Secur-Fit Advanced Outcomes Study

Clinical Study Protocol

A prospective, post-market, multi-center evaluation of the clinical outcomes of the Secur-Fit Advanced Hip Stem

Sponsor:	*Stryker Orthopaedics* *325 Corporate Drive* *Mahwah, NJ 07430* *201-831-5000*
Study Product:	*Secur-Fit Advanced Hip Stem*
Protocol Number:	*75*
510(k) Clearance Number:	*K122853 – February 1, 2013*

Version 3.0

Date: 17 August 2022

Protocol Change History

Version	Description	Changed By
A	New	Kristin L. Given
1.0	Final	Kristin L. Robinson
2.0	Amended Version 1.0 – Section 15.3 Subject Stipends or Payments has been edited to incorporate language regarding inclusion of subject stipends for protocol-related visits.	Candice Kelly

3.0	Change: ***Number Cases*** *Previous language*: Cases will be enrolled until 326 cases have received the Secur-Fit Advanced Hip Stem. *New language*: Cases will be enrolled until 314 cases have received the Secur-Fit Advanced Hip Stem. *Rationale for Change*: Reduction of cases to 314 poses no risk to the statistical analysis and demonstration of long-term safety and effectiveness of the Secur-Fit Advanced Hip Stem. Change: ***Primary Objective*** *Previous language*: To evaluate and determine the success rate, defined as absence of stem revision for aseptic loosening or femoral fracture, at 5 years postoperative with the Secur-Fit Advanced Hip Stem. *New language*: To evaluate and determine the success rate, defined as absence of stem revision for aseptic loosening or device-related femoral fracture, at 5 years postoperative with the Secur-Fit Advanced Hip Stem. *Rationale for Change*: Clarification that femoral fractures which are unrelated to the study device will not be included in primary analysis. Change: ***Secondary Objective*** *Previous language:* To evaluate rate of femoral fracture among patients implanted with the Secur-Fit Advanced Hip Stem within 30 days postoperative, and compare with rates reported for other primary hip stems in the literature. *New language*: To evaluate rate of device-related femoral fracture among patients implanted with the Secur-Fit Advanced Hip Stem within 30 days postoperative, and compare with rates reported for other primary hip stems in the literature	Candice Kelly

Version	Description	Changed By
	Rationale for Change: Clarification that femoral fractures which are unrelated to the study device will not be included in the secondary endpoint evaluation. Change: ***Secondary Objective*** *Previous language*: To demonstrate that surgeons can use the Secur-Fit Advanced Hip Stem to consistently match a preoperative plan for femoral head center, offset and leg length postoperatively. *New language*: [*Removal of endpoint*] *Rationale for Change*: This secondary objective is no longer required to support Stryker's business needs, and removal does not affect safety or performance.	

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List of Abbreviations

ADE	Adverse Device Effect
AE	Adverse Event
AP	Anteroposterior
BMI	Body Mass Index
CFR	Code of Federal Regulations
CP	Commercially Pure
CSM	Clinical Study Manager
DCR	Data Clarification Request
EC	Ethics Committee
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
GCP	International Conference of Harmonisation Good Clinical Practice
HA	Hydroxylapatite
HHS	Harris Hip Score
HIPAA	Health Insurance Portability and Accountability Act
ICMJE	International Committee of Medical Journal Editors
IRB	Institutional Review Board
LEAS	Lower Extremity Activity Scale
PER	Product Experience Report
PI	Principal Investigator
QOL	Quality of Life
ROM	Range of Motion
SAE	Serious Adverse Event
SC	Study Coordinator
SF-12	Short Form-12
THA	Total Hip Arthroplasty
UADE	Unanticipated Adverse Device Effect
UHMWPE	Ultra High Molecular Weight Polyethylene

Study Synopsis

Title	A prospective, post-market, multi-center evaluation of the clinical outcomes of the Secur-Fit Advanced Hip Stem
Short Title	Secur-Fit Advanced Outcomes Study
Protocol Number	75
Type	Post-market
Methodology	This study is a prospective, open-label, post-market, non-randomized, multi-center clinical evaluation of the Secur-Fit Advanced Hip Stem for primary total hip arthroplasty (THA) with a cementless application in a consecutive series of patients who meet the eligibility criteria. The total enrollment goal for the study is 314 cases, all of which will receive the Secur-Fit Advanced Hip Stem.
Study Duration	1. Follow-up of each primary THA case to 10 years 2. Enrollment period of 24 months 3. Approximate 12-year total duration
Study Center(s)	5 to 8 investigational centers
Hypothesis	The success rate of the Secur-Fit Advanced femoral stem, defined as absence of stem revision for aseptic loosening or device-related femoral fracture, is no worse than 99% at 5 years postoperative with a non-inferiority margin of 2.5%.

Objectives	**Primary:** • To evaluate and determine the success rate, defined as absence of stem revision for aseptic loosening or device-related femoral fracture, at 5 years postoperative with the Secur-Fit Advanced Hip Stem. **Secondary**: • To evaluate all-cause revision and removal rates with the Secur-Fit Advanced Hip Stem and compare with those reported for other primary hip stems in the literature. • To evaluate rate of device-related femoral fracture among patients implanted with the Secur-Fit Advanced Hip Stem within 30 days postoperative, and compare with rates reported for other primary hip stems in the literature. • To demonstrate the close relationship between the seating height of the Secur-Fit Advanced Hip Stem and its associated femoral broach.

Additional Data Collection	• Function and health related quality of life (QOL) will be compared between the Secur-Fit Advanced Hip Stem and published results for other primary hip systems, the following outcomes measures will be collected: o Harris Hip Score (HHS) o Short Form-12 (SF-12) o Lower Extremity Activity Scale (LEAS) o EQ-5D 1-year, 2-year and 5-year SF-12,LEAS and HHS will be presented with respect to improvement from preoperative scores. EQ-5D data will be summarized and presented. • An additional Follow-up Questionnaire will be administered annually in postoperative years 3, 4 and 6-10 to assess patient satisfaction and pain, and to capture adverse events. • Radiographic stability and complications will be compared between those implanted with the Secur-Fit Advanced Hip Stem and published results for other primary hip systems.
Number of Cases	Cases will be enrolled until 314 cases have received the Secur-Fit Advanced Hip Stem.

