the historical control group. Published complication rates with similar devices, as well as complications related to cementless acetabular replacement, will be reviewed.
Number of Subjects	Cases will be enrolled until 240 cases have received the Tritanium® Acetabular Shell • Treatment 1: 120 cases with X3® polyethylene insert • Treatment 2: 120 cases with MDM™ liner and ADM/MDM™ X3® insert
Diagnosis and Main Inclusion/Exclusion Criteria	Inclusions: A. Patient has signed an IRB approved, study specific Informed Patient Consent Form. B. Patient is a male or non-pregnant female age 18 years or older at time of study device implantation. C. Patient has primary diagnosis of Non-Inflammatory Degenerative Joint Disease (NIDJD). D. Patient is a candidate for a primary cementless total hip replacement. E. Patient is willing and able to comply with postoperative scheduled clinical and radiographic evaluations and rehabilitation.

Diagnosis and Main Inclusion/Exclusion Criteria	Exclusions: F. Patient has a Body Mass Index (BMI) ≥ 40. G. Patient has an active or suspected latent infection in or about the affected hip joint at time of study device implantation. H. Patient has a neuromuscular or neurosensory deficiency, which limits the ability to evaluate the safety and efficacy of the device. I. Patient is diagnosed with a systemic disease (e.g. Lupus Erythematosus) or a metabolic disorder (e.g. Paget's Disease) leading to progressive bone deterioration. J. Patient is immunologically suppressed or receiving steroids in excess of normal physiological requirements (e.g. > 30 days). K. Patient requires revision surgery of a previously implanted total hip replacement or hip fusion to the affected joint. L. Patient has a known sensitivity to device materials. M. Patient is a prisoner.
Study Device	Required Components: • Tritanium® Acetabular Shell Acetabular components must be used in a cementless application.
Reference Therapy	Literature control and Trident® HA Hemispherical Shell

Ancillary Devices	The following ancillary devices are permissible: • Stryker X3® polyethylene inserts (120 cases) • Stryker MDM™ liners with ADM/MDM™ X3® polyethylene inserts (120 cases) • Stryker LFIT™ CoCr, BIOLOX *delta* and alumina ceramic heads (in cases where the MDM™ liner is used, only 22.2 mm and 28 mm heads are permissible) • Stryker Universal Adapter Sleeves (for use with BIOLOX *delta* universal ceramic heads) • Compatible Stryker femoral stems • Stryker Orthopaedics Torx Bone Screws

Statistical Methodology	Primary: The 90% confidence interval of the success rate will be computed at 5 years postoperative. For the non-inferiority comparison, the lower bound of this 90% confidence interval will be compared with 94%. For the superiority comparison, the lower bound of this 90% confidence interval will be compared with 99%. Secondary: • A Fisher's exact test or Chi-square test will be used to compare the usage of screw fixation between the Tritanium® Acetabular Shell and Trident® X3® Polyethylene Insert studies. If there are any statistically significant differences in baseline variables (e.g. age, gender, diagnosis) between the groups, they will be addressed as covariates and ANOVA or ANCOVA will be used. • A two-sample t-test or Wilcoxon test will be used to compare the HHS, SF-12 and LEAS score at 1-year, 3-year, and 5-year follow-up between the Tritanium® Acetabular Shell and Trident® X3® Polyethylene Insert studies. If there are any statistically significant differences in baseline variables (e.g. age, gender, diagnosis) between the groups, they will be addressed as covariates and ANOVA or ANCOVA will be used. • EQ-5D health states will be converted to numerical results using the appropriate value set and presented in table format. • Adverse event (AE) rates will be listed and tabulated, with 95% confidence intervals presented. • Radiographic data will be summarized in table format.

Evaluation Schedule

Evaluation	Pre-op X-rays (-1 yr) eCRFs (-4 mn)	Intra-op	6-wk ± 2 wks	1-yr ± 2 mn	2-yr ± 2 mn	3-yr ± 3 mn	4-yr ± 4 mn	5-yr ± 4 mn	6-yr ± 4 mn	7-yr ± 4 mn	8-yr ± 4 mn	9-yr ± 4 mn	10-yr ±4mn
Inclusion/ Exclusion	X												
Demographics & Medical History	X												
Preoperative HHS	X												
Surgical Details		X											
Postoperative HHS			X	X		X		X		Optional			Optional
SF-12	X		X	X	X	X	X	X		Optional			Optional
LEAS	X		X	X	X	X	X	X		Optional			Optional
EQ-5D	X		X	X	X	X	X	X		Optional			Optional
Radiographs: Antero-posterior (AP) pelvis, AP femur, lateral	X		X	X		X		X		Optional			Optional
Follow-up Questionnaire									X	X	X	X	X

HHS: The HHS is a subjective outcomes tool completed by the investigator that measures function, pain and motion.

SF-12: The SF-12 is a 12-item patient questionnaire that evaluates general health and wellbeing.

LEAS: The LEAS is a self-administered patient evaluation designed to reflect patient activity.

EQ-5D: The EQ-5D is a standardized instrument for use as a measure of health outcome.

Follow-up Questionnaire: The Follow-up Questionnaire is a short patient questionnaire intended to provide information on patient satisfaction, pain, and whether or not there have been any revisions or removals since the last follow-up visit.

1 Introduction

This document is a protocol for a human research study. This study will be conducted in compliance with the protocol, Good Clinical Practice (GCP) Standards, associated Federal regulations and all applicable research requirements.

1.1 Background

Cementless acetabular components for total hip arthroplasty (THA) became popular in the United States in the early 1980s, primarily due to poor long-term results with cemented cups. Superior radiographic performance has been reported for cementless cups as compared with cemented fixation.[1] Cementless acetabular components require initial implant stability to allow for bone ingrowth or ongrowth, which provides long-term durability of the prosthesis when properly achieved.[2] To this end, there are several surface options available for cementless acetabular fixation; titanium fibermesh, sintered bead surfaces, and plasma spray are some widely used examples, all with good clinical history.[3] In a recent publication, the 20-year Kaplan-Meier survivorship of a titanium fibermesh cup was reported at 96%.[4] Similarly positive results have been reported at slightly shorter time points for both sintered bead surfaces[5] (0.7% revision for aseptic loosening at 9.5 years) and plasma sprayed surfaces[6] (0% revision for aseptic loosening at 8.5 years).

Tritanium® technology is now available in a primary application and provides a three-dimensional, commercially pure (CP) Titanium matrix that resembles trabecular bone, allowing for enhanced acetabular fixation[7] and joint stability.[8] Studies have shown the superiority of 3-D surfaces when compared to 2-D surfaces[9], as well as improved biological fixation with CP Ti as compared to alloys.[10] An example of the superiority of the Tritanium® coating to other coatings can be seen in a pre-clinical study[11] examining the canine *in vivo* bone response to six test surfaces. Bone penetration for Tritanium® surfaces was significantly greater than for all other test surfaces (titanium beads with and without PA and cobalt chrome beads with and without PA) at 12 weeks. Mechanically, the failure strength of the surface-to-bone attachment for Tritanium® surfaces was significantly greater than that of all other test surfaces at the 12-week time point. Both bone penetration and failure strength increased significantly between the 6- and 12-week time points.

Stryker has introduced a porous coated cementless acetabular cup for primary THA, the Tritanium® Acetabular Shell. The basic design of the Tritanium® Acetabular Shell is similar to other cementless acetabular cups which are currently commercially distributed. The Tritanium® Acetabular Shell's design features are based upon the previous success of Stryker's cementless Trident® hemispherical acetabular shells.

Table 1. Tritanium® Acetabular Shell Design Features

Product	Identifying Features	Based upon Clinical History of the Following	Existing Shell Closest to Same Design Features
Tritanium® Acetabular Shell	Hemispherical, solid and cluster hole designs Ti6Al-4V (Titanium alloy) substrate CP Titanium porous coating	Trident® Tritanium®Acetabular Shell; Trident® Hemispherical Acetabular Shell	Trident® Tritanium® Acetabular Shell

The Tritanium® Acetabular Shell shares design similarities with the Trident® Tritanium® and Trident® Hemispherical uncemented acetabular shells. The Trident® Hemispherical shells are the design upon which the Tritanium® family of acetabular shells is based; these shells are manufactured from a Ti6Al-4V substrate into a hemispherical geometry and have an arc-deposited coating of CP Ti to increase surface roughness. The Tritanium® family of shells retains the geometry and substrate material of this predecessor design, but replaces the arc-deposited CP Ti coating with a three dimensional porous coating of the same CP Ti material.

The Tritanium® Acetabular Shell is very similar in design and surface characteristics to the Trident® Tritanium® Acetabular Shell that is currently used in revision applications. A prospective, post-market, non-randomized, open-label, multi-center clinical study of the **Trident® Tritanium® Acetabular Shell** (product family 509-02-XXX) is currently in the subject enrollment phase. This study evaluates the use of the Trident® Tritanium® Acetabular Shell for revision of the acetabular component of a previously failed THR in a consecutive series of cases. A total of 244 cases are anticipated. Presently, there are 15 sites in the United States participating and 239 subjects enrolled. Data collection is on-going with the initially enrolled subjects just entering the 3-year follow-up interval. To date, there have been nine reported revisions. Six of these were reported as related to surgery or

infection; two were reported as related to the device; relation to the device in the case of the remaining revision is unknown as the revision was discovered at a site close-out visit and the investigator was no longer at the institution and therefore not available for consultation.

The Trident® Hemispherical Acetabular Shell is one of the earlier Stryker acetabular devices upon which the design of the Tritanium® Acetabular Shell is based. The Exeter® + Crossfire™ US Outcomes Study is a prospective, consecutive series of primary THRs of Exeter® Femoral Stems with Orthinox® Femoral Heads and is a source of clinical data on the performance of the Trident® Hemispherical Acetabular Shell. Subjects participating in this study were implanted with a cemented Exeter® Femoral Stem and an Orthinox® Femoral Head, in combination with a cementless **Trident® Hemispherical Acetabular Shell** (a.k.a. Trident® AD Acetabular Shell, product family 540-01-XXX) and a Crossfire™ polyethylene insert. Enrollment took place at two sites in the United States and is closed with a total of 147 cases. To date, there have been three reported acetabular revisions and one report of acetabular loosening. Two of the acetabular revisions were secondary to infection and one was secondary to recurrent dislocation. Mean follow-up is 4.9 years.

A review of the data collected suggests that the Trident® Tritanium® Acetabular Shell and the Trident® AD Acetabular Shell have performed appropriately for their intended use and present no new risks.

Mid-term clinical and radiographic outcomes have been reported for a competitive product (Trabecular Metal™ Monoblock Acetabular Component System; Zimmer® Inc, Warsaw, IN) of similar design to the subject device.[12] In a prospective study, 156 primary THAs in 143 patients were followed for a minimum of 8 years (maximum of 10 years). The average HHS improved from 44.0 $\pm$ 13.8 (4-86.75) preoperatively to 97.0 $\pm$ 6.2 (58.85-100) at the latest follow-up evaluation. Three revisions were reported during the follow-up period; one acetabular component was revised for repeated dislocation and two were revised due to late hematogenous infection. All retrieved components were stable at the time of removal.

This clinical study is necessary to compare the success of the Tritanium® Acetabular Shell to the reported success of products of similar design. The objective of the study is to show that the study device performs no worse than similar devices at 5 years postoperative with

extended follow-up to 10 years. The study also provides a unique opportunity to collect longitudinal data on the performance of the new MDM™ liner.

The MDM™ liner is a highly polished cobalt chrome liner that utilizes a Trident® locking mechanism to create a dual mobility bearing when coupled with the Tritanium® acetabular cup system, a ADM/MDM™ X3® polyethylene head/insert and a 22.2 mm or 28 mm femoral head.

The concept of dual mobility was first defined by Professor Gilles Bousquet in 1976. This concept combines the advantages of Charnley's low friction arthroplasty principle and the McKee theory of using a large femoral head to maximize stability.[12] The modular dual mobility (MDM™) liner locks into the Tritanium® acetabular shell using the Trident® locking mechanism allowing for the use of the ADM/MDM™ X3® polyethylene insert and femoral head to create the dual mobility system. The polyethylene insert freely rotates within the MDM™ liner as well as positively captures a prosthetic femoral head. Thus, there are two distinct points of articulation in which range of motion (ROM) is accommodated.

The MDM™ liner introduces the concept of dual articulation to existing, non-dual mobility acetabular shells. Acetabular shell options are important in order to intraoperatively address varying bone densities. The MDM™ liner, coupled with acetabular shells designed with the Trident® locking mechanism, such as the Tritanium® Acetabular Shell, combines the advanced fixation technology of Tritanium® with the large diameter X3® mobile bearing articulation to achieve initial and long-term stability and preserve ROM. By offering this unique combination of benefits, the pairing of Tritanium® technologies with the MDM™ provides surgeons with options to treat a wide variety of patients.

While the MDM™ liner allows for the introduction of dual mobility in various acetabular shell options it is the polyethylene insert which helps accommodate a larger femoral head. X3® ultra high molecular weight polyethylene (UHMWPE) is a highly cross-linked polyethylene manufactured through a proprietary process to maintain mechanical strength, crystallinity, density and stabilize free radicals. X3® UHMWPE was designed to reduce the wear characteristics of conventional UHMWPE. Large diameter femoral head sizes have become more common as surgeons are looking for additional product solutions to help increase patient ROM and stability.

1.2 Investigational Device

The Tritanium® Acetabular Shell, cleared for use under FDA 510(k) K081171, is a hemispherical acetabular shell with a 3D surface for biological fixation, fabricated from CP Ti. The shell is built upon the design features and clinical history of the existing Trident® Tritanium®, Trident® AD, and Trident® HA hemispherical acetabular shells. The device is designed with a roughened surface and high coefficient of friction to resist micromotion and promote initial fixation. The Tritanium® Acetabular Shell, intended for use in a cementless application, is available in sizes from 44 mm through 66 mm and is compatible with Trident® polyethylene liners and acetabular screws. This advanced technology is designed to address the need for improved initial and biological fixation. Data in support of these marketing claims will be collected in the Tritanium® Primary Acetabular Shell Study.

1.3 Preclinical Data

The following articles have been published on preclinical studies of the Tritanium® technology:

1. Frenkel SR, Jaffe WL, Dimaano F, Iesaka K, Hua T. (2004). **Bone response to a novel highly porous surface in a canine implantable chamber.** *J Biomed Mater Res B Appl Biomater.,71(2),* 387-91.

   This study examined the canine *in vivo* bone response to six test surfaces at 6 and 12 weeks after implantation. The surfaces tested were A) titanium (Ti) beads, B) Ti beads with PA, C) Cobalt chrome (CoCr) beads, D) CoCr beads with PA, E) Tritanium®, and F) Tritanium® with PA. Bone penetration into the test surfaces was shown to increase significantly between 6 and 12 weeks for both the coated and uncoated Tritanium®; bone penetration for both Tritanium® surfaces was significantly greater than for all other test surfaces at 12 weeks. Mechanically, the failure strength of the surface-to-bone attachment again increased significantly between 6 and 12 weeks for both Tritanium® surfaces, and was significantly greater than that of all other test surfaces at the 12-week time point.
2. Higuera CA, Inoue N, Lim JS, Zhang R, Dimaano N, Frassica FJ, Chao EY. (2005).**Tendon reattachment to a metallic implant using an allogenic bone plate augmented with rhOP-1 vs. autogenous cancellous bone and marrow in a canine model.** J Orthop Res.,*23(5),* 1091-9.

In this study, the supraspinous tendon was reattached unilaterally to a modified Enhanced Tendon Anchor (ETA) implant with a Tritanium® surface in two canine groups. Allogenic bone plates saturated with rhOP-1-collagen putty were used in the first group (OP); plates saturated with autogenous cancellous bone and marrow were used in the second group (BM). At 15 weeks, gait analysis showed 78% and 81% recovery of preoperative weight-bearing in the OP and BM groups, respectively. The ultimate tensile strength of the reattachment was 24% and 38% of the intact contralateral side in the OP and BM groups, respectively; the difference between the two was not significant. There was evidence of tendon-bone insertion transitional zones, tissue ingrowth and adhesion to the metallic surface in both groups.

3. Zhang R, Brown PR, Dimaano N, Hawkins M. (2003). **Enhancement of bone ingrowth with a titanium foam surface in a canine intramedullary rod model.** *Trans Soc for Biomat.,* 327.

   Intramedullary rods of Ti alloy were coated with CP Titanium as either a foam or a double layer of beads. These rods were inserted into the canine femoral intramedullary cavity through the osteotomy of the greater trochanter and harvested femurs were examined at 4 and 16 weeks. At 4 weeks, the median average depth of bone ingrowth in the Ti foam coating was 82%, compared to 35% for the Ti beads. At 16 weeks, the depths were measured at 81% and 51% for the foam and beads, respectively. The bone ingrowth in the Ti foam dramatically increased (15% to 80%) from 4 weeks to 16 weeks postoperatively, and was significantly higher than ingrowth into the Ti beads (37%) at 16 weeks.

4. Bobyn JD, Toh KK, Hacking SA, Tanzer M, Krygier JJ. (1999). **Tissue response to porous tantalum acetabular cups: a canine model.** *J Arthroplasty, 14(3),* 347-54.

