Multi-Center, Non-Controlled, Prospective Radiostereometric Analysis of the Pinnacle Acetabular Shell

SHORT TITLE: Pinnacle RSA Study

Protocol Number: DSJ_2018_02

Version Rev 5: 25 March 2022

Clinical Sponsor:

DePuy Synthes Joint Reconstruction
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Warsaw, IN 46581

PPD

PPD, Vice President, Clinical and External Research

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Investigator Signature Page

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Document Type	Revision	Effective Date
Original	1	March 27, 2019
Administrative	2	July 2, 2019
Administrative	3	October 16, 2019
Amendment	4	April 17, 2020
Amendment	5	March 25, 2022

I have read this protocol and agree to conduct this clinical investigation in accordance with the design and specific provisions outlined herein. I understand the protocol and I understand I am solely responsible to ensure the investigation is conducted in accordance with Good Clinical Practices (GCP), applicable country regulations, the Declaration of Helsinki, the signed clinical study contract with the Sponsor and with the protocol outlined herein. I will conduct this study as outlined therein and will make reasonable effort to complete the study within the time period designated by the Sponsor.

I will provide copies of the protocol and all pertinent information to all individuals responsible to me who will assist in the conduct of this study. I will discuss this material with them to ensure they are fully informed regarding the device and the conduct of the study.

I will fulfill the requirements of my Research Ethics Board (REB)/Ethics Committee (EC), or other oversight committee(s), to ensure complete and continual oversight of this clinical investigation. I will use an Informed Consent Document approved by the Sponsor and my reviewing REB/EC (where required).

I agree to report all information or data in accordance with the protocol and, in particular, I agree to report any serious adverse events, device related adverse events, or procedure related adverse events as defined in this protocol to the Sponsor, and comply with all adverse event reporting requirements of my reviewing REB/EC. I agree to permit he Sponsor, its authorized representatives, my reviewing REB/EC, and any regulatory authority/body access to all records relating to the clinical investigation.

The below signature confirms I have read and understood this protocol and its associated amendments or attachments and will accept respective revisions or amendments provided by the Sponsor.

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Signature of Principal Investigator: **Date**

Printed Name

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1 STUDY SUMMARY

Clinical Sponsor	DePuy Synthes Joint Reconstruction
Title	Multi-Center, Non-Controlled, Prospective Radiostereometric Analysis of the Pinnacle Acetabular Shell
Short Title	Pinnacle RSA Study
Protocol Number	DSJ_2018_02
IDE/IND Number	Not Applicable
Indication	Total Hip Arthroplasty (THA)
Study Article Description	Pinnacle Acetabular Shell (Sector, Gription, no screws), AltrX Polyethylene Liner and Corail Femoral Stem
Study Design	Multi-Center, Non-randomized, Non-Controlled, Prospective
Study Population	Males and Females, aged 21 or older, who are undergoing primary, unilateral THA
Number of Subjects	N = 90, with equal enrollment across three approaches: posterior (N=30), lateral (N=30) and anterior (N=30)
Number of Sites	2 (Canadian)
Enrollment Timeframe	9 months
Subject Follow-Up	Subjects will be seen at the following intervals: Preoperative, operative, 6 weeks, 3 months, 6 months, 1 year and 2 years postoperatively
Study Objectives	• To establish the mean subsidence profile of the Pinnacle Acetabular Shell using model-based RSA over the first two years post-implantation
Endpoints	<u>Primary:</u> • RSA measured mean superior cup migration (subsidence: Y translation in mm) at 2 years for each surgical approach separately, as well as combined <u>Secondary:</u> • RSA measured subsidence of the Pinnacle Acetabular Shell at 3 months, 6 months and 1 year • Other RSA measurements (X and Z translations in mm, X, Y, and Z rotations in degrees, and maximal total point motion in mm) at all time points • Linear head penetration at 1 year and 2 years for each surgical approach separately, as well as combined • Functional and health status as measured with Harris Hip Score, HOOS Jr. and Forgotten Joint Score (FJS-12) <u>Exploratory:</u>