Inclusion/Exclusion Criteria	Inclusions: A. Patient has signed an IRB/EC approved, study specific Informed Patient Consent Form. B. Patient is a male or non-pregnant female, skeletally mature and age 21-75 years at time of study device implantation. C. Patient has a diagnosis of Non-Inflammatory Degenerative Joint Disease. D. Patient is a candidate for primary total hip arthroplasty. E. Patient is willing and able to comply with postoperative scheduled clinical and radiographic evaluations and rehabilitation. Exclusions: F. Patient has previously undergone open surgical intervention on the operative hip. G. Patient has a prior femoral fracture, with or without deformity, on the operative side. H. Patient has an existing total hip replacement on the contralateral side. I. Patient requires simultaneous bilateral total hip replacement. J. Patient has a Body Mass Index (BMI) > 45. K. Patient has an active or suspected latent infection in or about the affected hip joint at time of study device implantation. L. Patient has a neuromuscular or neurosensory deficiency that would create an unacceptable risk of instability, prosthesis fixation failure or complications in postoperative care, or which limits the ability to evaluate the safety and efficacy of the device.

Inclusion/Exclusion Criteria	Exclusions (continued): M. Patient has bone stock that is inadequate for support or fixation of the prosthesis, or is diagnosed with a systemic disease (e.g. Lupus Erythematosus) or a metabolic disorder (e.g. Paget's disease) leading to progressive bone deterioration. N. Patient is immunologically suppressed or receiving steroids in excess of normal physiological requirements (e.g. > 30 days). O. Patient has a known sensitivity to device materials. P. Patient is a prisoner.
Study Device	**Secur-Fit Advanced Hip Stem** Required Components : 1. Secur-Fit Advanced Femoral Stem The femoral component must be used in a cementless application. Stryker acetabular components and femoral bearing heads must be used according to this study protocol. The following ancillary devices are permissible: • Compatible Stryker femoral bearing heads • Compatible Stryker acetabular shells, liners and inserts The compatible Stryker head and acetabular components are listed in the surgical protocol.

Statistical Methodology	**Primary Objective:** o 5-year success rate of the Secur-Fit Advanced Hip Stem with an endpoint of revision for aseptic loosening or device-related femoral fracture will be compared with a 99% success rate, with a 2.5% noninferiority margin. **Secondary Objectives:** o The Kaplan-Meier survival curve of revision/removal for the Secur-Fit Advanced Hip Stem will be displayed. o The rate of device-related femoral fracture within 30 days of index THA will be reported. o The mean amount of unintended exposure or countersink of the femoral component upon final seating will be presented.

Evaluation Schedule

Evaluation	Preop X-rays (-1 yr) CRFs (-4 mos)	Intraop	6 weeks (± 3 wks)	1 year (± 2 mos)	2 years (± 2 mos)	3 years (± 3 mos)	4 years (± 4 mos)	5 years (± 4 mos)	6 years (± 4 mos)	7 years (± 4 mos)	8 years (± 4 mos)	9 years (± 4 mos)	10 years (±4 mos)
Inclusion/ Exclusion	**X**												
Demographics & Medical History	**X**												
Preoperative Functional Evaluation	**X**												
Preoperative Digital Template	**S**												
Surgical Details		**X**											
Postoperative Functional Evaluation			**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**
Lauenstein lateral and anteroposterior (AP) pelvis radiographs	**X**		**X**	**X**	**X**			**X**		**Optional**			**Optional**
Follow-up Questionnaire			**As needed**	**As needed**	**As needed**	**X**	**X**	**As needed**	**X**	**X**	**X**	**X**	**X**

X: Evaluation is required for all cases.
S: Templating and preoperative plan will be collected for a subset of patients at select sites.

Functional Evaluation: The Functional Evaluations include the HHS, 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 well-being.
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 dislocation, patient satisfaction, pain and whether or not there have been any revisions or removals of the study device 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

THA is one of the most clinically successful and cost-effective interventions in health care. Numerous surgeons have reported excellent long-term results in terms of reducing pain, improving function and QOL in patients with debilitating hip disease.[1]

Cemented as well as cementless hip stems have shown good results in THA, even in younger patients.[2] Implant design may contribute to the success of an implant. In a multi-center study of 251 cases receiving proximally hydroxyapatite-coated straight, collarless femoral stems manufactured from titanium alloy (OmniFit HA), radiographic evaluations performed by D'Antonio et al.[3] indicated a high rate of early and continuing fixation and consistent adaptive bone remodeling around the stem through 6 years postoperative. Fifteen-year results from the same study demonstrated excellent long-term survivorship with a revision rate of 0.6% for both aseptic loosening and mechanical failure of the femoral stem.[4] Additionally, in a series of 31 bilateral patients implanted with OmniFit HA, Schwarzkopf et al.[5] observed femoral component survivorship of 100% through the 23-year follow-up period for the 27 patients available.

Following the design philosophy of the successful OmniFit HA stem, the next generation of double-wedge, metaphyseal filling stems introduced by Stryker was the Secur-Fit family. The main design change from OmniFit to Secur-Fit was the addition of a proximal roughened titanium surface to which the hydroxyapatite (HA) is applied. The neck angle of the Secur-Fit stem is 132°; this angle is decreased to 127° in the Secur-Fit Plus design to produce increased femoral offset. In a retrospective review of 105 cases implanted with either Secur-Fit or Secur-Fit Plus at 5 to 10 years postoperative, Incavo et al.[6] reported that all stems achieved and maintained stable fixation. Equal leg lengths were achieved in 82% of Secur-Fit cases and 92% of Secur-Fit Plus cases, leading the authors to note that availability of both a standard- and high-offset option may facilitate soft-tissue balancing intraoperatively without adversely affecting postoperative leg length.