   A total of 22 porous tantalum acetabular cups were implanted without cement in 11 dogs and studied for 6 months. Stable bone-implant interfaces were seen in all cases upon histological, radiographic and scanning electron microscopic evaluation. The depth of bone ingrowth varied from 0.2 mm to 2 mm (maximum achievable in this implant design). Mean bone ingrowth was 16.8% $\pm$ 5.7%; in peripheral regions of the cup where bone-implant contact was most consistent, this increased to 25.1% $\pm$ 10.1%.

Table 2. Bench Tests Conducted on the Tritanium® Acetabular Shell

Description of the test	Report ID
Evaluation of Bone Response to Porous Surfaces Using a Canine Total Hip Model	RD-08-009
Particle Sintered Foam (PSF) - The Morphological, Metallurgical, and Chemical Properties of the Coating and Substrate Matrices	RD-08-010
Particle Sintered Foam (PSF) - A Mechanical Characterization of the Coating System and the Underlying Substrate	RD-08-016
Evaluation of Press Fit Stability of Tritanium® PSF Acetabular Shells with PA coating	RD-09-021
In-vitro and In-vivo Biological Evaluation of Particle Sintered Titanium Foam	RD-05-033
Evaluation of Deformation of Tritanium® PSF Shells for Ease of Liner Assembly	RD-08-046
Evaluation of Press Fit Stability of Tritanium® PSF Acetabular Shells	RD-08-049
Evaluation of Fatigue Strength of Tritanium® Ingrowth Hemispherical Acetabular Shell.	RD-08-092

Copies of all test reports are available at Stryker Orthopaedics.

1.4 Clinical Data to Date

Solid back and cluster hole versions of the Tritanium® Acetabular Shell are currently available in the United States. This study is the first prospective data collection on both versions of the device.

2 Study Objectives

2.1 Efficacy

2.1.1 Primary

The primary objective of this study will be to evaluate the success rate of cementless primary THR in hips implanted with the Tritanium® Acetabular Shell, as compared to the published results of similar acetabular components. Success will be defined as absence of acetabular shell revision for any reason at 5 years postoperative. It is expected that the survivorship of the Tritanium® Acetabular Shell group will be non-inferior to the survivorship reported in the literature for similar competitive devices.

2.1.2 Secondary

Usage of bone screw fixation will be recorded and compared between the Tritanium® Acetabular Shell group and the Trident® HA Hemispherical Shell group (Trident® X3® Polyethylene Insert Study).

Additionally, pain, function and health-related QOL data for the Tritanium® Acetabular Shell group will be collected at postoperative time points and compared with the subjects' preoperative status, as well as with the historical control group and with published literature for similar highly porous acetabular shells. It is expected that the HHS, SF-12 and LEAS outcomes in the study group will be comparable to the historical control. It is expected that the EQ-5D outcomes in the study group will be comparable to published results for similar devices.

Lastly, radiographic stability and complications between those implanted with the Tritanium® Acetabular Shell and the historical control group will be reviewed.

Clinical Outcomes:

Clinical outcomes will be evaluated via the total HHS, including pain, motion and function, preoperatively and at the 6-week, 1, 3, and 5-year visits. Additional HHS data will be obtained at the 7-year and 10-year time points at investigational sites that choose to bring their subjects back in for these optional visits.

Patient Outcomes:

Pain, function and health related quality of life (QOL) will be compared between the Tritanium® Acetabular Shell combined group, the literature and the above-referenced historical control group. The SF-12 is a 12 item patient self-assessment evaluating health and general wellbeing. The LEAS is a tool that has been developed and validated to evaluate the level of patient activity. The EQ-5D is a standardized instrument for use as a measure of health outcome. These tools will be used to assess patient health-related QOL and will be collected preoperatively at the 6-week, 1, 2, 3, 4 and 5-year visits. Patient outcomes data will also be obtained at the 7-year and 10-year time points at investigational sites that choose to bring their subjects back in for these optional visits, in addition to the required Follow-Up Questionnaire described below.

A Follow-Up Questionnaire will be administered annually in postoperative years 6-10 to assess patient satisfaction and pain, and to capture adverse events. This questionnaire will provide the survivorship information necessary to evaluate the primary objective of the study.

Radiographic Outcomes:

To assess radiographic stability as compared with the historical control, radiographs will be taken and collected in the AP pelvis, AP hip and lateral views for the preoperative, 6-week, 1, 3 and 5-year intervals. Additional radiographs will be obtained at the 7-year and 10-year time points at investigational sites that choose to bring their subjects back in for these optional visits.

The AP pelvis and AP hip views allow for observation of any conditions involving the sacral wings, iliac bones, ischium, pubis as well as the femoral head and neck. The lateral view allows for evaluation of the entire hip joint as well as the femoral head, neck and proximal shaft.[13] Suggested radiographic technique for the views required is included in Appendix A.

Radiographs will be evaluated by an independent reviewer throughout the course of the study. Radiographic analysis of the acetabular component will employ three zones

(Zone 1 – Zone 3) in the AP views.[14,15] Numerous parameters will be reviewed by zone, including radiolucency and migration. Radiolucency in at least 50% of a zone and measuring at least 1 mm in width is defined as radiolucency present. Cases that present with migration of greater than 5 mm in any direction or at least 2 mm radiolucency in all zones will be considered radiographic failures.

2.2 Safety

All operative site events as well as all serious adverse events (SAEs), excluding elective procedures, will be collected and compared to the historical control group and to published data. It is expected that the AE rates reported for hips implanted with the Tritanium® Acetabular Shell will be comparable to those reported in the literature for similar porous coated cementless acetabular shells and for the historical control group. Details regarding AE definitions, recording and reporting are in Section 8 of this protocol, Adverse Events.

3 Clinical Study Plan

3.1 Study Design

A prospective, post-market, multi-center design will be employed. Radiographs will be assessed by an independent reviewer.

3.2 Number of Centers

Cases will be enrolled at 7 to 12 centers. The enrollment goal ranges from 20 to 34 cases implanted with the Tritanium® Acetabular Shell per center. The enrollment goal range is dependent upon the number of participating centers as well as the relative rates of enrollment of the two treatment groups. Although a range is presented, there is no maximum limit to the number of cases that a center may enroll. In the event that a center far exceeds the overall enrollment goal or enrollment into one of the treatment groups is completed, Stryker may ask the center to cease enrollment so as not to skew the data. All participating centers will comply with the federal regulations regarding patient informed consent and IRB approval. Non-compliance of a study center may result in termination of the center's participation in the study.

3.3 Number of Subjects

Cases will be enrolled in this study until a total of 240 receive the Tritanium® Acetabular Shell. Half of these cases will use the X3® polyethylene insert alone as the bearing surface; the other half will use the MDM™ liner coupled with a compatible ADM/MDM™ X3® insert as the bearing surface. These treatment groups will not be separated into arms; instead, investigators will use their clinical judgement in determining the appropriate bearing for each case. If enrollment in one of the treatment groups begins to outpace that of the other, centers may be asked to enroll only those cases that are candidates for the bearing surface for which enrollment is lagging. Following this plan, cases will not be artificially placed into a treatment group to which they may not be best suited on the basis of the timing of their enrollment; consequently, there will be fewer opportunities for protocol deviations with regard to treatment.

Only the following ancillary devices may be used according to this study protocol:

- Stryker X3® polyethylene inserts (120 cases)
- Stryker MDM™ liners with ADM/MDM™ X3® polyethylene inserts (120 cases)
- Stryker LFIT™ CoCr heads or BIOLOX *delta* or alumina ceramic heads (in cases where the MDM™ liner is used, only 22.2 mm and 28 mm heads are permissible)
- Stryker Universal Adapter Sleeves (for use with BIOLOX *delta* universal ceramic heads)
- Compatible Stryker femoral stems
- Stryker Orthopaedics Torx Bone Screws

The Tritanium® Acetabular Shell is described in detail in Section 6 of this protocol, Device Description.

3.4 Estimated Study Duration

The enrollment period is estimated to be a maximum of 18 to 24 months; cases will be evaluated as per the evaluation schedule until each case reaches 10 years.

4 Eligibility

The following criteria will be used to distinguish patients eligible for enrollment into this study.

4.1 Inclusion Criteria

A. Patient has signed an IRB approved, study specific Informed Patient Consent Form.
B. Patient is a male or non-pregnant female age 18 years or older at time of study device implantation.
C. Patient has primary diagnosis of Non-Inflammatory Degenerative Joint Disease (NIDJD).
D. Patient is a candidate for a primary cementless total hip replacement.
E. Patient is willing and able to comply with postoperative scheduled clinical and radiographic evaluations and rehabilitation.

4.2 *Exclusion Criteria*

F. Patient has a Body Mass Index (BMI) ≥ 40.
G. Patient has an active or suspected latent infection in or about the affected hip joint at time of study device implantation.
H. Patient has a neuromuscular or neurosensory deficiency, which limits the ability to evaluate the safety and efficacy of the device.
I. Patient is diagnosed with a systemic disease (e.g. Lupus Erythematosus) or a metabolic disorder (e.g. Paget's disease) leading to progressive bone deterioration.
J. Patient is immunologically suppressed or receiving steroids in excess of normal physiological requirements (e.g. > 30 days).
K. Patient requires revision surgery of a previously implanted total hip replacement or hip fusion to the affected joint.
L. Patient has a known sensitivity to device materials.
M. Patient is a prisoner.

5 Subject Enrollment

5.1 Treatment Assignment

All subjects will receive the Tritanium® Acetabular Shell. Half of the cases will use the X3® polyethylene insert alone as the bearing surface; the other half will use the MDM™ liner coupled with a compatible ADM/MDM™ X3® insert as the bearing surface. Treatment assignment will be made based upon the clinical judgment of each investigator and enrollment into each treatment group will be monitored by Stryker to ensure equal distribution between the two groups.

5.2 Randomization

The study will enroll under a non-randomized study design.

6 Device Description

6.1 Study Device

The Tritanium® Acetabular Shell has been cleared for use in the United States; therefore, this study is considered a post-market assessment. All cases in this study will receive the Tritanium® Acetabular Shell. Half of the cases will use the X3® polyethylene insert alone as the bearing surface; the other half will use the MDM™ liner coupled with a compatible ADM/MDM™ X3® insert as the bearing surface. Only the following **Stryker compatible** ancillary devices may be used, according to this study protocol:

- Stryker X3® polyethylene inserts (120 cases)
- Stryker MDM™ liners with ADM/MDM™ X3® polyethylene inserts (120 cases)
- Stryker LFIT™ CoCr heads or BIOLOX *delta* and alumina ceramic heads (in cases where the MDM™ liner is used, only 22.2 mm and 28 mm heads are permissible)
- Stryker Universal Adapter Sleeves (for use with BIOLOX *delta* universal ceramic heads)
- Compatible Stryker femoral stems
- Stryker Orthopaedics Torx Bone Screws

Device Description:

The Tritanium® Acetabular Shell consists of a porous coated hemispherical cup available in solid back and cluster-hole designs, and is similar to other acetabular shells currently distributed. It is intended for cementless application and is designed for use with currently available Stryker MDM™ liners and polyethylene inserts. A description of the Tritanium® Acetabular Shell and compatible liner/insert/head combinations follows. Appendix B gives an overview of all protocol-specified components.

The X3® Polyethylene Insert is the next generation of highly cross-linked UHMWPE with excellent mechanical and fatigue properties. X3® polyethylene is a highly cross-linked polyethylene manufactured through a proprietary, step-wise sequential irradiation and annealing process through which the polyethylene receives 30 kiloGrays of gamma radiation and is then annealed below melting point to promote cross-linking. This highly cross-linked polyethylene has shown reduction in polyethylene wear with approximately the same mechanical properties of standard polyethylene.

The Modular Dual Mobility (MDM™) liner, cleared for use under FDA 510(k) K103233, features a highly polished cobalt chrome (CoCr) liner with a Trident® locking mechanism which will allow for compatibility with the Tritanium® acetabular cup system. The X3® polyethylene insert will articulate within the inner surface of the highly polished cobalt chrome liner. The polyethylene insert and 22.2 mm or 28 mm femoral head will combine to create the dual mobility bearing. The MDM™liner is available in sizes from 36 mm through 58 mm and is compatible with ADM/MDM™ X3® Inserts. The MDM™ system is designed to provide stability through the use of large diameter dual mobility liners and advanced fixation through the use of ancillary fixation and Tritanium® acetabular shells.

Tritanium® Acetabular Shell:

The catalog numbers for the Tritanium® Acetabular Shell permissible according to this study protocol will be in the following format, where 'XXX' varies by size:

500-03-XXX (solid back)
502-03-XXX (cluster hole)

X3® Polyethylene insert:

The catalog numbers for the X3® polyethylene inserts permissible according to this study protocol will be in the following format, where 'XXX' varies by size:

623-00-XXX (0°)

623-10-XXX (10°)

Table 3. Tritanium® Acetabular Shell/Liner/Head Compatibility

		Shell Size, Liner Alpha Code and Liner Thickness (mm)							
Tritanium® Acetabular Shell		**44**	**46**	**48**	**50, 52**	**54, 56**	**58, 60**	**62, 64**	**66**
X3® Liner Alpha Code		**A**	**B**	**C**	**D**	**E**	**F**	**G**	**H**
Anatomic Heads	44mm						3.8	5.4	7.1
	40mm					3.8	5.8	7.4	9.1
	36mm				3.9	5.9	7.9	9.4	11.2
Femoral Heads	32mm		3.9	4.9	5.9	7.9	9.9	11.4	13.2
	28mm	4.9	5.9	6.9	7.9	9.9	11.9	13.4	15.2
	26mm			7.9	8.9	10.9	12.9	14.4	16.2
	22mm	7.8	8.8	9.8	10.8	12.8	14.8	16.3	18.1

MDM™ Liner:

The catalog numbers for the MDM™ liner permissible according to this study protocol will be in the following format, where 'XXX' varies by size:

626-00-XXX

ADM/MDM™ X3® Polyethylene Insert:

The catalog numbers for the dual mobility polyethylene inserts permissible with the MDM™ Liner according to the study protocol will be in the following format, where 'XXX' varies by size:

1236-2-XXX

Table 4. MDM™ Liner/Insert/Head Compatibility Chart

MDM™ Liner	MDM™ Liner Trial	ADM/MDM™ X3® Insert	ADM/MDM™ Insert Trial	Required Femoral Head Size (mm)
626-00-36C	3200-36C	1236-2-242	1235-0-242	22.2mm
626-00-38D	3200-38D	1236-2-244	1235-0-244	22.2mm
626-00-42E	3200-42E	1236-2-848	1235-0-848	28mm
626-00-46F	3200-46F	1236-2-852	1235-0-852	28mm
626-00-48G	3200-48G	1236-2-854	1235-0-854	28mm
626-00-52H	3200-52H	1236-2-858	1235-0-858	28mm
626-00-54I	3200-54I	1236-2-860	1235-0-860	28mm
626-00-58J	3200-58J	1236-2-864	1235-0-864	28mm

Table 5. MDM™ Liner/Insert/Tritanium® Shell Compatibility Chart

Shell Size (mm), Liner Alpha Code						
Tritanium Hemispherical Shell	48	50,52	54,56	58,60	62,64	66
Liner Alpha Code	C	D	E	F	G	H
MDM CoCr Liner	36C	38D	42E	46F	48G	52H
Poly Insert OD (mm)	36	38	42	46	48	52
Poly Insert ID (mm)	22.2	22.2	28	28	28	28
Nominal Poly Thickness (mm)	6.7	7.7	6.8	8.8	9.8	11.8

Ancillary Devices:

Only compatible Stryker femoral stems, Stryker LFIT™ CoCr or BIOLOX *delta* or alumina ceramic heads, standard X3® inserts and MDM™ liners with ADM/MDM™ X3® inserts may be used as ancillary devices according to this study protocol.

The patented[a] sequential irradiation and annealing manufacturing process for X3® offers increased wear resistance[b] and virtually eliminates free radicals[c] while preserving mechanical properties[d,e,f,g]. X3® is irradiated by 3 MRads gamma radiation and annealed (heated below melting temperature) three times for a total cumulative dose of 9 MRads.

6.2 Device Retrieval Process

Stryker Orthopaedics will retrieve any Stryker component removed along with adjacent tissues (if applicable) for analysis to help characterize potential device-related complications. In the event that any Stryker component is removed from a study subject, the outlined procedure should be followed.