	• Analyses to examine the correlation of functional and health status outcomes vs. RSA observations may be explored <u>Safety:</u> • The type and frequency of serious, non-serious and device or procedure related AEs across all study intervals will be summarized
Inclusion Criteria	1. Individuals requiring primary THA for a severely painful and/or disabled joint from osteoarthritis, traumatic arthritis, rheumatoid arthritis, or congenital hip dysplasia, AVN of the femoral head or acute traumatic fracture of the femoral head or neck 2. Individuals who are able to speak, read and comprehend the informed patient consent document and willing and able to provide informed patient consent for participation in the study and have authorized the transfer of his/her information to DePuy Synthes 3. Individuals who are willing and able to return for follow-up as specified by the study protocol 4. Individuals who are a minimum age of 21 years at the time of consent 5. Individuals who are willing and able to complete the Subject Hip Outcomes questionnaires as specified by the study protocol
Exclusion Criteria	1. Individuals have active local or systemic infection 2. Individuals who have loss of musculature, neuromuscular compromise or vascular compromise that would impact rehabilitation following surgery 3. Individuals with poor bone quality, such as osteoporosis, where in the surgeon's opinion, there could be considerable migration of the prosthesis or require additional acetabular cup fixation using screws, or a significant chance of fracture of the femoral shaft and/or the lack of adequate bone to support the implant(s) 4. Individuals with Charcot's or Paget's disease 5. Individuals who, in the judgement of the investigator, would not be a candidate for protocol allowable components to be used for their THA 6. Women that are pregnant or lactating

	7. Individuals who have had a contralateral hip that was implanted less than 6 months prior to the time of consent into this study or individuals that expect to have a contralateral hip implanted in the following 6 months at the time of consent into this study 8. Individuals that have amputations in either leg that would impact rehabilitation following surgery 9. Individuals who are bedridden. 10. Individuals that have participated in a clinical investigation with an investigational product (drug or device) in the last three months 11. Individuals currently involved in any personal injury litigation, medical-legal or worker's compensation claims 12. Individuals, in the opinion of the Investigator, who are drug or alcohol abusers or have psychological disorders that could affect their ability to complete patient reported questionnaires or be compliant with follow-up requirements 13. Individuals diagnosed and taking prescription medications to treat a muscular disorder that limits mobility due to severe stiffness and pain such as fibromyalgia or polymyalgia 14. Subject has a medical condition with less than 2 years life expectancy 15. Individual has a BMI $\geq$45 kg/m^2.
Safety Assessments	Type and frequency of device or procedure related Adverse Events will be collected. Site Ethics Committees/REBs will provide oversight for study subject safety.
Sample Size	The purpose of this study is to summarize the mean subsidence (superior cup migration) of the acetabular shell as measured with RSA. Mean subsidence will be summarized at all time points with 95% confidence intervals, for each surgical approach separately, as well as combined; there are no hypotheses in this study. The standard deviation in observed subsidence values at 2 years post-op is anticipated to be approximately 0.2 mm. Based upon this standard deviation, a sample size of N=30 is anticipated to provide a 95% confidence interval for each surgical approach separately with a margin of error of approximately $2(0.2/\sqrt{30}) = 0.073$ mm for each, which is deemed to be an adequate level of precision by the Sponsor.
Statistical Analysis	There are no formal hypothesis tests for this study. Summary statistics of primary, secondary and exploratory outcomes will be provided, along with 95% confidence intervals. Summaries will

	be provided for each surgical approach separately, as well as combined.
Interim Analysis	An interim analysis will be conducted when all subjects have reached 1-year post-op in order to give product development an understanding of acetabular cup subsidence that might be expected for future product development purposes. There is no intention to utilize this interim analysis as a means to justify stopping the study early.
Determination if DMC/CEC required	Not Required
Time and Events Schedule	See below

1.1 TIME AND EVENTS SCHEDULE

Event / Visit	Pre-op		Operative	Prior to Discharge	6 Weeks	3 Months	6 Months	1 Year	2 Years
	-270 to DOS	-90 to DOS	Day 0	Day 1 to Discharge	28-56 d	60-120 d	135-225 d	275-455 d	640-820 d
Complete Screening Log		✓							
Obtain Informed Subject Consent		✓							
Verify Inclusion / Exclusion Criteria		✓							
Subject History		✓							
Harris Hip		✓			✓*	✓	✓	✓	✓
Hip Evaluation		✓			✓	✓	✓	✓	✓
HOOS Jr.		✓			✓	✓	✓	✓	✓
Forgotten Joint Score (FJS-12)					✓	✓	✓	✓	✓
Operative Details			✓						
Device Log			✓						
Unscheduled Visit Report ** (Interim Visit)					✓	✓	✓	✓	✓
Adverse Event			✓	✓	✓	✓	✓	✓	✓
End of Study (Withdrawal (W/D)) Form***					If W/D	If W/D	If W/D	If W/D	If W/D
AP View	✓				✓	✓	✓	✓	✓
Lateral View	✓				✓	✓	✓	✓	✓
RSA Exam (supine)					✓ (dbl exam)	✓	✓	✓	✓