The stem body design of the Secur-Fit Advanced Hip Stem is based on the Secur-Fit HA Hip Stem (K982032, K041170). Like the predicate for body design, the Secur-Fit Advanced Hip Stem is a straight stem with a normalization pattern on the anterior and posterior aspects of the proximal end to facilitate press-fit stability and load transmission to the proximal region of the femur. Based on 3-Dimensional simulations, these normalizations are designed to convert medial and lateral shear stresses to compressive forces, which may facilitate proximal loading.(RD-13-001). The distal portion of the stem has a polished tip, and the neck region has been polished and shot peened. The stem neck is designed with a Howmedica Osteonics V40 taper on the proximal end and is available in both 127° and 132° neck-stem angles. The Secur-Fit Advanced Hip Stem is manufactured from Titanium (Ti-6Al-4V) alloy with a commercially pure Titanium (CP Ti) and HA coating to establish good initial fixation.

1.2 Study Device

The Secur-Fit Advanced Hip Stem was cleared for use under FDA 510(k) K122853 on February 1, 2013. See Appendix A for the FDA clearance letter.

The Secur-Fit Advanced Hip Stem is intended for cementless, press-fit application, and will be available in nine sizes ranging from size 4 through 12. Sizes 4 and 5 are available with a 132° offset angle only; all other sizes are available in both 127° and 132° offset angles. Details of the device design are presented in Section 6, Device Description.

1.3 Preclinical Data

The following bench tests (with test report numbers) were conducted with the Secur-Fit Advanced Hip Stem:

Coating Thickness (MT01016)

The mean coating thickness for the titanium plasma sprayed coating and Pure-Fix HA coating was 0.446 mm and 0.058 mm respectively.

Tensile Bond Strength (MT01016)

The average tensile strength of the titanium plasma sprayed and Pure-Fix HA coated specimens were 39.11 MPa.

Shear Bond Strength (MT01016)

The average shear bond strength of the PureFix HA on the titanium plasma sprayed coating was 23.85 MPa.

Fatigue Strength (MT01016)

Fatigue strength of the Titanium Plasma sprayed and PureFix HA coating on the shot peened Ti6Al-4V ELI substrate was 552 MPa at ten (10) million cycles.

Abrasion Resistance (MT01016)

The average weight loss as a result of abrasion testing of the PureFix HA and Titanium plasma sprayed coupons was 1.57 mg.

Neck Fatigue Testing (RD-12-092)

All eight 127° Size 8 Secur-Fit Advanced Hip Stems successfully withstood 5340N (1200lbf) for ten million (10×10^6) cycles without failure and with no loss of mechanical integrity as specified by ISO 7206-6. Based on loading characteristics, the maximum head offset for the Size 4 stem is +5 mm.

Distal Fatigue Testing (RD-12-093)

Eight 127° Size 6 representative stems, which were plasma spray HA coated over plasma spray CP Ti proximal coating, were used for testing. The stems were oriented at 10° valgus/9° flexion at a potting level of 80 mm from the worst case (+12 mm) head center consistent with ISO 7206-4. All eight 127° Size 6 Secur-Fit Advanced Hip Stems successfully withstood 2300 N (517 lbf) for five million (5.0×10^6) cycles without failure and with no loss of mechanical integrity as specified by ISO 7206-4:2010.

The results of the bench top testing conducted for the new Secur-Fit Advanced Hip Stem identified acceptance criteria were met.
Copies of all test reports are available at Stryker Orthopaedics.

1.4 Clinical Data to Date

This study is the first Stryker sponsored multi-center prospective data collection on the Secur-Fit Advanced Hip Stem.

2 Study Objectives

2.1 Efficacy

2.1.1 Primary

The primary objective of this study is to evaluate the success rate of cementless primary total hip replacement with the Secur-Fit Advanced Hip Stem. Success will be defined as absence of femoral stem revision for aseptic loosening or device-related femoral fracture at 5 years postoperative. It is expected that the success rate of the Secur-Fit Advanced Hip Stem group will be non-inferior to the selected reference rate of 99% at 5 years postoperative.

2.1.2 Secondary

The secondary objectives of this study will include evaluation of all-cause revision and removal rates with the Secur-Fit Advanced Hip Stem and comparison with those reported for other primary hip systems in the literature.

Additionally, the rate of device-related femoral fracture among patients implanted with the Secur-Fit Advanced Hip Stem within 30 days postoperative will be evaluated and compared with rates reported for other primary hip stems in the literature.

The close relationship between the seating height of the Secur-Fit Advanced Hip Stem and its associated femoral broach will also be demonstrated by intraoperatively measuring the component exposure or countersink upon final seating.

2.1.3 Additional Data Collection

Clinical Outcomes:

Clinical outcomes will be evaluated with the total HHS, including pain, motion and function, preoperatively and at the 6-week, 1, 2 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 in for these optional visits.

Patient Outcomes:

Pain, function and health related QOL will be compared between the Secur-Fit Advanced Hip Stem and reports in the literature for other primary femoral stems on the market. The SF-12 is a 12 item patient self-assessment evaluating health and general well-being. 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 and at the 6-week, 1, 2, 3, 4, and 5-year time points.

A Follow-up Questionnaire will be administered annually in postoperative years 3, 4 and 6-10 to assess patient satisfaction and pain, and to capture AEs. This questionnaire, which will also be completed during each interval through 5 years postoperative at which the subject is not seen by the investigator, will provide the information necessary to create an accurate Kaplan-Meier Survival Curve. 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.

Radiographic Outcomes:

To assess radiographic stability as compared with other primary femoral stems, radiographs will be taken and collected in the low AP pelvis and Lauenstein lateral views for the preoperative, 6-week, 1, 2 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 low AP pelvis view allows for measurement of the position of the hip center, femoral offset and neck angle, and any leg length discrepancy. The Lauenstein lateral view allows for evaluation of the entire hip joint as well as the femoral head, neck and proximal shaft.[7] Suggested radiographic technique for the views required is included in Appendix C.

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 view.[8,9] Radiographic analysis of the femoral component will employ seven zones (Zone 1 - Zone 7) in the AP views and seven zones (Zone 8 – Zone 14) in the lateral view. Numerous parameters will be reviewed by zone, including radiolucency, hypertrophy, condensation 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 subsidence of greater than 5 mm, migration of greater than 5° in any direction or at least 2 mm radiolucency in all zones within a single view will be considered radiographic failures.