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[a] U.S. Patent # 6,174,934 6,372,814 6,664,308 6,818,020 7,517,919

[b] Stryker Orthopaedics Trident Acetabular Inserts made of X3 UHMWPE (unsterilized), 721-00-32E, show a 97% reduction in volumetric wear rate versus the same insert fabricated from N 2 \Vac gamma sterilized UHMWPE, 620-00-32E. The insert tested was 7.5 mm thick with an inner diameter of 32 mm. Testing was conducted under multi-axial hip joint simulation for 5 million cycles using a 32 mm CoCr articulating counterface and calf serum lubricant. X3 UHMWPE Trident acetabular inserts showed a net weight gain due to fluid absorption phenomena but yielded a positive slope and wear rate in linear regression analysis. Volumetric wear rates were 46.39 ± 11.42 mm^3 /10^6 cycles for N2 \Vac gamma sterilized UHMWPE inserts and 1.35 ± 0.68 mm^3 /10^6 cycles for X3 UHMWPE (unsterilized) Trident Acetabular Inserts. Although in-vitro hip wear simulation methods have not been shown to quantitatively predict clinical wear performance, the current model has been able to reproduce correct wear resistance rankings for some materials with documented clinical results.[iv, v, vi]

[iv] Wang A, et al. Tribology International, Vol. 31, No. 1-3:17-33, 1998.
[v] Essner A. et al. 44th Annual Meeting, ORS, New Orleans, Mar. 16-19, 1998:774.
[vi] Essner A. et al. 47th Annual Meeting, ORS, San Francisco, Feb. 25-28, 2001:1007

[c] X3 UHMWPE virtually eliminates free radicals, as measured by Electron Spin Resonance (ESR). A very low (noise level, near instrument detection limit) concentration of residual free radicals was detected in the X3 UHMWPE. A 99% reduction of free radicals (14 ± 2 x 10^{14} spins/gram versus 1550 ± 32 x 10^{14} spins/gram) was found when compared to N2Vac gamma sterilized UHMWPE.

[d] X3 UHMWPE maintains mechanical properties after accelerated oxidative aging. No statistical difference was found for Tensile Yield Strength, Ultimate Tensile Strength and Elongation as measured per ASTM D638 before and after exposure to ASTM F2003 accelerated aging (5 Atmospheres (ATM) of oxygen at 70ºC for 14 days). Tensile Yield Strength was 23.5 ± 0.3 MPa and 23.6 ± 0.2 MPa, Ultimate Tensile Strength was 56.7 ± 2.1 MPa and 56.3 ± 2.3 MPa and Elongation was 267 ± 7% and 266 ± 9% before and after accelerated oxidative aging, respectively.

[e] X3 UHMWPE resists the effects of oxidation. No statistical difference was found for Tensile Yield Strength, Ultimate Tensile Strength, Elongation, Crystallinity and Density as measured per ASTM D638, D3417 and D1505 before and after ASTM F2003 accelerated aging (5 ATM of oxygen at 70°C for 14 days). Tensile Yield Strength was 23.5 ± 0.3 MPa and 23.6 ± 0.2 MPa, Ultimate Tensile Strength was 56.7 ± 2.1 MPa and 56.3 ± 2.3 MPa, Elongation was 267 ± 7% and 266 ± 9%, Crystallinity was 61.7 ± 0.6% and 61.0 ± 0.5%, and Density was 939.2 ± 0.1 kg/m3 and 939.2 ± 0.2 kg/m3 before and after accelerated oxidative aging, respectively.

[f] "Improved Strength of Cross-linked UHMWPE Without Compromising Oxidation/Fatigue Resistance and Wear", Yau SS; Wang A, Lovell T. 2007 Combined ORS Poster #496.

[g] "Wear, oxidation and mechanical properties of a sequentially irradiated and annealed UHMWPE in total joint replacement", A.Wang, H.Zeng, S-S Yau, A. Essner, M. Manley and J. Dumbleton, Journal of Physics, D:Appl: Phys 39 (2006).

1. When revision of a study subject is scheduled, the study coordinator (SC) should contact the Clinical Study Manager (CSM) or Clinical Study Associate (CSA) assigned to the project, as soon as possible.
2. The CSM or CSA will send a retrieval container to the SC.
3. After the device is explanted, the SC or an identified Stryker field representative will retrieve the device and place it in the retrieval container.
4. The SC, an identified field representative or the CSM/CSA will complete a Product Experience Report (PER).
5. If not completed by the CSM or CSA, the PER should be faxed to Stryker Product Surveillance at 201-831-6775, as well as to Stryker Clinical Research at 201-831-6454.
6. The PER should be attached to the retrieval container and sent to Product Surveillance. A de-identified operative report should be included, when available.
7. The CSM or CSA will follow up with Product Surveillance to obtain a PER number.
8. A summary of results will be provided to the investigator upon his/her request.

7 Evaluations

7.1 Preoperative Visit

During the preoperative visit, patients that are possible candidates for this study will be screened to determine if they meet the inclusion/exclusion criteria. If the patient is a candidate, the investigator will propose participation in the study to the patient, according to GCP guidelines. Patients must sign an IRB approved study consent form prior to participating in any study related activities. Consent must be obtained within four months of surgery.

Once the subject has been consented, preoperative data will be collected including: demographics, medical history, HHS, AP hip, AP pelvis and lateral radiographs, SF-12, LEAS and EQ-5D.

All preoperative data must be collected within 4 months of the scheduled date of surgery, with the exception of radiographs, acceptable within 1 year of the scheduled date of surgery. All information collected preoperatively will be used to quantify the sample population and compare postoperative progress.

7.2 Surgery

Surgical details will be collected from the operative notes and at the time of surgery.

7.3 6-week Visit

During the 6-week visit (± 2 weeks), the following evaluations will be collected: HHS, SF-12, LEAS, EQ-5D, AP hip, AP pelvis and lateral radiographs.

7.4 Annual Follow-up Visits

Clinical data will be collected via office visit by the investigator at the following annual postoperative intervals: 1-year, 3-year and 5-year. Tools for postoperative evaluation will be the HHS, AP hip, AP pelvis and lateral radiographs.

Patient outcomes data will also be collected via patient questionnaires. At each of the 1-year, 3-year and 5-year follow-up visits, the SF-12, LEAS and EQ-5D are required. These same questionnaires are also required at 2-year and 4-year intervals, and may be completed during an office visit or sent to the subject to be completed, initialed and dated and returned to the investigative site.

All clinical data, radiographs, and patient outcomes data must be collected within ± 2 months of the 1-year and 2-year anniversary dates. For remaining annual time points, the window expands to ± 3 months of the 3-year anniversary date and ± 4 months of the 4-year and 5-year anniversary dates.

The initial phase of the study will continue for 5 years after surgery and include collection of the previously described radiographs, HHS, and SF-12, LEAS and EQ-5D patient questionnaires. In the second phase of the study, all subjects will complete a brief satisfaction questionnaire annually at the 6-year, 7-year, 8-year, 9-year and 10-year follow-up intervals. This form may be completed by the SC during a patient telephone interview, or by the patient either at home or during a clinic visit. The questionnaire will be used to obtain the following information, at a minimum:

- Patient satisfaction with the hip replacement
- Presence of any pain in the study hip
- Any surgeries performed on the study hip

The questionnaire will also provide information on any revisions and enable calculation of the Kaplan-Meier survival curve necessary to meet the primary endpoint of the study.

Additionally, at investigational sites that choose to continue collecting clinical and radiographic data during the second phase of the study, subjects will be evaluated again at 7 and 10 years after surgery.

8 Adverse Events

8.1 Reporting of Adverse Events

The AE reporting requirements for this study are as follows:

- All AEs that meet the definition of serious, excluding elective procedures
- All AEs related to the operative site, regardless of seriousness

Elective procedures meeting the definition of an SAE do not need to be reported as AEs according to this study protocol. Examples of such elective procedures include, but **are not limited to**, the following commonly seen events:

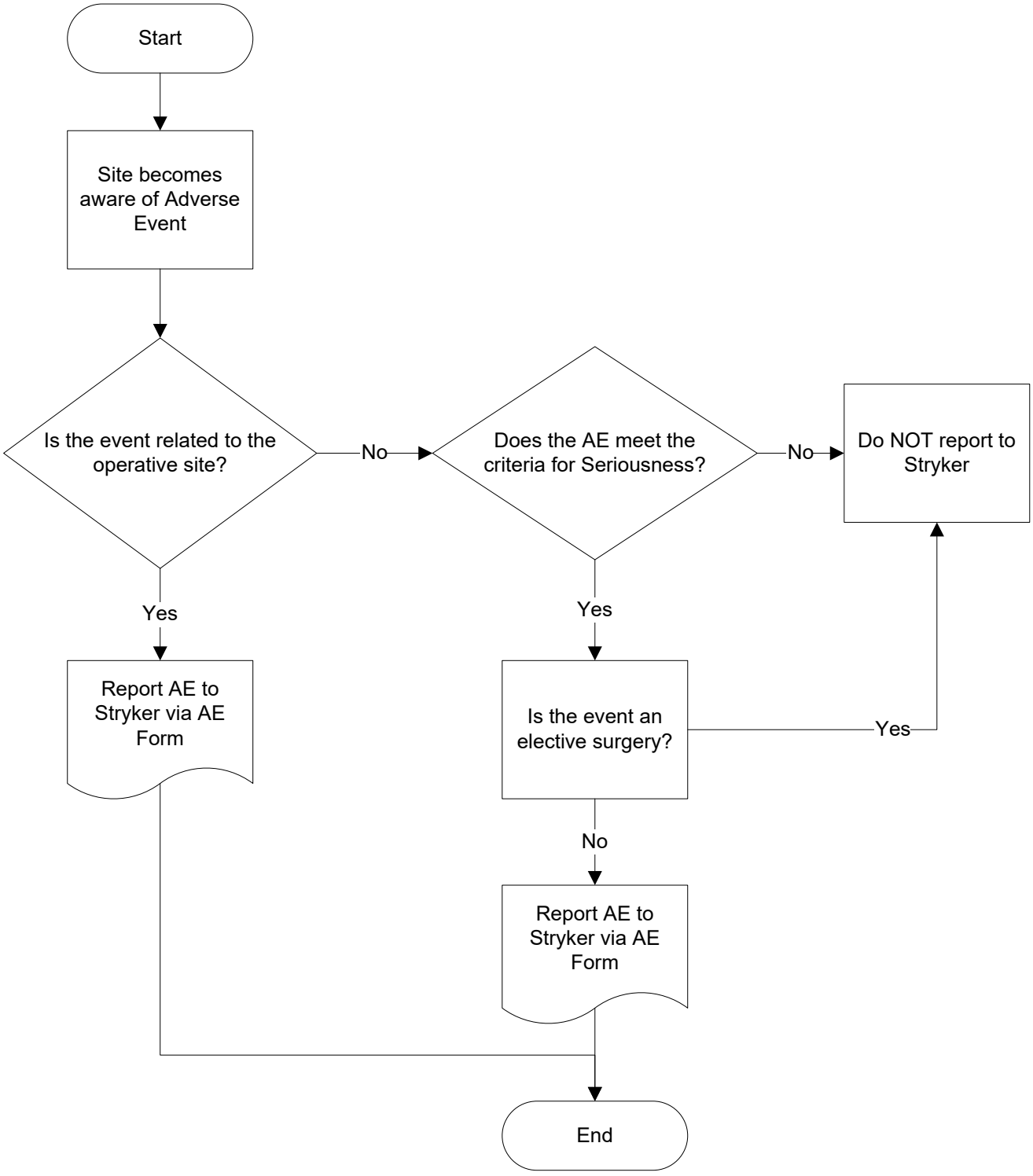
- Contralateral THR
- Total Knee Replacement
- Rotator Cuff Surgery
- Cataract Surgery

Such events will not be captured on the AE electronic Case Report Form (eCRF) but rather will be captured on the postoperative functional evaluation at the 6-week, 1-year, 3-year, and 5-year, time points. Additional events of this nature will be captured on the 7-year and 10-year functional evaluations if the investigator chooses to bring subjects in for these optional visits. On these functional evaluations, investigators and SCs will be prompted to question subjects as to whether they have seen a doctor for any reason, been hospitalized for any reason or have a current impediment to their function.

Additionally, SCs will be responsible for following up with the subjects regarding any questionable responses received on the satisfaction questionnaire administered in postoperative years 6 through 10. If it is determined upon this further investigation that a protocol-defined adverse event has occurred, the SC will be responsible for completing an AE eCRF and submitting the event to the sponsor, and reporting to the IRB as required.

The following decision tree facilitates identification of AEs for which reporting is required under this study protocol:

Figure 1
Adverse Event Decision Tree



General Physical Examination Findings

At screening for inclusion into the study, any clinically significant abnormality should be recorded as a preexisting condition and reported on the Demographics eCRF. From the time of consent

forward, any new clinically significant findings or abnormalities that meet the definition of a protocol defined AE must also be recorded and documented as an AE.

Adverse Event Reporting Period

The study period during which AEs must be reported is normally defined as the period from the initiation of any study procedures to the end of the study treatment follow-up. The start of study procedures is considered to be the point of consent. Any AEs which fit the protocol defined reportable events must be reported from the time of consent until study completion.

At each contact with the subject the investigator must seek information on AEs by specific questioning and, as appropriate, by examination. Information on protocol defined AEs should be recorded immediately in the source document and also in the appropriate AE module of the eCRF. All clearly related signs, symptoms and abnormal diagnostic procedure results should be recorded in the source document and grouped under one diagnosis as appropriate. The clinical course of each event should be followed until resolution or until it is determined at the end of the study that the AE will not resolve.

8.2 General Adverse Event Definitions

Following is a list of general AE definitions. For the purposes of this study, only SAEs, excluding elective procedures, as well as all AEs related to the operative site should be reported.

Adverse Event

An **AE** is any untoward medical occurrence in a clinical investigation subject, which changes the medical baseline of the subject. An AE can be an unfavorable and unintended sign, symptom or disease, whether or not related to the study device (AEs may also be referred to as complications). See Section 8.1, Reporting of Adverse Events, for the AE reporting requirements for this study.

Anticipated Adverse Event

An **anticipated AE** is an AE, of which the nature, severity or degree of incidence is known and identified in applicable product labeling, published literature or study protocol. The list of anticipated events is provided in Section 12, Risk/Benefit Assessment.

Serious Adverse Event

A **SAE** meets one or more of the following definitions:

- Resulted in in-patient hospitalization
- Resulted in prolonged existing hospitalization
- Resulted in persistent or significant disability/incapacity
- Resulted in permanent impairment of a body function or permanent damage to a body structure
- Necessitated medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure
- Was a life-threatening situation
- Resulted in patient death

Elective procedures meeting the definition of an SAE do not need to be reported as AEs according to this study protocol.

Adverse Device Effect

An **adverse device effect** (ADE) is a negative change in the subject's health that may have been caused by, or associated with, the use of the device.

Unanticipated Adverse Device Effect

An **unanticipated adverse device effect** (UADE) is any serious adverse effect on health, safety or any life-threatening problem or death caused by, or associated with, a device if that effect is a problem or death not previously identified in nature, severity or degree of incidence, or any other unanticipated serious problem associated with a device and related to the rights, safety or welfare of subjects.

8.3 Study Sponsor Notification by Investigator

Of reportable AEs, certain events must be submitted to Stryker within 24 hours for timely notification:

Adverse events that require time sensitive reporting:

An adverse event should be reported to the study sponsor (CSM or CSA) either by telephone/fax/email within 24 hours of the site's becoming aware of the event if any of the following apply:

- The AE is considered by the investigator to be device related or if the investigator is uncertain regarding the device related assessment;
- The AE required a reoperation of the study hip or a revision of any study hip components.

An AE eCRF must be completed by the investigator within 24 hours. If a SAE occurs, the de-identified source documentation must be uploaded to the Subject Binder of Stryker's Electronic Data Capture (EDC) system, within 24 hours of the investigative center's SAE awareness. See Section 11, Data Management, for additional details of Stryker's EDC system. These reports will be evaluated by Stryker to determine if a PER is required.

It is recommended that all other reportable adverse events are reported on eCRFs and submitted to Stryker within 2 weeks.

At the time of the initial report, the following information should be provided:

- Subject number
- A description of the event
- Date of onset
- Current status
- Whether study treatment was discontinued
- Investigator assessment of the association between the event and the study treatment

8.3.1 Ethics Committee/Institutional Review Board Notification by Investigator

Reports of AEs (including follow-up information) must be submitted to the Ethics Committee (EC) or Institutional Review Board (IRB) according to their specific requirements. Copies of each report and documentation of EC/IRB notification and receipt will be kept with the investigator's study files.

8.4 Recording of Adverse Events

All protocol defined AEs occurring during the study period must be recorded; this includes events that occur between visit intervals. The clinical course of each event should be followed until resolution or stabilization.

8.5 Medical Monitoring

It is the responsibility of the investigator to oversee the safety of the study at his/her center. This safety monitoring will include careful assessment and appropriate reporting of AEs, as previously noted. Stryker will conduct formal investigations via the Product Surveillance Department of those AEs which are submitted through our PER System.

9 Statistical Plan

9.1 Efficacy

9.1.1 Primary Efficacy Parameters

The primary efficacy parameter is acetabular component revision for any reason.

9.1.2 Secondary Efficacy Parameters

The secondary efficacy parameters include:

- The usage of screw fixation
- HHS at the 1-, 3- and 5-year follow-up visits
- SF-12 scores at the 1-, 3- and 5-year follow-up visits
- LEAS at the 1-, 3- and 5-year follow-up visits
- EQ-5D at the 1-, 2-, 3-, 4- and 5-year follow-up visits
- Follow-Up Questionnaire annually in postoperative years 6-10

9.1.3 Primary Efficacy Hypothesis

The null hypothesis, H_0, is that the success rate at 5 years postoperative is less than δ. The alternative hypothesis, H_a, is that the success rate at 5 years postoperative is greater than or equal to δ. When δ = 94%, the hypothesis is a test for non-inferiority. When δ=99%, the hypothesis is a test for superiority.