* ROM optional at 6 weeks only
** As Needed
*** As Applicable

2 INTRODUCTION

2.1 Background

Hip replacement, or arthroplasty, is a surgical procedure in which the diseased or damaged parts of the hip or hip joint are removed and replaced with prosthetic implants in the proximal femur (stem) and the acetabulum (cup or shell). The most common reason that people have hip replacement surgery is the wearing out of the hip joint as a result of osteoarthritis. Other conditions, such as rheumatoid arthritis (a chronic inflammatory disease that causes joint pain, stiffness and swelling), avascular necrosis (loss of bone caused by insufficient blood supply), injury (such as fracture), and bone tumors also may lead to breakdown of the hip joint and the need for hip replacement surgery.

2.2 Radiostereometric Analysis (RSA)

Radiostereometric Analysis is an accurate method of determining the migration of orthopaedic implants such as total hip arthroplasties. RSA is able to measure micromotion of the hip implant and this information can determine the early fixation of the implant in a short period of time. To date, there are no known publications on RSA data evaluating migration of the Pinnacle Acetabular Shell. Therefore, in order to evaluate future hip replacement products, a baseline value for the Pinnacle Acetabular Shell must be determined.

2.3 Study Article Description

Pinnacle Acetabular Shells come in several configurations based on the number of screw holes available in the implant. The shells also are available in different fixation surfaces. In this study, the Sector style cup with Gription Porous Coating (Pinnacle Acetabular Shell) will be evaluated for micromotion. Gription Porous Coating combines macrotexture and microtexture topographies allowing cell adhesion and proliferation.

2.4 Benefits/Risks

2.4.1 Benefits

The primary goal of total hip arthroplasty is the anatomic reconstruction of the hip joint, resulting in favorable prosthetic joint load and function. Mechanically, the goals are to create a stable articulation with an optimized range of motion, restore biomechanics for muscular efficiency and equalize limb lengths.

2.4.2 Risks

The most commonly reported adverse events related to the study device are:

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

The following may occur with any hip arthroplasty, including the study device:

GENERAL

- Change in position of the prosthetic components
- Early or late loosening of the prosthetic components
- Fatigue fracture of the femoral stem
- Excessive wear or fracture of the bearing components
- Early or late infection
- Peripheral neuropathies. Subclinical nerve damage may also occur as a result of surgical trauma
- Tissue reactions, osteolysis, and/or implant loosening caused by metallic corrosion, allergic reactions, wear or particulate debris

INTRAOPERATIVE

- Acetabular perforation
- Femoral shaft perforation, fissure or fracture, which may require the use of internal fixation
- Trochanteric fracture
- Damage to blood vessels
- Temporary or permanent nerve damage
- Subluxation or dislocation of the hip joint due to implant size or configuration selection, positioning of components and /or muscle and fibrous tissue laxity
- Lengthening or shortening of the affected extremity

EARLY POSTOPERATIVE

- Cardiovascular disorders including venous thrombosis, pulmonary embolism and myocardial infarction
- Hematoma and/or delayed wound healing
- Pneumonia and/or atelectasis
- Subluxation or dislocation

LATE POSTOPERATIVE

- Trochanteric avulsion from excessive muscular tension, weight-bearing, or inadvertent intraoperative weakening of the trochanter
- Aggravation of problems in the ipsilateral or contralateral knee and ankle joints
- Femoral or acetabular fracture due to trauma or excessive loading
- Bone resorption which may contribute to the deterioration of fixation and eventual loosening of the implant
- Periarticular calcification or ossification which may lead to a decrease in joint mobility and range of motion
- Traumatic arthrosis of the ipsilateral knee secondary to intraoperative positioning of the extremity during surgery
- Subluxation or dislocation

3 PURPOSE

3.1 Primary Objective and Endpoint

The primary objective is to establish the mean superior cup migration of the Pinnacle Acetabular Shell using model-based RSA over the first two years post-implantation. The primary endpoint is the mean vertical subsidence (Y translation, also known as superior cup migration) at 2 years as measured with RSA. This will be summarized for each surgical approach separately, as well as combined.