2.2 Safety

All operative site events occurring at any time as well as all serious adverse events (SAEs) occurring in the perioperative period (intraoperative to hospital discharge) will be collected and compared to published data. It is expected that the AE rates reported for the Secur-Fit Advanced Hip Stem will be comparable to those reported in the literature for other primary femoral stems on the market. 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

3.2.1 Centers for Standard Data Collection

Cases will be enrolled at five to eight centers. The enrollment goal is approximately 41 cases per center utilizing the Secur-Fit Advanced Hip Stem but will vary dependent upon the number of participating centers. Although a goal 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 enrollment goal, 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 Institutional Review Board (IRB) or Ethics Committee (EC)

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 until a total of 314 cases receive the Secur-Fit Advanced Hip Stem.

3.4 Estimated Study Duration

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

To allow for a learning curve with the use of the device, enrollment of cases into the study will commence when three cases have been completed at the center using the Secur-Fit Advanced Hip Stem.

4 Eligibility

The following criteria will be used to distinguish patients eligible for enrollment into this study. Proper implant selection must consider design, fixation, and environmental variables including: patient weight, age, bone quality and size, activity level and pre-operative level of health, as well as the surgeon's experience and familiarity with the device.

4.1 Inclusion Criteria

A. Patient has signed an IRB/EC approved, study specific Informed Patient Consent Form.
B. Patient is a male or non-pregnant female, skeletally mature and age 21-75 years at time of study device implantation.
C. Patient has a diagnosis of Non-Inflammatory Degenerative Joint Disease.
D. Patient is a candidate for primary cementless total hip arthroplasty.
E. Patient is willing and able to comply with postoperative scheduled clinical and radiographic evaluations and rehabilitation.

4.2 Exclusion Criteria

F. Patient has previously undergone open surgical intervention on the operative hip.
G. Patient has a prior femoral fracture, with or without deformity, on the operative side.
H. Patient has an existing total hip replacement on the contralateral side.
I. Patient requires simultaneous bilateral total hip replacement.
J. Patient has a Body Mass Index (BMI) > 45.
K. Patient has an active or suspected latent infection in or about the affected hip joint at time of study device implantation.
L. Patient has a neuromuscular or neurosensory deficiency that would create an unacceptable risk of instability, prosthesis fixation failure or complications in postoperative care, or which limits the ability to evaluate the safety and efficacy of the device
M. Patient has bone stock that is inadequate for support or fixation of the prosthesis, or is diagnosed with a systemic disease (e.g. Lupus Erythematosus) or a metabolic disorder (e.g. Paget's disease) leading to progressive bone deterioration.
N. Patient is immunologically suppressed or receiving steroids in excess of normal physiological requirements (e.g. > 30 days).
O. Patient has a known sensitivity to device materials.
P. Patient is a prisoner.

5 Subject Enrollment

5.1 Treatment Assignment

All subjects will receive the Secur-Fit Advanced Hip Stem.

5.2 Randomization

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

6 Device Description

6.1 Study Device

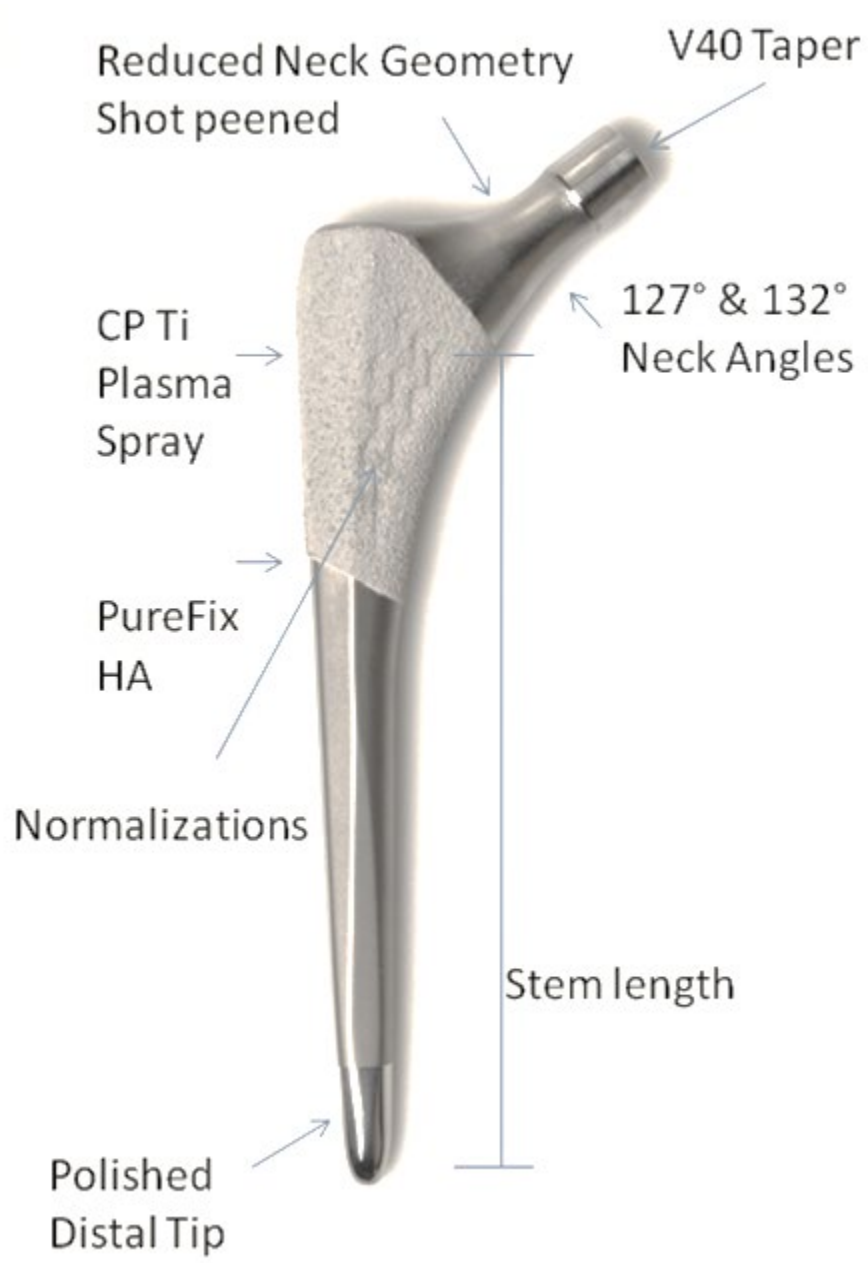
The Secur-Fit Advanced Hip Stem has been cleared for use in the United States; therefore, this study is considered a post-market assessment. All cases in this study will receive the Secur-Fit Advanced Hip Stem.