H_0: $p < \delta$

H_a: $p \geq \delta$

9.1.4 Primary Efficacy Analysis

A case success is defined as no incidence of revision or removal of the acetabular component within 5 years. A 90% confidence interval of the success rate will be computed at 5 years postoperative. If the lower bound of this confidence interval is greater than 94%, the non-inferiority hypothesis will be supported. If the lower bound of this confidence interval is above 99%, the superiority hypothesis will be supported. The Kaplan-Meier survival curve of revision or removal of the acetabular component will also be displayed using SAS/PROC LIFETEST.

9.1.5 Secondary Efficacy Analysis

A two-sided 0.05 alpha level will be used.

For comparison of usage of bone screw fixation between the Tritanium® Primary Acetabular Shell Study and the Trident® X3® Polyethylene Insert Study, a Chi-square test or Fisher's exact test will be used. If there are any statistically significant differences in baseline variables (e.g. age, gender, diagnosis) between the groups, they will be addressed as covariates and ANOVA or ANCOVA will be used.

For comparison of HHS, and SF-12 and LEAS at 1, 3 and 5 years postoperative between the Tritanium® Acetabular Shell and Trident® X3® Polyethylene Insert studies, a t-test or Wilcoxon test will be used. If there are any statistically significant differences in baseline variables (e.g. age, gender, diagnosis) between the groups, they will be addressed as covariates and ANOVA or ANCOVA will be used.

EQ-5D values and changes from baseline will be presented for each interval. Data from the Follow-Up Questionnaire will be used as an input to the Kaplan-Meier survival curve for postoperative years 6-10; any adverse events collected via the Follow-Up

Questionnaire will be reported on a separate Adverse Event eCRF and included in the safety analysis.

9.2 Safety Parameters

9.2.1 Safety Parameters

Safety parameters will include:

- All AEs reported
- Radiographic stability at each postoperative visit
- Revision or removal rates

9.2.2 Safety Analysis

All AEs will be listed, tabulated and summarized by event, number and percent of cases/subjects. AE rates and 95% confidence intervals will be presented.

For categorical variables, such as radiographic stability, the number and percent in each category will be presented.

9.3 Missing Data

No missing data will be imputed for the primary analysis and secondary analyses.

9.4 Statistical Methodology

9.4.1 Data Summary

The following is a detailed proposal of statistical analyses planned for data collected during the study.

Descriptive statistics will be computed for all preoperative conditions and demographic parameters. That is, for continuous data (e.g. HHS), the N, mean, median, standard deviation, minimum and maximum will be computed. For categorical data (e.g. gender), the frequency will be computed. If appropriate, the data will be presented by two cohorts in the Tritanium® Primary Acetabular Shell Study.

Descriptive statistics and statistical comparisons for important demographic, efficacy and safety variables will be provided in tables.

A survival analysis for revision of the acetabular component will be performed.

9.4.2 Sample Size Calculation

A literature review shows that at 5 years of follow-up there is a 97.9% to 99.6% success rate in similar devices using revision or removal of the acetabular component as the defining factor. Based on these results, it should be a reasonable assumption that the base success rate of revision or removal of the Tritanium® Acetabular Shell will be approximately 99% at 5 years. Using a base success rate of 99% from the literature and a delta of 5%, it was calculated that 142 total cases implanted with the Tritanium® Acetabular Shell would be needed to prove non-inferiority with 95% power. With a minimum of 142 cases analyzed, the primary hypothesis of the study will be met if the lower bound of the 90% confidence interval for the 5-year success rate is greater than 94%. By factoring in a 20% lost to follow-up rate within a 5-year period, the required sample size increases to 177 cases. Cases will continue to be enrolled until a total of 240 cases are implanted with the Tritanium® Acetabular Shell; half of these cases will use the X3® polyethylene insert alone as the bearing surface and the other half will use the MDM™ liner coupled with a compatible ADM/MDM™ X3® insert as the bearing surface.

9.4.3 Interim Analyses and early Stopping Considerations

No interim analysis is planned.

9.4.4 Efficacy Patient Populations

9.4.4.1 Efficacy

Per protocol population:

The study population for analysis will include all subjects who receive the Tritanium® Acetabular Shell. This does not include cases censored from analysis or cases that are unavailable for evaluation at the 5-year primary endpoint.

The primary and secondary efficacy analyses will be based on the per protocol population.

9.4.4.2 Safety

Safety Population:

The safety population will include all non-censored subjects who received the Tritanium® Acetabular Shell.

9.4.4.3 Survival Analysis

Modified intent to treat population:

Subjects enrolled in the study who received the Tritanium® Acetabular Shell will be included in the survival analysis.

9.4.4.4 Censored Cases

In the event that a protocol deviation occurs which could affect patient outcome, the data for the affected patient will be censored from the Efficacy and Safety Patient Populations. All cases that fall into this category will be reported separately.

10 Study Procedures

10.1 Subject Recruitment and Screening

Patients will be recruited at the study centers during preoperative visits through normal referral patterns. All patients recruited for this study will have the capacity to give informed consent. Advertising for the study at each center will be at the discretion of the investigator. See Appendix C for samples of study advertisements. All handouts, brochures, advertisements, etc. must be approved by the IRB prior to the dissemination of any recruitment materials to potential subjects.

10.2 Patient Informed Consent and Guidelines

All patients for this study will be provided a consent form describing this study and providing sufficient information for them to make an informed decision about their participation. The informed consent must contain all elements required by the FDA under 21 CFR Part 50, in addition to any other elements required by state, local and institutional policies. See Appendix D for a copy of the Model Informed Patient Consent. This consent form will be submitted with the protocol for review and approval by the IRB for the study. All patients must provide written consent after having had adequate time to consider their participation in the study. The formal consent of a

patient, using the IRB approved consent form, must be obtained before that patient is submitted to any protocol related procedures that are not part of normal care. Written documentation of consent must be provided on the consent's signature page in addition to a note in the patient medical records indicating the date that consent was obtained. The investigator-designated research professional obtaining the consent must also sign this consent form. The patient or their legal representative should receive a signed copy of the consent according to GCP guidelines.

The procedure for obtaining informed consent is outlined below:

- Use a current IRB approved copy of the consent form.
- Review the consent thoroughly with the patient before having them sign.
- After the patient has consented to the procedures, ensure he/she signs and dates the consent form.
- The person obtaining consent also signs and dates the signature page.
- Provide a copy of the consent to the patient.
- If required, provide the hospital with a copy of the signed consent.
- Maintain the signed original in the patient's study chart.

10.3 Early Withdrawal of Subjects

When and How to Withdraw Subjects

In the event that the subject is discontinued by the investigative center prior to the final study evaluation, the subject will be notified by the center that he/she is no longer in the study and a Study Termination eCRF will be completed.

The following is a list of reasons for which subjects may be withdrawn and the date of termination that should be used on the Study Termination eCRF in each situation. This list is not all inclusive:

Termination Reason	**Date of Termination**
Death	Date of death
Investigative center termination	Date of study close-out visit
Lost to follow-up	Date Stryker termination approval given
Voluntary withdrawal	Date subject notified center of withdrawal
Revision/removal of study device	Date of revision/removal procedure

Study device not implanted	Date of surgery
Surgery not performed	Date Stryker termination approval given

At the time of study surgery it is required that the following components are implanted:

- Tritanium® Acetabular Shell
- Stryker X3® polyethylene inserts (120 cases)
- Stryker MDM™ liners with ADM/MDM™ X3® polyethylene inserts (120 cases)
- Stryker LFIT™ CoCr heads, BIOLOX *delta* or alumina ceramic heads
- Stryker Universal Adapter Sleeves (for use with BIOLOX *delta* universal ceramic heads)
- Compatible Stryker femoral stems
- Stryker Orthopaedics Torx Bone Screws

Revision or removal of the Tritanium® Acetabular Shell constitutes a failure and study termination for the subject.

If MDM™ liner, acetabular insert (either X3® or ADM/MDM™ X3®) or femoral head exchange is required during the study, the event is considered a reoperation and does not constitute a failure or study termination.

If femoral stem revision is required during the study, the event is considered a reoperation and does not constitute a failure or study termination.

If the subject fails to return for his/her follow-up appointments, every effort should be made to contact the subject to assess his/her health status. If after attempting to contact the subject through three documented phone calls and a certified letter, the subject still does not respond, he/she will be considered lost to follow-up. A Study Termination eCRF will be completed **only after notifying Stryker of the subject's status** and **being given approval to terminate**.

In the event a subject does not have surgery, Stryker should be contacted to discuss if/when the surgery will be rescheduled. If the surgery is rescheduled more than 4 months from the date of preoperative data collection, the subject will need to be re-consented, all preoperative data will need to be re-collected and all original preoperative data will need to be removed from the database. If the surgery is not to be rescheduled or if the subject is no longer considered an

appropriate study candidate, a Study Termination eCRF may be completed **only after notifying Stryker of the subject's status** and **being given approval to terminate**.

When a subject completes the study according to protocol, including the final study evaluation, a Study Termination eCRF will be completed.

11 Data Management

11.1 Database

Data will be collected at each center and entered into Stryker's Electronic Data Capture (EDC) system. The system can be accessed remotely by each investigative center and the data entered will be managed by Stryker. Subject data will be processed and monitored according to the protocol schedule by Stryker or Stryker representatives. Draft specifications to support eCRFs are provided in Appendix E.

11.2 Confidentiality

This study will comply with the 2002 privacy rule of the Health Insurance Portability and Accountability Act (HIPAA). As such, Stryker will only collect that information which is necessary to support the objectives of the clinical study. Stryker will take precautions to ensure that data received is as de-identified as possible. In the case that some identified information is received, Stryker will ensure that any identifying information will not be reported. Study subjects will authorize Stryker to use their health information in support of the clinical study during the informed consent process. Should a subject choose to withdraw authorization, Stryker may use data collected prior to the withdrawal of authorization in order to maintain data integrity.

11.3 Source Documents

Source data is all information, original records of clinical findings, observations, or other activities in a clinical study necessary for the reconstruction and evaluation of the study. Source data are contained in source documents. Examples of these original documents and data records include: hospital records, clinical and office charts, study worksheets, laboratory notes, memoranda, subject questionnaires, pharmacy dispensing records, recorded data from automated instruments, radiographs, subject files, and records kept at the pharmacy, at the laboratories and at medico-technical departments involved in the clinical study.

All data points collected during follow-up visits must be documented in the subject's chart. This includes ROM values, pain and function as well as AEs and additional comments. The informed consent process should also be documented in the patient chart. Monitors, defined further in Section 13, will be comparing the eCRFs against source documents for adequacy. The monitors will seek to draw a reference between each data point on the eCRF and the subject's chart. Thus, one cannot derive pain, ROM or function based on a chart note that reads "Patient doing well." Every effort should be made to ensure complete source documentation.

Centers are required to create a source documentation plan including any applicable source documentation worksheets prior to enrollment.

11.4 Electronic Case Report Forms

The study eCRFs are the primary data collection instrument for the study. All data requested on the eCRF must be recorded. All missing data must be explained.

For specific instructions on eCRF completion, please consult the Guide to Case Report Forms provided under separate cover. It is recommended that eCRFs be completed, signed by the investigator and returned to Stryker within 2 weeks of the evaluation date.

11.5 Data Clarification Requests

If errors or omissions are noted by Stryker upon receipt of the eCRFs, a data clarification request (DCR) will be sent to the center for clarification. Queries should be answered in a clear and comprehensible manner. If the clarification requires a change to data captured on an eCRF, Stryker will modify the eCRF accordingly. Modified eCRFs need not be printed and included in conjunction to answered DCRs.

11.6 Protocol Deviations

Any deviation from this protocol will be reported to Stryker as well as to the EC/IRB according to their reporting procedures. Protocol Deviations for this study include, but are not limited to, the following:

- Informed consent deviations, including but not limited to:
    - Study procedures performed prior to informed consent
    - Incorrect informed consent version used
- Patient enrolled does not meet the inclusion/exclusion criteria
- Protocol specified study component(s) not implanted
- Visit deviations, including:
    - Unavailable primary endpoint

- One or more required eCRFs/radiographs not done
- Evaluations occurred outside of protocol specified time window
- Un-evaluable radiographs
- Missed visit

If the center anticipates a possible protocol deviation, the investigator or SC should contact Stryker for guidance.

11.7 Records Retention

It is the investigator's responsibility to retain study essential documents for 2 years after the date of the final report, or in the case of non-compliance, 2 years after the date of investigative center termination. These documents should be retained for a longer period if required by an agreement with Stryker.

12 Risk/Benefit Assessment

12.1 *Risk Category*

There are no additional risks associated with participating in this study over and above that of the primary THR procedure.

12.2 Potential Risk

The study involves the routine assessment of a primary THR procedure. The Tritanium® Acetabular Shell has been cleared for use by the FDA and will be used according to its labeling. Assessment involves questionnaires, patient and physician assessments, and routine radiographs. The information collected will be kept confidential and will comply with the HIPAA.

While the expected life of THR components is difficult to estimate, it is finite. These components are made of foreign materials, which are placed within the body for the potential restoration of mobility or reduction of pain. However, due to the many biological, mechanical and physiochemical factors which affect these devices but cannot be evaluated in vivo, the components cannot be expected to indefinitely withstand the activity level and loads of normal healthy bone.

Adverse effects associated with primary THR include the following:

Serious complications may be associated with any total joint replacement surgery. These complications include, but are not limited to: infection; genitourinary disorders; gastrointestinal disorders; vascular disorders, including thrombus; bronchopulmonary disorders, including emboli; myocardial infarction or death.

With all implanted devices, asymptomatic, localized progressive bone resorption (osteolysis) may occur around the prosthetic components as a consequence of foreign-body reaction to the particulate matter of metal, UHMWPE and/or ceramic. Particulate is generated by interaction between components as well as adhesion, abrasion and fatigue. Secondarily, particulates can also be generated by third body wear. Osteolysis can lead to future complications, including loosening, necessitating the removal and replacement of prosthetic components.

Early and late loosening of total hip components can occur. Early biomechanical 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.

Dislocation of the hip prosthesis can occur due to inappropriate patient activity, trauma or other biomechanical considerations.

Malseating of the acetabular liner can occur during surgery.

Peripheral neuropathies, circulatory compromise and heterotopic bone formation may occur.

Intraoperative fissure, fracture, or perforation of the femur, acetabulum or trochanter can occur due to impaction of the component into the prepared femoral canal or acetabulum. Postoperative femoral or acetabular fracture can occur due to trauma, the presence of defects or poor bone stock.

If bone screws are used, appropriate selection of bone screw length and location is essential to avoid damage to underlying soft tissue structures. Perforation of the pelvic wall can result in internal bleeding and possible damage to vital organs.

Metal sensitivity reactions have been reported following joint replacement.

AEs may necessitate reoperation, revision, arthrodesis of the involved joint, girdlestone or amputation of the limb.

12.3 *Expected Complications and Rates of Occurrences*

Complications associated with total hip arthroplasty procedures, such as those performed with the Tritanium® Acetabular Shell, have been reported. These include the potential for: injury to the hip's neurovascular structures, loosening of the components, malseating of the acetabular liner, heterotopic bone formation, infection, deep vein thrombosis, pulmonary embolism, metal sensitivity reactions, intraoperative or postoperative fracture of the femur or acetabulum, and the need for re-operation, revision, arthrodesis of the involved joint, girdlestone or amputation of the limb. The safety objective will compare the complication rates of the Tritanium® Acetabular Shell to published rates.

12.4 Protection Against Risks

Subjects will be treated in the best medical judgment of the investigator, regardless of the study protocol. If an investigator must deviate from the written protocol to protect the health or wellbeing of the subject, this deviation will be promptly reported to both the EC/IRB and Stryker.

12.5 *Potential Benefits to the Subject*

There is no guarantee that subjects will personally benefit from inclusion in this study. Subjects may undergo more thorough screening and follow-up than non-study patients and may benefit from this increased surveillance. This study seeks to provide clinicians information about this system/device by comparing this treatment/device to published results for other treatments/devices. Information gathered in this study may benefit others undergoing this procedure in the future.

13 Study Monitoring, Auditing, and Inspecting

13.1 Study Monitoring Plan

Monitors are persons employed by sponsors to review the conduct of clinical studies to assure that the clinical investigators abide by their obligations to conduct clinical studies properly. Proper monitoring ensures adequate protection of the rights of human subjects, the safety of subjects involved in a clinical investigation and the quality and integrity of data submitted as a result of the investigation.

This study will be monitored at least once per year, with additional visits as necessary. The investigator will allocate adequate time for such monitoring activities. The Investigator will also ensure that the monitor or other compliance or quality assurance reviewer is given access to all study-related documents and study-related facilities and has adequate space to conduct the monitoring visit. The monitor will review all source documents and compare them to the data contained in the eCRFs, in addition to performing a periodic review of regulatory documents such as EC/IRB approvals. The monitors will need the following when they visit:

- An area where they can review study data
- Subject binders
- Patient charts pulled at the center, or access to relevant electronic medical records
- Regulatory documents
- Time to meet with the SC and the Investigator

13.2 Auditing and Inspecting

A quality assurance audit is a form of review that provides additional confidence to the sponsor concerning the validity and accuracy of clinical study data that must be submitted to the FDA or for publication. The purpose of investigator audits is to ensure that the investigator has maintained all study information according to the sponsor's protocol and standard operating procedures and in compliance with FDA regulations.