3.2 Secondary Objectives and Endpoints

Secondary objectives are:

- To establish the subsidence profile of the Pinnacle Acetabular Shell; this will be accomplished by determining the mean subsidence at 3 months, 6 months and 1 year as measured with RSA.
- Other RSA measurements (X and Z translations in mm, X, Y, and Z rotations in degrees, and maximal total point motion in mm) at all time points.
- Linear head penetration (in mm) at 1 year and 2 years. This will be summarized for each surgical approach separately, as well as combined.
- Functional and health status will be measured with Harris Hip Score, HOOS Jr. and Forgotten Joint Score (FJS-12).

3.3 Exploratory Objectives and Endpoints

The following will be summarized as exploratory analyses:

-
- Analyses to examine the correlation of functional and health status outcomes vs. RSA observations may be explored.

3.4 Safety Endpoints

The type and frequency of serious, non-serious, and device or procedure related AEs across all study intervals will be summarized.

3.5 Device Description

All components involved in this clinical investigation are commercially available. The part numbers allowed by this protocol are listed in Appendix A.

Pinnacle Acetabular Shell

The shells are designed to assemble with the polyethylene insert. The style utilized in this clinical investigation are the Gription-coated, Sector Series shells.

AltrX Polyethylene Liner

The liners are available as several options: Neutral, +4 Neutral, +4 10°, and Lipped. It is at the surgeon's discretion as to which version is most appropriate for the individual study subject.

Femoral Head

Only Articul/eze 12/14 metal heads are allowed for this clinical investigation. Suggested head size will be 32 mm diameter for acetabular cup sizes of 48-54 mm, and 36 mm diameter for sizes 56-66 mm; other on-label combinations are allowable for this protocol.

Corail Femoral Stem

The Corail femoral stem is an HA coated stem available in several sizes. Three offset options are available and is at the surgeon's discretion as to which size and offset is most appropriate for the individual study subject.

4 SUBJECT DEFINITION

This study will include subjects aged 21 or older who are scheduled to undergo unilateral joint replacement. Subjects who do not meet all inclusion criteria or who meet any of the exclusion criteria will be excluded from study consideration and participation. Subjects who meet all entry criteria and are properly consented may be excluded from further participation due to study withdrawal, see Section 8 for details.

4.1 Inclusion Criteria

Subjects meeting all the following specific criteria will be considered for participation in the study:

a) Individuals requiring primary THA for a severely painful and/or disabled joint from osteoarthritis, traumatic arthritis, rheumatoid arthritis, or congenital hip dysplasia, AVN of the femoral head or acute traumatic fracture of the femoral head or neck.
b) Individuals who are able to speak, read and comprehend the informed patient consent document and willing and able to provide informed patient consent for participation in the study and have authorized the transfer of his/her information to DePuy Synthes.
c) Individuals who are willing and able to return for follow-up as specified by the study protocol.
d) Individuals who are a minimum age of 21 years at the time of consent.
e) Individuals who are willing and able to complete the Subject Hip Outcomes questionnaires as specified by the study protocol.

4.2 Exclusion Criteria

Subjects will be excluded from participation in the study if they meet any of the following criteria:

a) Individuals have active local or systemic infection.
b) Individuals who have loss of musculature, neuromuscular compromise or vascular compromise that would impact rehabilitation following surgery.
c) Individuals with poor bone quality, such as osteoporosis, where in the surgeon's opinion, there could be considerable migration of the prosthesis or require additional acetabular cup fixation using screws, or a significant chance of fracture of the femoral shaft and/or the lack of adequate bone to support the implant(s).
d) Individuals with Charcot's or Paget's disease.
e) Individuals who, in the judgement of the investigator, would not be a candidate for protocol allowable components to be used for their THA.
f) Women who are pregnant or lactating.
g) Individuals who have had a contralateral hip that was implanted less than 6 months prior to the time of consent into this study or individuals that expect to have a contralateral hip implanted in the following 6 months at the time of consent into this study.
h) Individuals that have amputations in either leg that would impact rehabilitation following surgery.
i) Individuals who are bedridden
j) Individuals that have participated in a clinical investigation with an investigational product (drug or device) in the last three months.
k) Individuals currently involved in any personal injury litigation, medical-legal or worker's compensation claims.
l) Individuals, in the opinion of the Investigator, who are drug or alcohol abusers or have a psychological disorder that could affect their ability to complete patient reported questionnaires or be compliant with follow-up requirements.