The Secur-Fit Advanced Hip Stem is a straight stem intended for cementless, press-fit application. It is a non-porous coated femoral stem with a fit and fill design to provide rotational stability. The stem body design is based on the Secur-Fit HA Hip Stem. Like the predicate for body design, the Secur-Fit Advanced Hip Stem is a straight stem with a normalization pattern on the anterior and posterior aspects of the proximal end (depicted in Figure 1) to facilitate press-fit stability and load transmission to the proximal region of the femur. Based on 3-Dimensional simulations, these normalizations are designed to convert medial and lateral shear stresses to compressive forces, which may facilitate proximal loading.(RD-13-001). Medial curvature of the stem is proportional and size-specific.

The Secur-Fit Advanced Hip Stem will be fabricated from Titanium (Ti-6Al-4V) Alloy, with a CPTi plasma spray coating covered with a HA powder (Pure-Fix HA). The distal portion of the stem has a polished tip, and the neck region has been polished and shot peened.

The Secur-Fit Advanced Hip Stem will be available in 9 sizes ranging from size 4 through 12; the catalog numbers are listed in Table 1. Stem length will range from 110 mm to
160 mm, increasing in length as the stem size increases. Stem length is measured from the medial calcar point to the distal tip of the stem. The stem's neck is designed with a Howmedica Osteonics V40 taper on the proximal end similar in design to the Accolade II.

Figure 1: Secur-Fit Advanced A/P View



The only difference in the V40 taper of the Secur-Fit Advanced Hip Stem to the Accolade II is the taper length. The neck lengths of the Secur-Fit Advanced Hip Stem range from 26 mm to 40 mm and grow with stem size. Additionally, the necks are available in two angles (127° and 132°) that provide dual head offsets. Sizes 4 and 5 are available with a 132° offset angle only; all other

sizes are available in both 127° and 132° offset angles. Overall femoral offsets achievable with a +0 mm head range from 31.5 mm to 53.7 mm.

Table 1: Secur-Fit Advanced Stem Offsets

STEM	CATALOG NUMBER	NECK ANGLE (°)	STEM SIZE	STEM LENGTH (mm)	NECK LENGTH (mm)	FEMORAL OFFSET WITH +0mm HEAD (mm)	DISTAL TIP DIAMETER* (mm)
Secur-Fit Advanced 127°	1601-06127	127	6	120	28	37.2	6.9
	1601-07127	127	7	130	32	41.5	7.4
	1601-08127	127	8	136	32	42.4	8.1
	1601-09127	127	9	142	36	46.9	8.9
	1601-10127	127	10	148	36	48.1	9.7
	1601-11127	127	11	155	40	52.6	9.7
	1601-12127	127	12	160	40	53.7	10.7
Secur-Fit Advanced 132°	1601-04132	132	4	110	26	31.5	5.1
	1601-05132	132	5	115	26	32.5	6.0
	1601-06132	132	6	120	26	33.6	6.9
	1601-07132	132	7	130	30	37.5	7.4
	1601-08132	132	8	136	30	38.4	8.1
	1601-09132	132	9	142	34	42.6	8.9
	1601-10132	132	10	148	34	43.8	9.7
	1601-11132	132	11	155	38	47.9	9.7
	1601-12132	132	12	160	38	49.0	10.7

The following femoral component catalog numbers are permissible according to this study protocol and are in the following format, where 'XX' varies by size:

1601-XX127

1601-XX132

The full listing of permissible femoral component catalog numbers may be found in Appendix D.

Additionally, only the following **Stryker compatible** ancillary devices may be used, according to this study protocol:

- Compatible Stryker femoral bearing heads
- Compatible Stryker acetabular shells, liners and inserts

The compatible Stryker head and acetabular components are listed in the surgical protocol.

For reference, compatible femoral heads and acetabular components are listed in Table 2 and Table 3 below. In the case of any uncertainty regarding device compatibility, the current version of the Secur-Fit Advanced surgical protocol should be reviewed.

Table 2: Femoral Head Compatibility

HEAD	HEAD SIZE	HEAD OFFSETS
CoCr V40	22	+0, +3, +8
	26	-3, +0, +4, +8, +12
	28	-4, +0, +4, +8, +12
	32	-4, +0, +4, +8, +12
	36	-5, -4, +0, +4, +5, +8, +10
	40	-4, +0, +4, +8, +12
	44	-4, +0, +4, +8, +12
Alumina V40	28	-2.7, +0, +4
	32	-4, +0, +4
	36	-5, +0, +5
Alumina C-Taper (when used with C-Taper Sleeve – catalog # 17-0000E)	28	-2.5, +0, +5
	32	-2.5, +0, +5
	36	-5, +0, +5
delta BIOLOX V40	28	-4, -2.7, +0, +4
	32	-4, +0, +4
	36	-5, -2.5, +0, +2.5, +5, +7.5
delta BIOLOX C-Taper (when used with C-Taper Sleeve – catalog # 17-0000E)	28	-2.5, +0, +2.5, +5
	32	-2.5, +0, +2.5, +5
	36	-5, -2.5, +0, +2.5, +5, +7.5
delta BIOLOX Universal Taper (when used with Universal Taper Sleeve- catalog #6519-T-XXXX)	28	-2.5, +0, +4
	32	-2.5, +0, +4
	36	-2.5, +0, +4
	40	-2.5, +0, +4
	44	-2.5, +0, +4