The investigator will permit study-related monitoring, audits, and inspections by the EC/IRB, Stryker and/or government regulatory bodies of all study related documents (e.g. source documents, regulatory documents, data collection instruments, study data). The investigator will ensure the capability for inspections of applicable study-related facilities.

14 Ethical Considerations

This study is to be conducted according to United States standards of GCPs and applicable government regulations including 21 CFR Parts 50 and 56 as well as 45 CFR Parts 160 and 164.

This protocol and any amendments will be submitted to a properly constituted independent EC/IRB for formal approval of the study conduct. The decision of the EC/IRB concerning the

conduct of the study will be made in writing to the investigator and a copy of this decision will be provided to Stryker before commencement of this study. The investigator may be asked to provide a list of EC/IRB members and their affiliates to Stryker, if available.

All patients considered for this study will be provided a consent form describing this study and providing sufficient information for patients to make an informed decision about their participation. This consent form must be modified to contain center specific information and submitted with the protocol for review and approval by the EC/IRB for the study. The formal consent of a patient, using the IRB approved consent form, must be obtained before that patient is submitted to any study procedure. This consent form must be signed by the patient or legally acceptable surrogate and the investigator-designated research professional obtaining the consent.

15 Study Finances

15.1 Funding Source

This study is financed by Stryker Orthopaedics.

15.2 Conflict of Interest

Any investigator who has a conflict of interest with this study (e.g. patent ownership, royalties or financial gain greater than the maximum allowable by their institution) must have the conflict reviewed by their EC/IRB or a properly constituted Conflict of Interest Committee with a Committee-sanctioned conflict management plan that has been reviewed and approved by Stryker prior to participation in this study.

15.3 Subject Stipends or Payments

At pre-determined study visit intervals, Stryker may reimburse subjects with a modest stipend for protocol-required data collection. This stipend system and reimbursement amounts must be approved by the Institution's IRB prior to implementation.

Subject attrition can occur for a variety of reasons, including a subject's loss of health insurance coverage. In a case where a patient has lost health insurance coverage and no other coverage is available, Stryker may, on a case-by-case basis, reimburse investigators for office visits and radiographic charges for subjects involved in this study in order to facilitate data retrieval. The physician or the office staff should contact the CSM prior to scheduling the subject to discuss this possibility and receive pre-approval. After receipt of the completed data forms, the physician

must submit either evidence of coverage denial (e.g. explanation of benefits) or a letter explaining that the subject does not have insurance. Other visits, procedures and assessments done other than those specified in the protocol will not be reimbursed. Reimbursement may be provided under the following conditions:

- Study subjects lose insurance coverage after enrollment into the study
- An insurance carrier refuses to pay for a follow-up visit and/or radiographs
- An insurance carrier refuses to provide a subject referral to see the investigator for follow-up

Under extreme circumstances, and with prior approval, Stryker may reimburse a subject for the cost of transportation to and from the investigator's office for a protocol-required office visit.

This policy is the same for all participating study subjects and does not bias against any particular subject or study cohort.

16 Publication Plan

It is anticipated that publication of the multi-center study results will be compiled and submitted to a peer-reviewed journal at the time the study cohort reaches 3, 5 and 10 years of follow-up. Additional publication proposals may be made by investigators at any time and will be considered.

This study will utilize the guidelines for authorship published by the International Committee of Medical Journal Editors (ICMJE). This guidance can be referenced at www.icmje.org.

Publications will be facilitated by the Chair and the primary investigator (PI) of the study. Both individuals will be chosen by Stryker. The PI is solely focused on the multi-center publications and progress towards those publications, including recurring updates to centers, center motivation as well as authorship. If the PI does not produce a draft of a publication within 90 days of receiving the results data, Stryker will delegate the responsibility to other investigators in the study at its discretion. The Chair reviews all additional publications proposed by participating investigators based upon the study results prior to study completion, on an ongoing basis. This review includes whether or not a proposal will be pursued, as well as imposition of guidelines as to publication completion and criteria.

The following summarizes the possible roles of these parallel positions:

Chair	**PI**
Contributes to study design	Contributes to study design
Assists with study questions requiring expert clinical opinion	Assists with study questions requiring expert clinical opinion
Assists with identification of investigators	Assists with identification of investigators and maintains performance
Reviews additional publication proposals submitted by investigators	Updates investigators on progress towards multi-center results
Contributing author, if ICMJE guidelines met	Primary author, multi-center publication of primary endpoint data

At the completion of the study, each participating study investigator shall have independent publication privileges for his/her own center's results. These manuscripts and abstracts will be delayed until after the 3, 5 and 10-year multi-center publications are submitted. All publications of the data shall be submitted to Stryker for review prior to submission for publication. Stryker shall not edit or otherwise influence the publications other than to ensure that confidential information is not disclosed, that no off-label use of Stryker devices is promoted, and that the data is accurately represented. Any publications resulting from this study must be submitted to Stryker for review at least 60 days prior to submission of publication.

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Appendix A

Suggested Radiographic Technique

Suggested Radiographic Technique[i]

The following views are required preoperatively and at each postoperative interval specified according to the evaluation schedule to enable evaluation of the implant-bone interface.

- AP pelvis
- AP femur
- Lateral femur

General Requirements

A. Appropriate corrections in radiological exposure setting are needed for obese subjects.
B. At least a 14"x17" sized film should be used.
C. If the subject is **bilateral** and a view showing both hips is submitted, **two copies of that view are required**.
D. Both digital and film radiographs are acceptable. **Digital films must be in uncompressed DICOM format.**
E. Each image must have:
    a. Subject's identification number
    b. Subject's initials
    c. Date of radiograph
    d. Indication of operative side in the study
    e. Markers for right and left sides, as applicable
    f. Visit interval

AP Pelvis

If the subject is bilateral, two copies of the AP pelvis radiograph are needed.

A. Standard technique
    a. 100 cm tube to film distance.
    b. The subject should be supine with his/her sacrum flat against the table and legs in full extension, internally rotated 15°, compensating for the normal anteversion of the femoral neck.
    c. The x-ray beam should be directed perpendicular to the film cassette and must be centered on the pubic ramus.

d. The iliac bones, sacrum, pubis, ischium, femoral heads, femoral necks and both the greater and lesser trochanter must be visible on film as shown below.

Refer to Figure 1 for an acceptable AP pelvis radiograph.

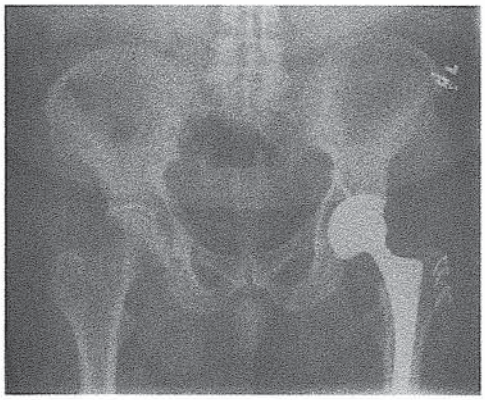

Figure 1. AP Pelvis View – Acceptable

AP Femur

A. Standard technique
   a. The subject should be supine with his/her sacrum flat against the table and legs in full extension, internally rotated 15°.
   b. The film cassette should be placed immediately below the table, parallel to the subject's frontal plane.
   c. The x-ray beam should be directed perpendicular to the film cassette and should be centered toward the center of the involved femoral head.

Refer to Figure 2 for an acceptable AP femur radiograph.

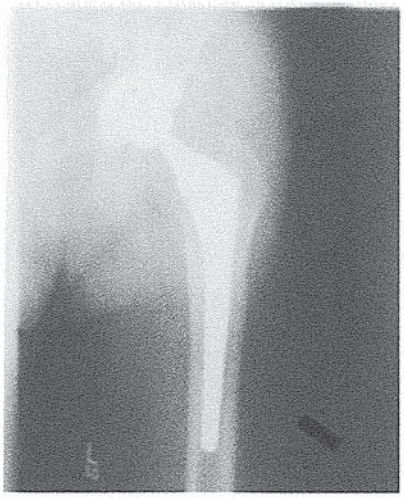

Figure 2. AP Femur View – Acceptable

Refer to Figure 3 for AP subject positioning.

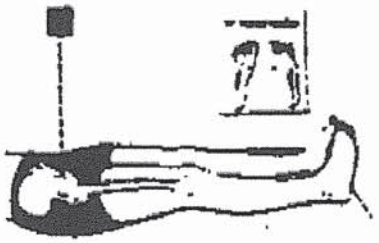

Figure 3. AP Positioning

Lateral Femur[ii,iii]

A. Standard technique
    a. The subject should be supine with the involved leg flat against the table.
    b. The knee of the involved leg should be flexed 90° and the thigh drawn up to at least a 45° angle.
    c. The x-ray beam should be directed over the lesser trochanter, perpendicular to the proximal femur.
    d. The entire hip joint must be visible.

Refer to Figure 3 for an acceptable lateral radiograph.

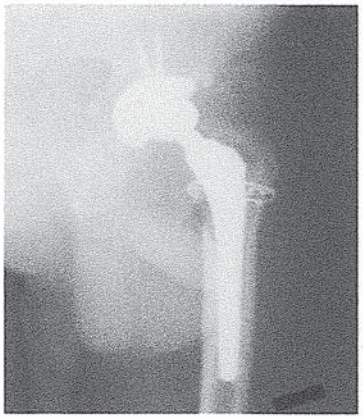

Figure 3. Lateral View – <u>Acceptable</u>

Refer to Figure 4 for subject positioning.

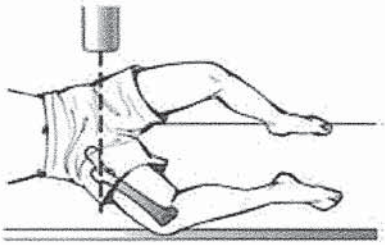

Figure 4. Lateral Positioning

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Appendix B

Component List

Tritanium® Acetabular Shell
Protocol-Specified Component List

Catalog Number	Description
Tritanium® Hemispherical Solid Back Shell	
500-03-44A	44mm
500-03-46B	46mm
500-03-48C	48mm
500-03-50D	50mm
500-03-52D	52mm
500-03-54E	54mm
500-03-56E	56mm
500-03-58F	58mm
500-03-60F	60mm
500-03-62G	62mm
500-03-64G	64mm
500-03-66H	66mm
Tritanium® Cluster Hole Shell	
502-03-44A	44mm
502-03-46B	46mm
502-03-48C	48mm
502-03-50D	50mm
502-03-52D	52mm
502-03-54E	54mm
502-03-56E	56mm
502-03-58F	58mm
502-03-60F	60mm
502-03-62G	62mm
502-03-64G	64mm
502-03-66H	66mm

Appendix C

Study Advertisements

Clinical Trial with Tritanium® Acetabular Shell

Dr. (name) of (practice) is participating in a clinical study evaluating a new primary hip replacement for cementless use in patients who are eligible for a primary total hip replacement.

The **Tritanium® Acetabular Shell** is a hemispherical shell that will be used to replace the surface of your natural hip socket. This shell features a three dimensional commercially pure Titanium foam coating to enhance initial fixation and long-term stability.[1,2] The **Tritanium® Acetabular Shell** is intended for cementless, press-fit use. It is compatible with other Stryker components as well. This system is currently being sold throughout the world and is implanted in patients who need primary hip surgery.

Dr. (name) is one of 7 to 12 surgeons nationwide selected to enroll qualifying patients into this clinical study. The data collected will be used to evaluate both short and long-term (10-year) performance of the components following surgery.

The study includes males and non-pregnant females 18 years of age or older. These patients must be candidates for a primary hip replacement. These patients must also be able to comply with requirements following surgery including weight bearing restrictions and self-evaluation questionnaires. Enrolled patients will be required to come in for an evaluation before surgery and at 6 weeks, 1 year, 3 years and 5 years after surgery. X-rays will be taken at these follow-up evaluations. A short satisfaction questionnaire will be required annually at years 6 through 10 after surgery. The doctor may choose to perform further follow-up evaluations and x-rays at 7 years and 10 years.

Meeting all of the above criteria does not guarantee participation in the study. Further consultation and a screening evaluation with the physician are necessary to ensure this is the right study for you. Study personnel at the site will explain

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[1] Stryker Orthopaedics Test Report 08-009: Evaluation of bone response to porous surfaces using a canine total hip model.
[2] Stryker Orthopaedics Test Report 07-077.

all the details of the study to you so you can make an informed decision as to whether or not you would like to participate.

If you are interested in participating in this study, please contact Dr. (name) or (study coordinator name) at the numbers listed below for further details.

Your request for information about this study in no way commits you to participate. In order to participate, you will have to meet specific criteria and sign a consent form that details all aspects of the study, the device and the risks associated with primary hip surgery.

Dr. (name)
Practice Name
Telephone Number

Study Coordinator Name
Title
Telephone Number

Appendix D

Model Informed Patient Consent

Model Informed Patient Consent

I. Study Title: Post-market Study of the Stryker Orthopaedics Tritanium® Acetabular Shell

II. Description of the Study

You have been asked to take part in this research study because your physician has determined that you need surgery to replace your hip joint. A total of approximately 240 subjects from 7 - 12 different clinics will be participating in this study.

The purpose of this study is to evaluate the success rate of cementless primary hip replacement with the Tritanium® Acetabular Shell as compared to similar competitive devices as reported in scientific journals, through absence of revision of the acetabular shell at 5 years postoperative. We (Stryker Orthopaedics, implant manufacturer and sponsor of the study, and your physician) are doing this study to find out if Stryker Orthopaedics' Tritanium® Acetabular Shell is at least as good as hips implanted with similar competitive devices.

Your doctor and his staff will ask you some questions during this visit. Based on the requirements of the study, you may or may not be chosen to be in the study.

Fitting all of these requirements does not mean you will be in the study. The doctor also has to examine you to make sure the study is right for you. The staff at the doctor's office will tell you everything about the study. Then you can decide if you want to be in the study or not.

You will be in the study for the next 10 years. Your doctor will examine you before surgery and during surgery. You will have surgery and your doctor will tell us the details of your surgery. During the visit before surgery you will need to fill out forms about your health. Your doctor will also collect other information and x-rays that would be collected at a normal visit.

He will then examine you for the study after your surgery. During your visits to the doctor after surgery, your doctor will figure out how well your hip is working and take x-rays. These x-rays are the same kind you would have if you were not in the study.

At your visits to the doctor after surgery, your doctor will ask you to fill out questionnaire forms. These forms will be about your health. Some of these visits and/or forms may be completed remotely (via videoconferencing, telephone or email), if approved by your doctor's Institutional Review Board (IRB). These visits will follow the evaluation schedule below:

Surgeon Evaluations	Before Surgery	6 Weeks	1 Year	2 Years	3 Years	4 Years	5 years
Demographics and Current Medical Conditions	X						
Harris Hip Score	X	X	X		X		X
AP Pelvis X-ray	X	X	X		X		X
AP Femur X-ray	X	X	X		X		X
Lateral X-ray	X	X	X		X		X
Patient Questionnaires							
SF-12	X	X	X	X	X	X	X
LEAS	X	X	X	X	X	X	X
EQ-5D	X	X	X	X	X	X	X

Finally, you will be asked to complete a short questionnaire regarding your satisfaction with the results of your hip replacement at 6, 7, 8, 9, and 10 years after surgery. This questionnaire may be completed at home and mailed to your doctor, during an office visit, or during a telephone call with study personnel. An office visit at 7 and 10 years after surgery is optional.

III. Condition and Care after Surgery

Your doctor will give you specific instructions regarding your care and rehabilitation after your surgery. As with any surgery, your body takes time to heal. That amount of time will be related to the extent of the surgical procedure and your general physical condition. During this period of healing, you may experience postoperative pain, perhaps lasting several months after the operation.

You will be told to use walking aids (crutches, walker or cane) for a period of time after your surgery. The use of these walking aids will lessen pressure and weight loads on your hip, which is thought to increase the chances for a stable implant. You have been informed that you must follow your physician's orders, including those regarding the use of walking aids.

The goal of this surgery is to lessen pain and increase your hip function. You will need to see your physician at 6 weeks, 1, 3 and 5 years after your surgery for evaluation of your artificial hip joint. Your physician may choose to perform further follow-up evaluations and x-rays at 7 years and 10 years.

IV. Possible Risks and Discomforts

This study involves the routine assessment of a primary hip replacement procedure. The Food and Drug Administration (FDA) has cleared the device used in this study for sale in the United States. There are no additional risks associated with participating in this study over and above that of the primary hip surgery. You may need to spend a little more time in the doctor's office to fill out paperwork. If at any time new information is developed during this research study which may affect your willingness to participate, the information will be provided to you.