m) Individuals diagnosed and taking prescription medications to treat a muscular disorder that limits mobility due to sever stiffness and pain such as fibromyalgia or polymyalgia.
n) Subject has a medical condition with less than 2 years life expectancy.
o) Individual has a BMI $\geq$45 kg/m^2.

4.3 Definition of Subject Enrollment

A patient will be considered enrolled when they have provided signed Informed Consent Document (ICD) to participate in this Investigation, which includes authorization of the release of his/her Protected Health Information (PHI).

5 STUDY DESIGN

This study is designed as a prospective, multi-center, non-randomized, non-controlled study. This study does not limit the procedures involved in the treatment of the subject as long as the protocol specified products are utilized.

5.1 Subject Enrollment

No protocol specified activities can be completed until written Informed Consent is obtained for that Subject. Standard of care radiographs that have been taken prior to consent may be used for the purposes of the protocol as long as they were taken within 270 days of surgery.

5.1.1 Subject Screening and Informed Consent

As patients are being scheduled for primary, unilateral THA, the Principal Investigator or a trained designee at each of the sites will conduct a preliminary screen to determine if the patient meets general requirements for the study. If a patient appears to be eligible, delegated staff will offer study participation to those patients. Having explained the study purpose to the Subject, the Investigator or trained designee shall offer to answer any of the Subject's questions. If the Subject then agrees to participate, his or her willingness must be documented via his/her name, signature and date on the REB's approved ICD and this document countersigned and dated by the person taking consent. The signed ICD will then be placed into the Subject's Medical Record. Screening, consenting and enrollment are illustrated in Figure 5.1.

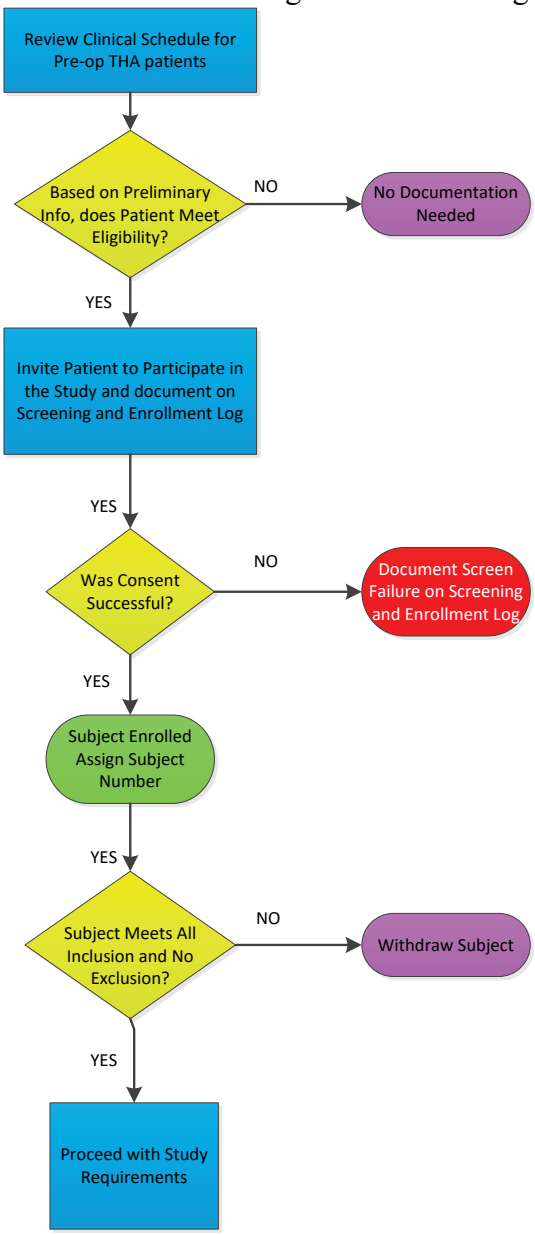
The Principal Investigator is responsible for ensuring that no subject will be included in the study without adequate informed consent. Failure to obtain and properly document this process is in violation of 21 CFR Part 50, the Declaration of Helsinki and this study protocol. All ICDs must have approval by the responsible REB. Consent of a subject needs to come from the Subject themselves and be documented on an ICD.