*Maximum head offset for Size 4 stem is +5

Table 3: Secur-Fit Advanced Compatible Acetabular Components

Trident X3 Acetabular Inserts
Trident Crossfire Elevated Rim Liners
Trident Crossfire Poly Liners, 10° or 0° profile
Trident Crossfire Eccentric Poly Liners, 10° or 0° profile
Trident Poly Liners, 10° or 0° profile
Trident Eccentric Poly Liners
Trident Constrained Insert
Crossfire Series II Inserts (2041C, 2042C, 2043C, S2301, S2302)
Series II Inserts, and Series II Eccentric Inserts
Constrained Liner
Series I Inserts
System 12 Inserts (Standard and Crossfire)
All Poly Cup
Trident All Poly Cup
Crossfire Trident All Poly Cup
UH1
Centrax Bipolar
PCA Acetabular Insert
Precision Acetabular Components
Trident N_2/Vac Polyethylene Inserts
Trident Hemispherical Solid Back Shells
Trident Hemispherical PS HA
Trident Hemispherical Shells (AD and AD-HA)
Trident PSL HA Solid Back Shells
Trident Hemispherical Cluster Shells
Trident PSL HA Cluster Shells
Trident Hemispherical Multi-Hole Shells
Tritanium Acetabular Shell System
Trident Porous Titanium Acetabular Components
Restoration ADM
MDM
Exeter X3 RimFit Cup

6.2 Device Retrieval Process

Stryker Orthopaedics will retrieve the Secur-Fit Advanced Hip Stem and/or adjacent tissues for analysis to help characterize potential device-related complications. In the event that the Secur-Fit Advanced Hip Stem is removed from a study subject, the procedure outlined in the Retrieved Implant Analysis Protocol (Appendix E) should be followed. In addition:

1. When revision of a study subject is scheduled, the study coordinator (SC) should contact the Clinical Study Manager (CSM) or other Stryker Clinical Research personnel assigned to the project, as soon as possible.
2. Stryker Clinical Research 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, following the instructions in Appendix E.
4. The SC, an identified field representative or Stryker Clinical Research will complete a Product Experience Report (PER).
5. If not completed by Stryker Clinical Research, the PER should be faxed or emailed to Stryker Product Surveillance at 201-831-6775 or soprodexreports@stryker.com, as well as to Stryker Clinical Research at 201-831-6454 or to the Clinical Research email addresses listed on the Sponsor Contact Sheet.
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. Stryker Clinical Research 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/EC approved Informed Patient Consent Form prior to participating in any study related activities. Consent must be obtained within 4 months prior to surgery.

Once the patient has been consented, preoperative data will be collected including: demographics, medical history, HHS, SF-12, LEAS, EQ-5D, AP pelvis and Lauenstein lateral radiographs. At sites participating in the preoperative planning subset, investigators will submit digital images of each subject's preoperative template as well as additional information regarding planned biomechanical parameters and devices to be implanted.

All preoperative data must be collected within 4 months prior to the scheduled date of surgery, with the exception of radiographs, acceptable within 1 year prior to 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 (± 3 weeks), the following evaluations will be collected: HHS, SF-12, LEAS, EQ-5D, AP pelvis and Lauenstein lateral radiographs.

In the event that an in-person visit cannot be conducted and radiographs cannot be obtained, a Follow-up Questionnaire will be completed via mail, online completion (if available), or telephone interview with the subject by investigative site personnel.

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, 2-year and 5-year. Tools for postoperative evaluation at each of these intervals will be the HHS, AP pelvis and Lauenstein lateral radiographs. In the event that an in-person visit cannot be conducted and radiographs cannot be obtained, a Follow-up Questionnaire will be completed via mail, online completion (if available), or telephone interview with the subject by investigative site personnel.

Patient outcomes data will also be collected with the Follow-up Questionnaire, SF-12, LEAS, and EQ-5D patient questionnaires at each office visit and at the 3-year and 4-year intervals via mail or online completion, if available.

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 through 10-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, SF-12, LEAS and EQ-5D patient questionnaires. In the second phase of the study, all subjects will complete a brief Follow-up 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 subject telephone interview, or by the subject either at home or during a clinic visit. The questionnaire will be used to obtain the following information, at a minimum:

- Subject 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.

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 and occur within the perioperative period (intraoperative to hospital discharge)
- All AEs related to the operative site, regardless of seriousness or time of occurrence