There are, however, standard risks associated with hip surgery. These include but are not limited to: moderate to severe pain; crack/fracture (breakage) of femoral (thigh) or acetabular (pelvic) bones or components; migration (movement) of components; subsidence (sinking) of components; dislocation (to move out of normal position) of components; discomfort related to malseating of one of the components; sensitivity to metal components (femoral [thigh] and acetabular [pelvic]); revision (removal) of one or more of the components; loosening and infection; wear (rubbing) of the components which could lead to bone loss; peripheral neuropathies (any disorder of the nerves involving your legs); nerve damage; abnormal bone formation; circulatory compromise (changes in circulation related to your heart, blood and lymph vessels, to varying degrees); genitourinary disorders (related to urination); gastrointestinal disorders (related to the stomach and intestines); vascular disorders (related to blood vessels: including thrombus [blood clot]); bronchopulmonary disorders (related to the bronchi tubes and lungs, such as pneumonia); emboli (plugged vessel); myocardial infarction (heart attack) or death.

V. Potential Benefits

While there is no guarantee that you will personally benefit from inclusion in this study, information gathered in this study may benefit others undergoing primary hip surgery in the future.

You will have incentives to return for annual follow-up visits through a patient retention program. Patients enrolled into the study are encouraged to complete all of their required follow-up visits. You will be offered a stipend in the form of a debit card for various follow-up visits held in your doctor's office. You must complete all of the applicable questionnaires and evaluations in order to receive the stipend per visit. You can learn more about the program from your study doctor and his staff. This stipend should not influence your decision to participate in the study.

VI. Other Types of Treatment

You have discussed alternative treatments with your surgeon, which include but are not limited to: conservative non-surgical treatment, cemented or cementless total hip replacement utilizing other commercially available components, hip fusion or no treatment at all.

You may decline to participate in this study. This will not change any procedures associated with your hip surgery. Your physician can provide detailed information about this treatment and the benefits of various treatment options available to you. You should feel free to discuss your alternatives with your physician.

VII. Making Financial Information Known

Your doctor and/or the research institution may receive compensation from the manufacturer of your implant device(s) to cover the time and/or expenses associated with this Study or for other services. If you require any further information please consult your doctor or his staff about this issue.

VIII. Privacy

If you say yes to participate in this study, your medical records and identity will be kept confidential to the extent permitted by law and will not be released without your written permission.

By signing this consent form, you agree to allow representatives from the study sponsor to review your medical records. Some of this information will be provided to the study sponsor and its agents and contractors, and as required by law, review boards and other people who are required to watch over the safety and effectiveness of medical products and therapies and the conduct of research. Your name and identity will not be revealed in those reports.

IX. Cost to Be in the Study

Your procedure is a routine primary hip surgery and should be covered by your insurance carrier. You will not be paid for participating in this study.

X. Device Retrieval Analysis Study

I understand that the Stryker Orthopaedics Tritanium® Primary Acetabular Shell Study has a protocol for the analysis of retrieved devices in the event that any study component(s) that I have had implanted by Dr. <Investigator's Name> are removed during the course of the investigation.

I understand that Stryker Orthopaedics Corporation (implant manufacturer and Sponsor), requests my Physician to send my retrieved study component(s) to the Product Surveillance department at Stryker Orthopaedics for evaluation as part of my participation in the investigational study.

I hereby authorize my Physician and his staff to provide my retrieved study component(s), name, birth date, Patient Information Form and any and all information about my hip surgery to Stryker Orthopaedics for the purposes of evaluating my retrieved device(s) and reporting the results of the analysis to my Physician and Stryker Orthopaedics Corporation.

My Physician will be provided with the results of this analysis. I understand that the device(s) will not be returned to me, nor will I receive the results of any tests, analysis, or evaluations on the returned device(s).

I understand that, except for sending my retrieved study component(s) to The Cleveland Clinic Foundation and Stryker Orthopaedics, my retrieved study component(s) will not be released to outside parties.

I understand that, except for providing my individually identifiable information to the Physician who performed my surgery, Stryker Orthopaedics Corporation and The Cleveland Clinic Foundation, my individually identifiable data will not be released to outside parties. I also understand that I may inspect or copy the information by requesting said information from my Physician.

I understand that I may revoke this authorization for release of my retrieved study component(s) and individually identifiable information at any time by notifying my Physician in writing, but I understand that doing so will have no effect on actions taken before the receipt of my revocation.

I will have confidentiality in all records kept about me. My agreement to participate in this implant retrieval analysis study is completely voluntary. I understand that I have the right to not participate and the right to withdraw from the study at any time of my choosing and that this will in no way compromise my care, delay my treatment, or affect any future medical care.

Please check one of the boxes below:

☐ I agree to allow the Sponsor to study any hip replacement parts removed from me.

☐ I do not want to allow the Sponsor to study any hip replacement parts removed from me.

_____ _____

Signature of Subject/Legal Representative Date

XI. Clinical Trial Website Posting

A description of this clinical trial will be available on http://www.Clinical Trials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

XII. Payment and Medical Treatment Related to Injury

Stryker Orthopaedics will not provide compensation or free medical treatment if you suffer any medical complications related to the surgery. <Investigator's name> should be contacted immediately at <Investigator's phone number> if such a complication occurs. No monetary compensation or free medical treatment will be made available by <Name of Hospital>. <Investigator's name> should inform you of the hospital's policy in such matters. Signing this consent in no way waives your legal rights or releases the investigator, the sponsor, the institution or its agents from liability or negligence.

XIII. Access to Data and Privacy

By participating in this study, you are authorizing your physician and his/her staff to provide your health information to the sponsor, its agents and contractors, and as required by law, review boards and other people who are required to watch over the safety and effectiveness of medical products and therapies and the conduct of research. This health information includes all information collected during the research. It may also include relevant health information in your medical records that may have been collected prior to your involvement in this research study.

The sponsor will only collect that information which is necessary to support the objectives of the research, and will take precautions to ensure that data received has your identifying information (name, address, etc.) removed as much as possible. National privacy laws no longer cover use or re-disclosure of your health information,

once received by the sponsor. However, in the case that some identified information is received, the sponsor will ensure that any identifying information will not be reported.

The sponsor will use your health information to conduct the study, as well as for additional purposes such as overseeing and improving the performance of its devices, proposals for developing new medical products or procedures and other business purposes.

This permission does not have an ending date, but you may take back this permission to release your health information at any time by notifying your physician in writing. Understand that doing so will have no effect on actions taken before that time. This consent, authorizing that your health information may be provided to those indicated, must be signed in order for you to participate in this research study. If this consent is revoked you can no longer participate in this research study. In any case, your authorization to release individually identifiable information will expire at the end of this study.

IV. People to Contact

If you have any questions you can call [IRB Name] IRB at [IRB Phone Number]. You can also ask them if you want to know your rights as part of the study. You should contact Dr. [Investigators Names] as soon as you can at [Phone Number] if you have an injury that is related to the study.

XV. Being in the Study

Being part of this study is your choice. If you do not choose to be in the study you will not lose any benefits that you are supposed to have. You can decide you do not want to be in the study anymore and will not lose the benefits you are supposed to have.

By signing and dating this form below, you are indicating that you have read and reviewed all sections of this Informed Consent Form, you have had all your questions answered, and you voluntarily consent to participate in this research study. If you do not sign this form, you will not be allowed to participate in the research study.

_____
Printed name of Subject/Legal Representative

_____ _____
Signature of Subject/Legal Representative Date Signed

_____ _____
Signature of Person conducting the consent process Date Signed

_____ _____
Signature of Investigator Date Signed

A signed and dated copy of this consent form must be given to the patient.

Appendix E

Draft Electronic Case Report Form Specifications

Stryker®
Orthopaedics

Tritanium® Primary Acetabular Shell

ADVERSE EVENT

GENERAL INFORMATION

SUBJECT INITIALS: _____ ONSET DATE: _____ (DD-MMM-YYYY) SUBJECT ID: _____

I. DESCRIPTION

A. OPERATIVE SITE EVENTS **(Check one event in Section A or Section B)**

- ○ Acetabular Component Loosening
- ○ Acetabular Crack / Fracture
- ○ Acetabular Insert Crack / Fracture
- ○ Acetabular Liner Malseating
- ○ Acetabular Migration (If > 3mm)
- ○ Acetabular Shell Crack / Fracture
- ○ Bursitis
- ○ Deep Joint Infection
- ○ Device Allergic Reaction
- ○ Dislocation
- ○ Hip Pain
- ○ Intra-Prosthetic Dislocation
- ○ Femoral Bearing Head Crack / Fracture
- ○ Femoral Component Loosening
- ○ Femoral Component Subsidence
- ○ Femoral Crack / Fracture
- ○ Femoral Neck Crack / Fracture
- ○ Femoral Stem Crack / Fracture
- ○ Heterotopic Bone Formation (Type III / IV)
- ○ Modular Junction Dissociation
- ○ Osteolysis
- ○ Reflex Sympathetic Dystrophy (RSD)
- ○ Sciatic Nerve Palsy
- ○ Soft Tissue Trauma
- ○ Subluxation
- ○ Superficial Wound Infection
- ○ Tendonitis
- ○ Trochanteric Crack / Fracture
- ○ Trochanteric Non-Union
- ○ Wound Hematoma
- ○ Wound Related (Specify)
- ◉ Other (Specify)

Adverse Event Code: _____

Adverse Event Description: _____

B. SYSTEMIC EVENTS

- ○ Cancer (Specify)
- ○ Cardiovascular (Specify)
- ○ Dermatologic (Specify)
- ○ Digestive (Specify)
- ○ DVT
- ○ Musculoskeletal (Specify)
- ○ Neurologic (Specify)
- ○ Pulmonary Embolism
- ○ Respiratory (Specify)
- ○ Thrombophlebitis
- ○ Trauma (Specify)
- ○ Urogenital (Specify)
- ○ Other (Specify)

C. WHEN DID THE EVENT OCCUR? ○ Pre-Op ○ Intra-Op ○ Post-Op

II. COMPLICATION / CONCURRENT MEDICAL EVENT

D. DESCRIBE CIRCUMSTANCES, INCLUDING HISTORY OR CAUSATIVE EVENT, SPECIFY SIGNS, SYMPTOMS AND DISEASES.

_____

E. DEVICE RELATED? *** If Yes or Uncertain - Contact Stryker within 24 hours. Explain and upload applicable de-identified source documentation to the Subject Binder.**

◉ Yes* ○ No ○ Uncertain* _____

F. SERIOUSNESS Does this event meet the definition of serious? ◉ Yes* ○ No *** If Yes, check all that apply.**

- ☐ Resulted in inpatient hospitalization
- ☐ Resulted in prolonged existing hospitalization
- ☐ Resulted in persistent or significant disability/incapacity
- ☐ Resulted in permanent impairment of a body function or permanent damage to a body structure
- ☐ Necessitated medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure
- ☐ Was a life threatening situation
- ☐ Resulted in patient death

*** Specify when Adverse Event became SERIOUS. If Serious date is the same as Onset Date, enter Onset Date.**

_____ (DD-MMM-YYYY)

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ADVERSE EVENT

III. TREATMENT

◉ Yes* ○ No * If Yes, specify below

Contact Stryker within 24 hours if the treatment is Revision/Removal or Re-Operation.

REVISIONS / REMOVALS: (Check all that apply)

For Stryker Implants, submit PER form and implant(s) to Stryker.

		Date of Treatment (DD-MMM-YYYY)
☒	Acetabular Shell (Complete Study Termination Form)	
☒	Acetabular Liner	
☒	Acetabular Insert	
☒	Femoral Bearing Head	
☒	Femoral Stem	
☒	Other	

RE-OPERATIONS: (Specify) **Re-Operations are for study hip only and include open manipulation/reduction. Do not include revision or removals.**

		(DD-MMM-YYYY)
☒		
☐		

OTHER TREATMENTS: (Specify)

Diagnostic tests are not considered Treatments (i.e. X-rays and MRIs should NOT be included).

			(DD-MMM-YYYY)
☒	Add Row / Reset		
	x		

RESOLUTION OF EVENT:

◉ Unresolved as of **(Update this information if the Event has been resolved)**

○ Resolved as of

(DD-MMM-YYYY)

IV. COMMENTS

FOR STRYKER USE ONLY

PER #

Reason for Save

Verification / Confirmation Method

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Tritanium® Primary Acetabular Shell

DEMOGRAPHICS

GENERAL INFORMATION

SUBJECT INITIALS: _____

VISIT DATE: _____ (DD-MMM-YYYY)

SUBJECT ID: _____

I. DEMOGRAPHICS

A. DATE OF BIRTH: _____ (DD-MMM-YYYY)

B. HEIGHT: _____ inches

C. WEIGHT: _____ lbs.

BMI _____

D. EDUCATION LEVEL:

- ◯ Less Than High School
- ◯ High School Diploma
- ◯ Greater Than High School

E. EMPLOYMENT STATUS:

- ◯ Working
- ◯ Not Working

F. GENDER:

- ◯ Male
- ◯ Female

G. ETHNICITY:

- ◯ Hispanic or Latino origin
- ◯ Not Hispanic or Latino origin

H. RACE:

- ☐ American Indian or Alaskan native
- ☐ Asian
- ☐ Black or African heritage
- ☐ Native Hawaiian or other Pacific Islander
- ☐ White

II. SMOKING AND ALCOHOL HISTORY

I. CIGARETTE USE:

- ◯ Non-smoker
- ◯ Current cigarette smoker
  (Specify # Packs/Day and # Years below)
- ◯ Ex-cigarette smoker
  (Specify # Packs/Day, # Years, and Date Stopped)

PACKS/DAY: _____ # YEARS: _____

Date Stopped _____ (DD-MMM-YYYY)

J. ALCOHOL USE:

- ◯ Have never had alcohol
- ◯ Have not had alcohol in the last year
- ◯ Less than 3 drinks a week
- ◯ 3 -7 drinks a week
- ◯ 8 - 14 drinks a week
- ◯ 15+ drinks a week

III.DIAGNOSIS

K. INITIAL DIAGNOSIS:

- ◯ Osteoarthritis
- ◯ Traumatic Arthritis
- ◯ Avascular Necrosis
- ◯ Other (Specify)

IV. PRESENT MEDICAL STATUS

L. CONCURRENT MEDICAL CONDITION:

- ☐ None
- ☐ Cancer
- ☐ Cardiovascular
- ☐ Dermatologic
- ☐ Digestive
- ☐ Endocrine / Metabolic
- ☐ Immunologic / Lymphatic
- ☐ Musculoskeletal
- ☐ Neurologic
- ☐ Psychologic
- ☐ Respiratory
- ☐ Substance Dependence
- ☐ Urogenital
- ☐ Other (Specify)

V. COMMENTS

Reason for Save	
Verification / Confirmation Method	

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Tritanium® Primary Acetabular Shell

INCLUSION / EXCLUSION

GENERAL INFORMATION

SUBJECT INITIALS:	OPERATIVE SIDE:	DATE INFORMED CONSENT SIGNED:	SUBJECT IDENTIFIER:
	○ Right ○ Left	(DD-MMM-YYYY)	

I. INCLUSION CRITERIA

	Yes	No	
A.	○	○	Patient has signed an IRB approved, study specific Informed Patient Consent Form.
B.	○	○	Patient is a male or non-pregnant female age 18 years or older at time of study device implantation.
C.	○	○	Patient has primary diagnosis of Non-Inflammatory Degenerative Joint Disease (NIDJD).
D.	○	○	Patient is a candidate for a primary cementless total hip replacement.
E.	○	○	Patient is willing and able to comply with postoperative scheduled clinical and radiographic evaluations and rehabilitation.

**** All of the above must be answered "Yes" for the patient to be enrolled in the study.**

II. EXCLUSION CRITERIA

	Yes	No	
F.	○	○	Patient has a Body Mass Index (BMI) > 40.
G.	○	○	Patient has an active or suspected latent infection in or about the affected hip joint at time of study device implantation.
H.	○	○	Patient has a neuromuscular or neurosensory deficiency, which limits ability to evaluate the safety and efficacy of the device.
I.	○	○	Patient is diagnosed with a systemic disease (e.g. Lupus Erythematosus) or a metabolic disorder (e.g. Paget's Disease) leading to progressive bone deterioration.
J.	○	○	Patient is immunologically suppressed or receiving steroids in excess of normal physiological requirements (e.g >30 days).
K.	○	○	Patient requires revision surgery of a previously implanted total hip replacement or hip fusion to the affected joint.
L.	○	○	Patient has a known sensitivity to device materials.
M.	○	○	Patient is a prisoner.

**** All of the above must be answered "No" for the patient to be enrolled in the study.**

COMMENTS

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LOWER EXTREMITY ACTIVITY SCALE (LEAS)

GENERAL INFORMATION

SUBJECT INITIALS:	VISIT DATE:	VISIT:	SUBJECT ID:
	(DD-MMM-YYYY)		

I. LOWER EXTREMITY ACTIVITY SCALE

Enter data as completed by the subject per paper questionnaire.