After Informed Consent, study subjects will be defined as 'enrolled'. Delegated office research staff will then assign a Subject ID number to each enrolled subject. Each subject will be identified by site or surgeon number (e.g. 01, 02) followed by -001 for the first subject, -002 for the second subject and so on. Together the site/surgeon number and the Subject number will comprise the unique Subject ID. This unique identifier will be recorded in the Subject's ICD, medical record and the Screening and Enrollment Log.

Delegated site research staff should then record the following information into the Screening and Enrollment Log:

- Subject ID;
- Date of Screening;
- If applicable, primary reason for not including the patient (e.g., does not satisfy eligibility criteria, not interested in participating).

Figure 5-1 Screening and Enrollment Process



6 STUDY PROCEDURES

6.1 Pre-Operative (-90 days to Day of Surgery)

Following informed consent and eligibility verification, the subject will have the following pre-operative health and functional status evaluations:

The subject's orthopaedic medical history and current diagnoses will be documented. Data collected will include but is not be limited to:

- Age, gender, height and weight
- History of concurrent or previous medical issues
- History of previous treatment to the index hip
- Harris Hip Score
- HOOS Jr.
- Radiographs
    - AP Femur*
    - Lateral

*The AP Femur is the preferred view at all time points, however an AP Pelvis will also be accepted.

The information collected from the 'Pre-Op' visit will be populated on the appropriate eCRFs as indicated in the Time and Events Table (Section 1.1). If pre-operative radiographs of sufficient quality were obtained within 270 days of surgery, then they do not need to be repeated just for the purpose of this study.

6.2 Operative (Day 0)

Each subject will receive an uncemented Corail femoral stem in combination with a Pinnacle Sector Acetabular cup. All subjects will receive a metal femoral head and an AltrX Polyethylene liner. No screw fixation of the Sector cup is allowed by this protocol. If the surgeon deems that screw fixation or any component other than those listed in the protocol is required for that subject, that subject will be withdrawn from the study. Subjects that are withdrawn pre-operatively or intra-operatively will be replaced in order to have 30 subjects in each surgical approach.

Three surgical approaches will be used for the purpose of this study: posterior, anterior, and lateral. Each surgeon shall perform the approach they are most comfortable with and have the greatest expertise. In general, subjects enrolled at the Winnipeg site will undergo a posterior approach or direct lateral approach. Subjects enrolled at the London site will undergo a direct anterior approach, direct lateral approach or posterior approach. Enrollment will be closely monitored to ensure a minimum of 30 subjects are enrolled in each surgical approach group. Once a group has reached 30 implantations, Investigators of that approach group will be informed to halt enrollment of further subjects. If over 30 subjects are enrolled per approach, the additional subjects will be treated as any other study subject (i.e. exams, follow-up, analysis).

Implant sizing shall be performed as per the surgeon's discretion for each individual subject and will not be standardized between sites. Approximately 5-10 tantalum beads will be placed into the

acetabulum. Bead placement will be standardized across study sites to reduce the possibility of un-useable RSA exams resulting from poor bead spacing or bead occlusion.

Any intra-operative adverse events will be captured as well as details of the surgery and implants/components used. The information collected from the 'Operative' time-point will be populated on the appropriate eCRFs as indicated in the Time and Events Table (Section 1.1).

6.3 Prior to Discharge (Day 1 to Discharge)

Subjects will undergo the standard of care for total hip arthroplasty at the participating sites, including bandaging, anti-coagulation, antibiotic and/or physiotherapy protocols. Adverse events and post-operative complications will be collected.

The information collected from the 'Prior to Discharge' time-point will be populated on the appropriate eCRFs as indicated in the Time and Events Table (Section 1.1).

6.4 6 Weeks (Day 28-56)

All subjects will undergo a model-based RSA examination. For all sites, the 6-week exam will be used as the reference examination. RSA radiographs will be obtained with subjects in a supine position. A duplicate RSA exam will be conducted at this time-point to calculate the intra-subject measurement error.