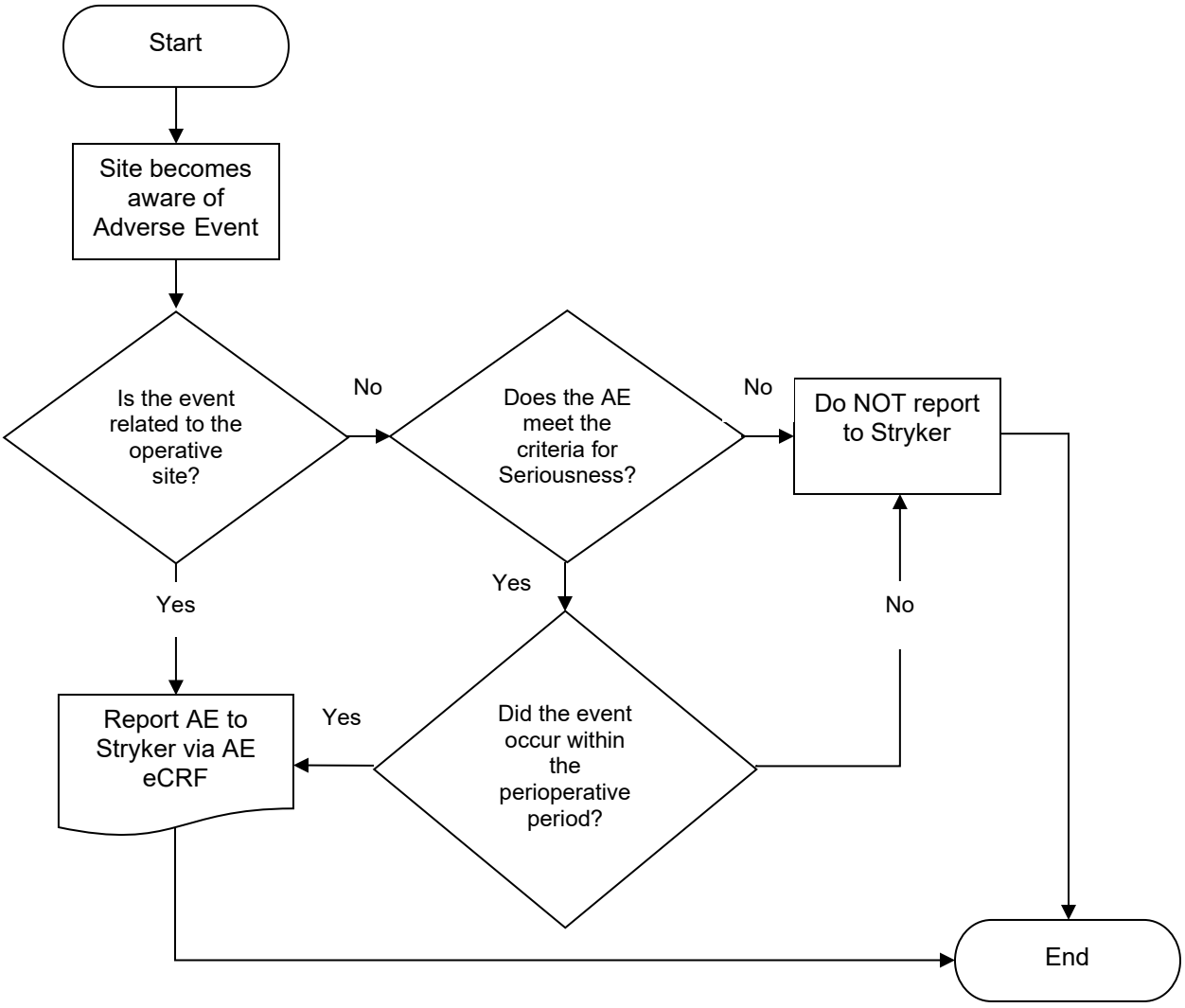
On postoperative functional evaluations, investigators and SCs will be prompted to question subjects as to whether they have seen a doctor for any reason, been hospitalized for any reason or have a current impediment to their function.

Additionally, SCs will be responsible for following up with the subjects regarding any questionable responses received on the Follow-up Questionnaire administered in postoperative years 6

through 10. If it is determined upon this further investigation that a protocol-defined AE has occurred, the SC will be responsible for completing an AE eCRF, submitting the event to Stryker and reporting to the IRB/EC, as required.

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

Figure 4. 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 the 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

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 Stryker Clinical Research either by telephone/fax/email within 24 hours of the site 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 within 24 hours. If a SAE occurs, the de-identified source documentation must be uploaded to the appropriate location within 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 AEs are submitted through eCRF entry 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 EC or 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 the success rate at 5 years postoperative with the Secur-Fit Advanced Hip Stem, where success is defined as absence of femoral stem revision and/or removal for aseptic loosening or device-related femoral fracture at 5 years postoperative.

9.1.2 Secondary Efficacy Parameters

The secondary efficacy parameters include:

- The all-cause revision and/or removal rates of the Secur-Fit Advanced Hip Stem;
- The rate of device-related femoral fracture among patients implanted with the Secur-Fit Advanced Hip Stem within 30 days postoperative; and
- The component exposure or countersink upon final seating intraoperative.

Additional data will be collected as noted in Section 2.1.3; related details are in Section 9.4.1 Data Summary.

9.1.3 Primary Efficacy Analysis

The primary hypothesis to be tested will be that the success rate at 5 years postoperative with the Secur-Fit Advanced Hip Stem is not worse than 99% with a non-inferiority margin of 2.5%.

That is, the following hypothesis will be tested:

H_0: Pt <= 99% - 2.5% H_A: Pt > 99%- 2.5%

Here, Pt is the success rate at 5 years postoperative with the Secur-Fit Advanced Hip Stem

A 90% two-sided confidence interval will be computed for the success rate at 5 years. If the lower bound of the confidence interval is greater than 96.5%, then the non-inferiority hypothesis will be supported.

9.1.4 Secondary Efficacy Analysis

The all-cause revision and/or removal rates of the Secur-Fit Advanced Hip Stem will be reported.

The rate of device-related femoral fracture among patients implanted with the Secur-Fit Advanced Hip Stem within 30 days postoperative will be evaluated.

The mean amount of unintended exposure or countersink of the femoral component upon final seating will be presented; standard deviation, median, minimum, and maximum will be displayed.

The analysis for the additional data collection is in 9.4.1 Data Summary.

9.2 Safety

9.2.1 Safety Parameters

Safety parameters include all protocol-defined adverse events as well as revision and/or removal rates. For details regarding protocol-defined adverse events, see Section 8.1.

9.2.2 Safety Analyses

The frequency and percentage of all protocol-defined adverse events will be tabulated. For details regarding protocol-defined adverse events, see Section 8.1.

9.3 Missing Data

No missing data will be imputed.

9.4 Statistical Methodology

9.4.1 Data Summary

Descriptive statistics will be computed for all baseline conditions and demographic parameters. That is, for continuous data, the N, mean, median, standard deviation, minimum and maximum will be computed. For categorical data, the frequency will be computed. The data will be presented by appropriate subgroups (e.g., center, gender).

A Kaplan-Meier survivorship curve will be displayed for revision and/or removal of the Secur-Fit Advanced Hip Stem for aseptic loosening or device-related femoral fracture.

A Kaplan-Meier survivorship curve will be displayed for all-cause revision and/or removal of the Secur-Fit Advanced Hip Stem.

For the additional data collected according to Section 2.1.3, data will be summarized according to visit. For parameters represented by continuous variables (e.g., ROM), the

summaries will consist of the N, mean, median, standard deviation, minimum, and maximum values. For categorical variables (e.g., Mobility from EQ-5D), the frequency and percentage in each category will be presented. A paired t-test will be performed to evaluate the change in clinical and patient outcomes, preoperative to 5 years within the Secur-Fit Advanced Hip Stem. The 1-year, 2-year and 5-year SF-12, LEAS and HHS will be presented with respect to improvement from preoperative scores.