1. ◯ I am confined to bed all day.
2. ◯ I am confined to bed most of the day except for minimal transfer activities (going to the bathroom, etc.).
3. ◯ I am either in bed or sitting most of the day.
4. ◯ I sit most of the day, except for minimal transfer activities, no walking or standing.
5. ◯ I sit most of the day, but I stand occasionally and walk a minimal amount in my house. (I may rarely leave the house for an appointment and may require the use of a wheelchair or scooter for transportation.)
6. ◯ I walk around my house to a moderate degree but I don't leave the house on a regular basis. (I may leave the house occasionally for an appointment.)
7. ◯ I walk around my house and go outside at will, walking one or two blocks at a time.
8. ◯ I walk around my house, go outside at will and walk several blocks at a time without any assistance (weather permitting).
9. ◯ I am up and about at will in my house and can go out and walk as much as I would like with no restrictions (weather permitting).
10. I am up and about at will inside my house and outside. I also work outside the house in a:
    ◯ minimally active job ◯ moderately active job ◯ extremely active job
11. I am up and about at will inside my house and outside. I also participate in relaxed physical activity such as jogging, dancing, cycling, swimming:
    ◯ occasionally (2-3 times per month) ◯ 2-3 times per week ◯ daily
12. I am up and about at will inside my house and outside. I also participate in vigorous physical activity such as competitive level sports:
    ◯ occasionally (2-3 times per month) ◯ 2-3 times per week ◯ daily

II. COMMENTS

Subject Initials are present on paper CRF? ◯ Yes ◯ No

Reason for Save

Verification / Confirmation Method

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NOTICE OF PROTOCOL DEVIATION

GENERAL INFORMATION

SUBJECT INITIALS: _____ **DATE OF DEVIATION:** _____ (DD-MMM-YYYY) **SUBJECT ID:** _____

I. DEVIATION INFORMATION

A. TYPE OF DEVIATION

- ○ **Informed Consent:**
  - ○ Study procedures performed prior to informed consent
  - ○ Incorrect informed consent version used
  - ○ Other _____
- ○ **Inclusion / Exclusion:** Subject enrolled does not meet the Inclusion / Exclusion criteria
- ○ **Treatment:** Protocol specified study component(s) not implanted (Check all that apply)

  ☐ Acetabular Shell* ☐ Acetabular Liner ☐ Acetabular Insert ☐ Femoral Bearing Head ☐ Femoral Stem

  * Complete Study Termination form
- ○ **Evaluation(s):** (Specify one visit below)

VISIT :	○	○	○	○	○	○	○	○	○	○	○	○
	Pre-Op	6 Week	1 Year	2 Year	3 Year	4 Year	5 Year	6 Year	7 Year	8 Year	9 Year	10 Year

  - ○ Missed entire visit (Select if entire visit did not occur; no CRF and X-ray completed)
    For a missed visit, record the day after visit interval window closure.
  - ○ Deviation in visit (Check all that apply and specify)
    - ☐ Required form(s)/X-ray(s) not done
    - ☐ Evaluation(s) occurred outside of protocol specified time window
    - ☐ Unevaluable X-ray (i.e. unreadable/poor quality)

    (If Deviation in visit, specify each form/X-ray)
    - ☐ EQ-5D
    - ☐ Follow-up Questionnaire
    - ☐ Functional Evaluation
    - ☐ LEAS
    - ☐ SF-12
    - ☐ X-ray - A/P Pelvis
    - ☐ X-ray - A/P Femur
    - ☐ X-ray - Lateral
- ○ **Adverse Event:** Protocol-specific Adverse Event reporting criteria not met - AE reported to Sponsor after 24 hours of knowledge of event.
- ○ **Other:** _____

B. Briefly describe the deviation and why this occurred.

_____

COMMENTS

_____

Reason for Save _____

Verification / Confirmation Method _____

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Tritanium® Primary Acetabular Shell

POST-OP FUNCTIONAL EVALUATION

GENERAL INFORMATION

SUBJECT INITIALS: _____ **VISIT DATE:** _____ (DD-MMM-YYYY) **VISIT** _____ **SUBJECT IDENTIFIER:** _____

I. PAIN

A. PAIN

- ◯ None, or ignores it
- ◯ Slight, occasional, no compromise in activities
- ◯ Mild, no effect on average activities, rarely moderate pain with unusual activity, may take aspirin
- ◯ Moderate pain, tolerable but makes concessions to pain. Some limitations of ordinary activity or work. May require occasional pain medication stronger than aspirin
- ◯ Marked pain, serious limitation of activities
- ◯ Totally disabled, crippled, pain in bed, bedridden

II. FUNCTION / GAIT

B. LIMP

- ◯ None
- ◯ Slight
- ◯ Moderate
- ◯ Severe or unable to walk

C. SUPPORT

- ◯ None
- ◯ Cane, long walks
- ◯ Cane, most of the time
- ◯ One crutch
- ◯ Two canes
- ◯ Two crutches, walker or unable to walk

D. DISTANCE WALKED

- ◯ Unlimited
- ◯ Six blocks
- ◯ Two or three blocks
- ◯ Indoors only
- ◯ Bed and chair only

III. FUNCTIONAL ACTIVITIES

E. STAIRS

- ◯ Normally without using a rail
- ◯ Normally using a railing
- ◯ In any manner
- ◯ Unable to use stairs

F. SOCKS / SHOES

- ◯ With ease
- ◯ With difficulty
- ◯ Unable

G. SITTING

- ◯ Any chair, 1 hour
- ◯ High chair, 1/2 hour
- ◯ Unable to sit comfortably in any chair

H. PUBLIC TRANSPORTATION

- ◯ Able to use
- ◯ Not able to use

I. ABSENCE OF DEFORMITY (Operative side only)

	Yes	No
Fixed flexion contracture < 30°	◯	◯
Fixed adduction < 10°	◯	◯
Fixed internal rotation in extension < 10°	◯	◯
Leg length discrepancy less than 3.2 cm	◯	◯

(Specify) _____ cm

J. RANGE OF MOTION (Operative side only)

Permanent (Fixed) Flexion	_____ °
Flexion to	_____ °
Abduction to	_____ °
Adduction to	_____ °
External Rotation in Extension to	_____ °
Internal Rotation in Extension to	_____ °

Before proceeding to the next section, click "Calculate HHS" button.
If changing any HHS data fields, click "Calculate HHS" button again.

Calculate HHS _____

Tritanium® Primary Acetabular Shell

POST-OP FUNCTIONAL EVALUATION

IV. EVENTS

K. Have there been any protocol defined Adverse Events since the last visit? ◯ Yes* ◯ No

*If Yes, complete an AE form for each.

USE THIS SECTION TO REPORT MEDICAL EVENTS OTHER THAN PROTOCOL DEFINED ADVERSE EVENTS.

L. Has the subject seen a doctor for any medical event since the last visit? ◯ Yes* ◯ No

*If Yes, specify:

M. Has the subject been hospitalized for any elective surgery since the last visit? ◯ Yes* ◯ No

*If Yes, specify (check all that apply)

*Provide Details

N. Is anything currently affecting the subject's function? ◯ Yes* ◯ No

*If Yes, specify:

V. COMMENTS

Reason for Save

Verification / Confirmation Method

Stryker®
Orthopaedics

Tritanium® Primary Acetabular Shell

PRE-OP FUNCTIONAL EVALUATION

GENERAL INFORMATION

SUBJECT INITIALS: _____

VISIT DATE: _____ (DD-MMM-YYYY)

SUBJECT IDENTIFIER: _____

I. PAIN

A. PAIN

- ◯ None, or ignores it
- ◯ Slight, occasional, no compromise in activities
- ◯ Mild, no effect on average activities, rarely moderate pain with unusual activity, may take aspirin
- ◯ Moderate pain, tolerable but makes concessions to pain. Some limitations of ordinary activity or work. May require occasional pain medication stronger than aspirin
- ◯ Marked pain, serious limitation of activities
- ◯ Totally disabled, crippled, pain in bed, bedridden

II. FUNCTION / GAIT

B. LIMP

- ◯ None
- ◯ Slight
- ◯ Moderate
- ◯ Severe or unable to walk

C. SUPPORT

- ◯ None
- ◯ Cane, long walks
- ◯ Cane, most of the time
- ◯ One crutch
- ◯ Two canes
- ◯ Two crutches, walker or unable to walk

D. DISTANCE WALKED

- ◯ Unlimited
- ◯ Six blocks
- ◯ Two or three blocks
- ◯ Indoors only
- ◯ Bed and chair only

III. FUNCTIONAL ACTIVITIES

E. STAIRS

- ◯ Normally without using a rail
- ◯ Normally using a railing
- ◯ In any manner
- ◯ Unable to use stairs

F. SOCKS / SHOES

- ◯ With ease
- ◯ With difficulty
- ◯ Unable

G. SITTING

- ◯ Any chair, 1 hour
- ◯ High chair, 1/2 hour
- ◯ Unable to sit comfortably in any chair

H. PUBLIC TRANSPORTATION

- ◯ Able to use
- ◯ Not able to use

I. ABSENCE OF DEFORMITY (Operative side only)

	Yes	No
Fixed flexion contracture < 30°	◯	◯
Fixed adduction < 10°	◯	◯
Fixed internal rotation in extension < 10°	◯	◯
Leg length discrepancy less than 3.2 cm	◯	◯

(Specify) _____ cm

J. RANGE OF MOTION (Operative side only)

Permanent (Fixed) Flexion	____ °
Flexion to	____ °
Abduction to	____ °
Adduction to	____ °
External Rotation in Extension to	____ °
Internal Rotation in Extension to	____ °

Before proceeding to the next section, click "Calculate HHS" button.
If changing any HHS data fields, click "Calculate HHS" button again.

Calculate HHS _____

IV. COMMENTS

_____

Reason for Save _____

Verification / Confirmation Method _____

Stryker®
Orthopaedics

Tritanium® Primary Acetabular Shell

SURGICAL DETAILS

Submit Surgical Details CRF ONLY if surgery is performed and subject receives study device.

GENERAL INFORMATION

SUBJECT INITIALS: _____ SURGERY DATE: _____ (DD-MMM-YYYY) SUBJECT ID: _____

I. SURGICAL DETAILS

A. APPROACH
- ◯ Anterior
- ◯ Anterolateral
- ◯ Posterior/ Posterolateral
- ◯ Dual Incision
- ◯ Lateral

B. MUSCLE REPAIR OR REATTACHMENT REQUIRED?
- ◯ Yes*
- ◯ No

*If Yes, which muscle group?
- ☐ External Rotators
- ☐ Gluteus Medius
- ☐ Other _____

C. NAVIGATION USED?
- ◯ Yes
- ◯ No

D. INCISION LENGTH
_____ cm

E. DURATION OF SURGERY
Skin to Skin _____ minutes

F. ESTIMATED BLOOD LOSS
_____ cc

II. PROSTHESES

G. PROSTHESES -
Upload a copy of the component label(s) implanted.

Acetabular Shell -
Go to Subject Information screen and enter data in Products tab.

	Reference #	Lot #
Acetabular Liner		
Acetabular Insert		
Femoral Bearing Head		
Femoral Stem		

H. OTHER? ◯ Yes* ◯ No

*If Yes, specify and upload a copy of the label(s).

Add Row / Reset	Other (Specify)	Reference #	Lot #
☒			

I. BONE SCREWS USED? ◯ Yes* ◯ No

*If Yes, specify and upload a copy of the label(s).

Add Row / Reset	Reference #	Lot #
☒		

J. INTRAOPERATIVE COMPLICATION?

If Yes, complete AE form. ◉ Yes ◯ No

K. DISCHARGED TO: (Check One)
- ◯ Skilled Nursing Facility
- ◯ Chronic Care Center
- ◯ Rehabilitation Unit
- ◯ Home
- ◯ Other: (Specify) _____

Discharge Date: _____ DD-MMM-YYYY

III. COMMENTS

Reason for Save _____

Verification / Confirmation Method _____

Submit

Stryker®

Orthopaedics

Tritanium® Primary Acetabular Shell

SF - 12 v2

GENERAL INFORMATION

PATIENT INITIALS:	VISIT DATE:	VISIT:	SUBJECT IDENTIFIER:
	(DD-MMM-YYYY)		

I. SF-12 Health Survey Standard

Enter data as completed by the subject per paper questionnaire.

1) In general, would you say your health is:

Excellent	Very Good	Good	Fair	Poor
○	○	○	○	○

2) The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

	Yes, Limited A Lot	Yes, Limited A Little	No, Not Limited At All
a. **Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf**	○	○	○
b. **Climbing several flights of stairs**	○	○	○

3) During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

a. **Accomplished less than you would like**

All of the time	Most of the time	Some of the time	A little of the time	None of the time
○	○	○	○	○

b. **Were limited in the kind of work or other activities**

All of the time	Most of the time	Some of the time	A little of the time	None of the time
○	○	○	○	○

4) During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

a. **Accomplished less than you would like**

All of the time	Most of the time	Some of the time	A little of the time	None of the time
○	○	○	○	○

b. **Did work or other activities less carefully than usual**

All of the time	Most of the time	Some of the time	A little of the time	None of the time
○	○	○	○	○

Stryker®

Orthopaedics

Tritanium Primary Acetabular Shell

SF - 12 v2

I. SF-12 (CONTINUED)

5) During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

Not at all	A little bit	Moderately	Quite a bit	Extremely
○	○	○	○	○

6) These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks...

a. **Have you felt calm and peaceful?**

All of the time	Most of the time	Some of the time	A little of the time	None of the time
○	○	○	○	○

b. **Did you have a lot of energy?**

All of the time	Most of the time	Some of the time	A little of the time	None of the time
○	○	○	○	○

c. **Have you felt downhearted and depressed?**

All of the time	Most of the time	Some of the time	A little of the time	None of the time
○	○	○	○	○

7) During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting friends, relatives, etc.)?

All of the time	Most of the time	Some of the time	A little of the time	None of the time
○	○	○	○	○

COMMENTS

Subject Initials are present on paper CRF? ○ Yes ○ No

Reason for Save

Verification / Confirmation Method

Stryker®
Orthopaedics

Tritanium® Primary Acetabular Shell
STUDY TERMINATION

GENERAL INFORMATION

SUBJECT INITIALS:

TERMINATION DATE:
(DD-MMM-YYYY)

SUBJECT IDENTIFIER:

I. STUDY TERMINATION

A. DID SUBJECT COMPLETE STUDY ACCORDING TO PROTOCOL?

◯ Yes ◯ No* *If No, answer questions B and C

B. CHECK ONE PRIMARY REASON BELOW:

Death (Complete AE form)

Investigative site terminated

Lost to follow-up

List efforts to contact patient:
- 1st phone call: (DD-MMM-YYYY)
- 2nd phone call: (DD-MMM-YYYY)
- 3rd phone call: (DD-MMM-YYYY)
- Certified letter sent (DD-MMM-YYYY)

Additional efforts:

Revision/Removal of Study Device (Complete AE form)

Study Device Not implanted (Specify below and complete Protocol Deviation form)

Subject Withdrawal

Surgery Not Performed (Specify below)

Other (Specify below)

C. WAS STUDY DEVICE IN PLACE AT DATE OF LAST CONTACT? Yes No

II. COMMENTS

Reason for Save

Verification / Confirmation Method

Appendix F

Product Labeling

stryker®
Howmedica
OSTEONICS

TRITANIUM Acetabular Component System

Howmedica Osteonics Corp.
325 Corporate Drive
Mahwah, NJ 07430
A subsidiary of Stryker Corporation

or

Benoist Girard
203 Bd de la Grande Delle – BP 8
14201 Hérouville-Saint-Clair Cedex
France
Telephone #: +1 201-831-5000

EC REP

Stryker France
ZAC Satolas Green Pusignan
Av de Satolas Green
69881 MEYZIEU Cedex
France

CE 0086

QIN4397 Rev. F

Refer to product label for CE Mark Status and Legal Manufacturer. The CE mark is only valid if also found on the product label.

Labeling Symbols

Attention, See Instructions for Use

Do Not Reuse

Sterilized using Irradiation

Sterilized using Hydrogen Peroxide

Sterilized using Ethylene Oxide

Use by Date

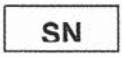
Date of Manufacture

Legal Manufacturer

Authorized Representative in the European Community

Catalog Number

Batch Code



Serial Number

QIN 4397 Rev. F

TRITANIUM Acetabular Component System English

Description

The HOWMEDICA OSTEONICS TRITANIUM Acetabular Shell consists of a metal acetabular shell with a Particle Sintered Foam (PSF) coating. The shells are intended for cementless fixation within the prepared acetabulum. The dome hole plugs are optional devices which are available to help seal the HOWMEDICA OSTEONICS TRITANIUM Acetabular Shell. The plugs are to be threaded into the dome hole of the shell.

Compatibility

Shell-to-Insert

- TRITANIUM Shells (500-03-XXX and 502-03-XXX) can be used with TRIDENT Polyethylene Inserts.
- TRITANIUM Shells (500-03-XXX, 502-03-XXX) are approved for use with TRIDENT Ceramic Inserts in the European Union member states and Australia. For use of TRITANIUM Shells (500-03-XXX,
  502-03-XXX) with TRIDENT Ceramic Inserts in other International markets, please consult the local market's Stryker representative.
- Tritanium Shells (500-03-XXX, 502-03-XXX) with TRIDENT Ceramic Inserts are not approved for use in the USA.