For the Follow-up Questionnaire, frequency and percentage will be computed for each category according to visits. Applicable lists based on Follow-up Questionnaire will be generated to capture AEs.

For radiographic data, data will be presented according to visits for available parameters. Frequency and percentage will be computed for radiolucency according to visit. Lists will be generated for migration over time. Radiographic failure will be evaluated, where radiographic failure is defined as subsidence of greater than 5 mm, migration of greater than 5° in any direction or at least 2 mm radiolucency in all zones within a single view.

Documentation of statistical analyses utilizing SAS® software version 9.1.3 or higher.

9.4.2 Sample Size Justification

With a reference value of 99% of success rate at 5 years, under the regular assumptions of 5% significance level (or 95% one-sided confidence interval), 80% power, 2.5% non-inferiority margin, the sample size is 277. After factoring a 15% lost to follow-up rate, the final sample size is 326. A significant decrease in screening/enrollment occurred after 2018, resulting in a final sample size of 314 cases.

9.4.3 Interim Analyses

No interim analysis is planned.

9.4.4 Analysis Population

Per Protocol Population: The study population for analysis will include all non-censored subjects who receive the Secur-Fit Advanced Hip Stem and are available for efficacy evaluation.

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

Safety Population: The safety population will include all non-censored subjects who received the Secur-Fit Advanced Hip Stem.

The safety analysis will be based on the safety population.

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. All handouts, brochures, advertisements, etc. must be approved by the IRB/EC prior to the dissemination of any recruitment materials to potential subjects. Study advertisement content may be found in Appendix F.

10.2 Patient Informed Consent and Guidelines

All patients for this study will be provided an Informed Patient Consent Form describing this study and providing sufficient information for them to make an informed decision about their participation. The Informed Patient Consent Form 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. For international sites, the applicable country regulations are required. See Appendix G for a copy of the Model Informed Patient Consent. This will be submitted with the protocol for review and approval by the IRB/EC 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/EC approved Informed Patient 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 Informed Patient Consent Form'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 Informed Patient Consent Form. The patient or his/her legal representative should receive a signed copy of the Informed Patient Consent Form, according to GCP guidelines.

The procedure for obtaining informed consent is outlined below:

- Use a current IRB/EC approved copy of the Informed Patient Consent Form.
- Review thoroughly with the patient before having them sign.
- After the patient has consented to the procedures, ensure he/she signs and dates the Informed Patient Consent Form.
- The person obtaining consent also signs and dates the signature page.
- Provide a copy of the Informed Patient Consent Form to the patient.
- If required, provide the hospital with a copy of the signed Informed Patient Consent Form.
- 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 for each treatment group:

Secur-Fit Advanced Hip Stem with any compatible Stryker acetabular components:

- Secur-Fit Advanced Hip Stem
- Compatible Stryker femoral head
- Compatible Stryker acetabular insert
- Compatible Stryker acetabular liner (if used)
- Compatible Stryker acetabular shell

Revision or removal of the Secur-Fit Advanced Hip Stem for device-related femoral fracture or aseptic loosening constitutes a failure. Revision or removal of the Secur-Fit Advanced Hip Stem for any reason requires study termination for the subject.

If revision of the femoral head or any acetabular component is required during the study, the event 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 H.

11.2 Confidentiality

This study will comply with the 2002 HIPAA privacy rule. 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 is not 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 include 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 preoperative and follow-up visits must be documented in the subject's chart. This includes range of motion 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 documented. All missing data must be explained. It is recommended that eCRFs be completed and electronically signed by the investigator within 2 weeks of the evaluation date.

11.5 Data Clarification Requests

If errors or omissions are noted by Stryker upon review of the data entered into the eCRFS, a data clarification request (DCR) will be sent to the center within the EDC system. Queries should be answered in a clear and comprehensible manner. If the clarification requires a change to study data, the EDC system will update the eCRF automatically with the data captured in the DCR response. The investigative center will be required to reapply their electronic signature to the modified eCRF. Modified eCRFs need not be printed and included in conjunction to answered DCRs.

11.6 Protocol Deviations

Any deviation from this protocol will be recorded in Stryker’s Clinical Trial Management System and must be reported to the EC/IRB by the investigational site according to their reporting procedures. Protocol Deviations for this study may include the following; this list may not be all-inclusive:

- 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

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 THA procedure.

12.2 Potential Risk

The study involves the routine assessment of a primary THA procedure. The Secur-Fit Advanced Hip Stem has been cleared for use by the FDA and will be used according to its labeling, included in Appendix I. Assessment involves questionnaires, patient and physician assessments as well as routine radiographs. The information collected will be kept confidential and will comply with the HIPAA privacy rule.

While the expected life of THA 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 THA 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 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.

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.

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 THA procedures, such as those performed with the Secur-Fit Advanced Hip Stem, 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 Secur-Fit Advanced Hip Stem 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 well being 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 device by comparing it to published results for other similar 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 monitoring 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, as applicable, and has adequate space to conduct the monitoring visit, when applicable. 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:

- An area where they can review study data, when monitoring is conducted on site
- Access to eCRF data for all cases
- Access to source documentation
- Regulatory documents
- Time to discuss findings 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 an Informed Patient Consent Form describing this study and providing sufficient information for patients to make an informed decision about their participation. This Informed Patient 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 EC/IRB approved Informed Patient Consent Form, must be obtained before that patient is submitted to any study procedure. This Informed Patient 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

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

Additionally, at pre-determined study visit intervals, Stryker may reimburse subjects with a modest stipend for protocol-required data collection. This stipend system must be approved by the Institution's IRB prior to implementation and will be based upon individual IRB approval from each site.

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 2, 5 and 10 years of follow-up. Early results with regard to surgical information and postoperative biomechanics may be published prior to the 2-year time point. Additional publication proposals may also 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 2, 5 and 10-year multi-center publications are submitted. Although Stryker will not be involved in coordinating these independent manuscripts, 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.

17 References

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