Acetabular Bone Screws

- HOWMEDICA OSTEONICS 6.5mm Bone Screws can be used with the dome screw holes of the acetabular shells.

Materials:

- ASTM F-620, ASTM F-136 Acetabular Shell
  Titanium 6Al-4V ELI Alloy
- ASTM F-1580 CP Titanium· TRITANIUM Coating
- ASTM F-67 CP Titanium Dome Hole Plugs

Indications

- Painful, disabling joint disease of the hip resulting from: degenerative arthritis, rheumatoid arthritis, post-traumatic arthritis or late stage avascular necrosis.
- Revision of previous unsuccessful femoral head replacement, cup arthroplasty or other procedure.
- Clinical management problems where arthrodesis or alternative reconstructive techniques are less likely to achieve satisfactory results.
- Where bone stock is of poor quality or is inadequate for other reconstructive techniques as indicated by deficiencies of the acetabulum.

The HOWMEDICA OSTEONICS TRITANIUM Acetabular Shell is intended for cementless use only.

Contraindications

- Any active or suspected latent infection in or about the hip joint.
- Any mental or neuromuscular disorder which would create an unacceptable risk of prosthesis instability, prosthesis fixation failure, or complications in postoperative care.
- Bone stock compromised by disease, infection or prior implantation which cannot provide adequate support and/or fixation to the prosthesis.
- Skeletal immaturity.

Warnings

- Do not reassemble a ceramic head and stem. Once a ceramic head has been assembled to a stem taper, it should never be reassembled to that stem or subsequently assembled to any other stem. In addition, a ceramic head should only be assembled to an unused stem taper. Once a stem taper has been assembled to any femoral head, it should never be subsequently assembled to any ceramic head component due to deformation of the stem's taper locking mechanism during initial stem/head assembly.
- Do not allow polished bearing areas and machined taper surfaces to come in contact with hard or abrasive surfaces, as scratching or in any way damaging these surfaces can significantly affect the structural integrity.
- Adaptor sleeve must be fully seated on the stem taper before the head is impacted. In no instance should any attempt be made to pre-assemble the adaptor sleeve to the ceramic bearing head.
- When using an adaptor sleeve, improper seating of the head and/or adaptor sleeve may result in a discrepancy in neck length, component disassociation and/or dislocation.
- Clean bearing surfaces of debris prior to assembly as foreign particles may cause accelerated bearing wear, which may lead to early failure of the device. Clean and dry machine taper surfaces to help ensure proper seating and assembly.
- Do not substitute another manufacturer's device for any of the Howmedica Osteonics' TRITANIUM System or TRIDENT System components because design, material, or tolerance differences may lead to premature device and/or functional failure. Components of the system have been specifically designed to work together. Any such use will negate the responsibility of Howmedica Osteonics Corp. for the performance of the resulting mixed component implant.
- Howmedica Osteonics Corp. strongly advises against the use of another manufacturer's bone screws with any HOWMEDICA OSTEONICS Acetabular System component, due to variations which exist between screw head and screw seat configurations.
- Do not use V40 alumina heads with CoCr stems.
- Do not use C-Taper alumina heads with CoCr stems without an adaptor sleeve.
- Do not use C-Taper alumina heads with Stainless Steel (Orthinox) stems.
- Avoid excessive verticalization of shell, which may accelerate bearing wear.
- Do not contour or bend an implant because it may reduce its fatigue strength and cause failure under load.
- Do not implant in obese patients because additional loading may lead to loss of fixation or device failure.
- Improper seating of the head may result in a discrepancy in neck length, component disassociation and/or dislocation.
- Ensure appropriate selection of bone screw length and location to help avoid damage to underlying soft tissue structures. Perforation of the pelvic wall can result in internal bleeding and possible damage to vital organs.

- Discard all damaged or mishandled implants. Never reuse an implant, even though it may appear undamaged. It may have small defects and internal stress patterns which may lead to early failure of the device.
- **Do not resterilize.**

Precautions

- Before clinical use, the surgeon should thoroughly understand all aspects of the surgical procedure and limitations of the device. Physicians must instruct patients in the limitations of the prosthesis, including, but not limited to, the impact of excessive loading through patient weight or activity, and be taught to govern their activities accordingly. If the patient is involved in an occupation or activity which includes substantial walking, running, lifting, or muscle strain, the resultant forces can cause failure of the fixation, the device, or both. The prosthesis will not restore function to the level expected with normal healthy bone, and the physician must advise the patient against having unrealistic functional expectations.
- Appropriate selection, placement and fixation of the total hip components are critical factors which affect implant service life. As in the case of all prosthetic implants, the durability of these components is affected by numerous biologic, biomechanic and other extrinsic factors, which limit their service life. Accordingly, strict adherence to the indications, contraindications, precautions and warnings for this product is essential to potentially maximize service life.
- If the ceramic component(s) fracture necessitating revision, take special care to remove all ceramic debris from the joint. Any remaining fragments could accelerate wear of the replacement components.
- Use caution when handling ceramic components during assembly because of the brittle nature of ceramic material.
- Intentional removal of an acetabular component can be accomplished by careful use of cutting burrs, thin and narrow osteotomes and cautious extraction forces. A threaded metal shell can be removed by carefully unscrewing the shell in a counterclockwise direction. If difficulty is encountered, the preceding techniques may be employed.
- Removal of an unloosened arc deposited or hydroxylapatite surface treated implant may require the use of special instruments to disrupt the interface at the implant surface.
- Care should be taken not to cut through surgical gloves when handling any sharp-edged orthopaedic device.

Utilization and Implantation

- The surgeon must be completely familiar with the implant system and surgical protocol, and complete preoperative planning should be carried out.
- The suggested surgical procedure should be strictly adhered to. Proper assembly of the ceramic inserts and the ceramic heads to their mating taper surfaces and proper assembly technique are critical to the success of ceramic hip systems.
- The recommended trial components should be used for size determination, trial reduction and range of motion evaluation, thus helping to preserve the integrity of the actual implants and their sterile packaging.
- Radiographic templates are available to help assist in the preoperative prediction of component size and style.
- The Surgical Protocol for the TRITANIUM Acetabular Component System provides additional procedural information.

Information for patients

- The surgeon must advise the patient of both the limitations of the reconstruction and the need for protection of the implant from full weight bearing until adequate fixation and healing have occurred. Excessive activity and trauma affecting the joint replacement have been implicated in failure of the reconstruction by loosening, fracture and/or wear of the prosthetic implants. Loosening of the components can result in increased production of wear particles, as well as damage to the bone, making successful revision surgery more difficult.
- The surgeon should caution the patient to limit activities and protect the replaced joint from unreasonable stresses, and to follow the instructions of the physician with respect to follow-up care and treatment.
- The surgeon should warn the patient of surgical risks and possible adverse effects. The surgeon should warn the patient that the device does not replicate a normal healthy joint, that the implant can break or become damaged as a result of strenuous activity or trauma, and that the device has a finite service life and may need to be replaced in the future.
- Transient bacteremia can occur in daily life. Dental manipulation, endoscopic examination and other minor surgical procedures have also been associated with transient bacteremia. To help prevent infection at the implant site, it may be advisable to use antibiotic prophylaxis before and after such procedures.

Adverse Effects

- While the expected life of total hip replacement components is difficult to estimate, it is finite. These components are made of foreign materials which are placed within the body for the potential restoration of mobility or reduction of pain. However, due to the many biological, mechanical and physiochemical factors which affect these devices but cannot be evaluated in vivo, the components cannot be expected to indefinitely withstand the activity level and loads of normal healthy bone.
- Dislocation of the hip prosthesis can occur due to inappropriate patient activity, trauma or other biomechanical considerations.
- Loosening of total hip 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 possibilty of bone erosion and/or pain.
- Fracture of ceramic components has been reported in a small percentage of cases.
- Intraoperative fissure, fracture, or perforation of the femur, acetabulum or trochanter can occur due to impaction of the component into the prepared femoral canal or acetabulum. Postoperative femoral or acetabular fracture can occur due to trauma, the presence of defects, or poor bone stock.
- If bone screws are used, appropriate selection of bone screw length and location is essential to help avoid damage to underlying soft tissue structures. Perforation of the pelvic wall can result in internal bleeding and possible damage to vital organs.
- Peripheral neuropathies, nerve damage, circulatory compromise and heterotopic bone formation may occur.
- Serious complications may be associated with any total joint replacement surgery. These complications include, but are not limited to: genitourinary disorders; gastrointestinal disorders; vascular disorders, including thrombus; bronchopulmonary disorders, including emboli; myocardial infarction or death.
- Acetabular pain may occur due to loosening of the implant.
- Metal sensitivity reactions have been reported following joint replacement.
- 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.
- With all implant devices, asymptomatic, localized progressive bone resorption (osteolysis) may occur around the prosthetic components as a consequence of foreign-body reaction to the particulate matter of cement, metal, Ultra-High Molecular Weight Polyethylene (UHMWPE) and/or ceramic. Particulate is generated by interaction between components and bone, primarily through wear mechanisms of adhesion, abrasion and fatigue. Secondarily, particulate can also be generated by third-body wear. Osteolysis can lead to future complications, including loosening, necessitating the removal and replacement of prosthetic components.
- Very small particles from metal and polyethylene components can be shed from the components during normal use and over time. Although most of this debris stays in the relevant joint (i.e. contained in the synovium) or is trapped by surrounding scar tissue, microscopic particles can be disseminated (migrate) throughout the body and on occasions have been described as accumulating in lymph nodes and other parts of the body. Although no significant medical complications have been reported as a result of these particles, their migration and/or accumulation in the body have been described in the literature. Given the insufficient time period during which patients with these devices have been followed and the fact that these devices are currently being used in younger patients and remain in the body for increasingly longer periods of time, it should be said that the long-term effects, if any, from these particles, is unknown. The long-term effects have been theorized to include:
  - Cancer: There is presently no scientific evidence that links metallic or polyethylene debris with cancer. However, the possibility cannot be ruled out.
  - Lymphadenopathy and Accumulation in Other Tissues/Organs: There have been a few reports of the accumulation of wear debris in lymph nodes (proximal and distal). Although no medical complications or disease process has been reported as stemming from these accumulations, their existence should be recognized to facilitate diagnosis and avoid confusion with suspicious lesions, cancerous or otherwise.
  - Systemic Disease: There has been some speculation that there could be an association between migration of debris and as yet unidentified systemic effects. It is possible that some long-term effect may be demonstrated at some point in the future, but because there is very little scientific data suggesting association between migration of debris and systemic disease, it is believed that the benefits of these devices clearly outweigh the potential risks for any such theoretical long-term effect.
- Surgeons should warn patients of the above listed potential effects including the finite service life of the device and the need for post-operative protection of the implant.

Sterilization

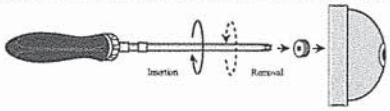
- These components have been sterilized by gamma radiation
- Do NOT re-sterilize.
- Autoclaving ceramic components can compromise their mechanical and structural integrity.
- Inspect the packaging of ALL sterile products for flaws before opening. In the presence of any flaws, assume the product is not sterile.
- Take care to prevent contamination of ANY components.
- Discard ALL nonsterile or contaminated product.

Single use devices cannot be explanted and subsequently reimplanted as the physical forces exerted by these actions may compromise the physical integrity, dimensions and/or surface finishes of the devices. Also, sterility cannot be assured for reused devices as cleaning and re-sterilization procedures have not been verified.

DOME HOLE PLUG ASSEMBLY INSTRUCTIONS

INSERTION:

- Once the acetabular shell is seated in the acetabulum, the dome hole plug may be inserted. Place the dome hole plug onto the captive twist head of the driver (secure by tapping on a hard surface). Insert the dome hole plug into the threaded dome hole of the shell. Turn the driver clockwise until the plug is seated firmly. Extract driver from plug.



REMOVAL:

- Removal of the plug is the same as insertion, except the driver is turned counterclockwise.

CAUTION: FEDERAL LAW (U.S.A.) RESTRICTS THIS DEVICE TO SALE BY OR ON THE ORDER OF A LICENSED PHYSICIAN.

Refer to product label for CE Mark Status and Legal Manufacturer. The CE mark is only valid if also found on the product label.

The following table contains a list of abbreviations that are used on Howmedica Osteonics Corp. product labeling:

Term	Abbreviation	Term	Abbreviation
Alpha Code	ALPH CDE	Neck	NK
Angle	ANG	Offset	OFFST
Degree	DEG or °	Outer Diameter	OD
Diameter	DIA	Package	Pkg.
Extra Deep	XDP	Right	RT c
Extra Large	XLGE	Screw Holes	SCR HLS
Extra Small	XSM	Side	SDE
Head	HD	Size	SZE
Height	HT	Small	SM
Inner Diameter	ID	Standard	STD
Insert	INSR	Taper	TPR
Large	LGE	Thickness	THKNS
Left	b LFT	Type	TYP
Length	LNTH	With	W/
Medium	MED	Without	W/O

Appendix G

510(k) Clearance Letter

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

JUL 22 2008

Howmedica Osteonics Corp.
% Ms. Kimberly Lane
Regulatory Affairs Specialist
325 Corporate Drive
Mahwah, NJ 07430

Re: K081171
Trade/Device Name: Tritanium® Acetabular Shell System
Regulation Number: 21 CFR 888.3358
Regulation Name: Hip joint metal/polymer/metal semi-constrained porous-coated uncemented prosthesis
Regulatory Class: Class II
Product Code: LPH
Dated: April 23, 2008
Received: April 24, 2008

Dear Ms. Lane:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Center for Devices and Radiological Health's (CDRH's) Office of Compliance at (240) 276-0120. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at (240) 276-3474. For questions regarding the reporting of device adverse events (Medical Device Reporting (MDR)), please contact the Division of Surveillance Systems at (240) 276-3464. You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Mark N. Melkerson

Mark N. Melkerson
Director
Division of General, Restorative
and Neurological Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K081171

Device Name: Tritanium® Acetabular Shell System

Indications for Use:

The indications for use of the total hip replacement prostheses include:

1. Painful, disabling joint disease of the hip resulting from: non-inflammatory degenerative arthritis, rheumatoid arthritis, post-traumatic arthritis, or late stage avascular necrosis.
2. Revision of previous failed femoral head replacement, shell arthroplasty or other procedure.
3. Clinical management problems where arthrodesis or alternative reconstructive techniques are less likely to achieve satisfactory results.
4. Where bone stock is of poor quality or inadequate for other reconstructive techniques as indicated by deficiencies of the acetabulum.

This acetabular shell is intended for cementless use only.

Prescription Use X (Part 21 CFR 801 Subpart D) AND/OR Over-The-Counter Use _____ (21 CFR 807 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE OF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

(Division Sign-Off)

Division of General, Restorative, and Neurological Devices

510(k) Number K081171

Health Questionnaire

English version for the US

stryker®

Tritanium® Primary Acetabular Shell
EQ-5D Health Questionnaire

VISIT:

Pre-op	6 Week	1 Year	2 Year	3 Year	4 Year	5 Year	7 Year	10 Year
○	○	○	○	○	○	○	○	○

SUBJECT ID: 6 9 (Study) | | (Site) | | | | | (Subject)

SUBJECT INIITIALS: | | |

By placing a checkmark in one box in each group below, please indicate which statements best describe your own health state today.

Mobility

I have no problems in walking about ❑
I have some problems in walking about ❑
I am confined to bed ❑

Self-Care

I have no problems with self-care ❑
I have some problems washing or dressing myself ❑
I am unable to wash or dress myself ❑

Usual Activities (*e.g. work, study, housework, family or leisure activities)*

I have no problems with performing my usual activities ❑
I have some problems with performing my usual activities ❑
I am unable to perform my usual activities ❑

Pain/Discomfort

I have no pain or discomfort ❑
I have moderate pain or discomfort ❑
I have extreme pain or discomfort ❑

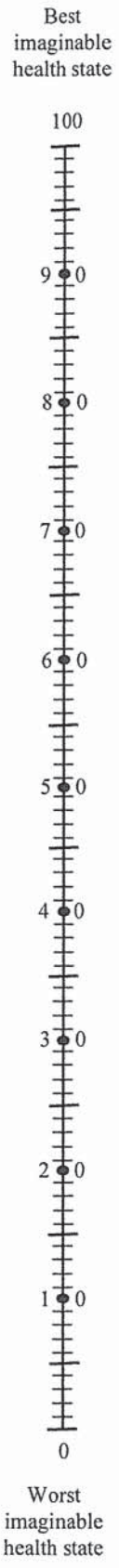
Anxiety/Depression

I am not anxious or depressed ❑
I am moderately anxious or depressed ❑
I am extremely anxious or depressed ❑

To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale how good or bad your own health is today, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your health state is today.

Your own health state today



SUBJECT ID: 6 9 (Study) ( ) (Site) ( ) (Subject)

VISIT:

Pre-op	6 Week	1 Year	2 Year	3 Year	4 Year	5 Year	7 Year	10 Year
○	○	○	○	○	○	○	○	○

Subject, please initial and date here

DATE: ( ) ( ) ( ) ( ) ( ) ( ) ( ) ( )
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