Additionally, the subject will have the following health and functional status evaluations:

- Harris Hip Score; ROM optional
- Hip Evaluation
- HOOS Jr.
- Forgotten Joint Score
- Adverse Events (if applicable)
- Radiographs
    - AP Femur
    - Lateral

The information collected from the '6 Week' visit will be populated on the appropriate eCRFs as indicated in the Time and Events Table (Section 1.1).
NOTE: Any subject that is unable to complete their 6 week visit due to the COVID-19 Pandemic can be replaced; as many endpoints use this timepoint as the baseline value. Subjects unable to complete their 6 week visit will not be withdrawn because of this missing visit but continue to be followed according to the protocol.

6.5 3 Month, 6 Month, 1 Year and 2 Year Visits

The subject will have the following health and functional status evaluations:

- Harris Hip Score
- Hip Evaluation
- HOOS Jr.
- Forgotten Joint Score
- Adverse Events (if applicable)
- Radiographs
    - AP Femur
    - Lateral
- RSA Exam (supine position)

The information collected from these visits will be populated on the appropriate eCRFs as indicated in the Time and Events Table (Section 1.1).

6.6 Unscheduled Visit

If a subject requires an additional visit during a study interval for their study hip, and is seen by one or more person listed on the Delegation of Authority Log, then the following information shall be repeated:

- Harris Hip Score
- Hip Evaluation
- HOOS Jr.
- Forgotten Joint Score
- Adverse Events (if applicable)

If a subject has an unscheduled visit after the 6 week interval (outside defined protocol window) for their study hip, with one or more person listed on the Delegation of Authority Log then the following information shall be collected:

- Harris Hip Score
- Hip Evaluation
- HOOS Jr.
- Forgotten Joint Score
- Adverse Events (if applicable)
- Radiographs
    - AP Femur
    - Lateral
- RSA Exam (supine position) if RSA Exam was not conducted in-window for previous visit. If subject is seen multiple times outside of the same defined protocol window, only one RSA Exam is required.

6.7 Radiostereometric Analysis (RSA)

The RSA analysis will be the responsibility of the Canadian RSA Network. In summary, model based RSA software (RSAcore, Leiden, Netherlands) will be used for analysis, employing computer-models of the DePuy Synthes implants and inserted beads representing the bone rigid body. A central analysis service will be employed to analyze anonymized radiographs in a standard manner. DePuy Synthes will provide production CAD models as required for this analysis.

Three-dimensional migration measurements will be made of the acetabular shell relative to the bone beads. The 6-week examination will be used as reference against which the 3-month, 6-month, 1-year and 2-year post-operative exams will be compared. Results obtained from the model based RSA software will be changes from the 6-week (baseline) examination and will report the following at 3 months, 6 months, 1 year and 2 years:

- X, Y and Z translation measurements in mm from baseline;
- X, Y and Z rotation measurements in degrees from baseline;
- Maximal total point motion (one measurement in mm of maximal migration).

Three-dimensional migration of the Pinnacle Acetabular Shell shall be determined from the software.

Linear head penetration (in mm) will be performed by examining the change in distance between the center of the femoral head and the center of the acetabular shell between the 6-week (baseline) exam and 1 year and 2 year exam. The femoral head center is determined by fitting a CAD sphere to the articular region of the femoral head (ignoring the trunnion area). The acetabular shell center is determined in a similar manner but also uses the silhouette of the cup face to determine its' centerpoint.

7 ADVERSE EVENT REPORTING

7.1 Adverse Events

An Adverse Event is any untoward medical occurrence in a subject, regardless if there is a relationship between the adverse event(s) and the study device(s).

At each evaluation of the subject enrolled in a clinical investigation, the Investigator determines whether any adverse events (AE) have occurred and determines their relationship to the study devices or procedure. For the purposes of this study, only serious adverse events (see Section 7.2), device and/or procedure related adverse events will be reported to the Sponsor.

All reportable adverse events, study device malfunctions and other product issues must be recorded in the medical records and entered into electronic Case Report Forms (eCRFs) within two weeks of awareness the AE occurred. Upon entry of an AE into the eCRF, designated members of the DePuy Synthes clinical team will receive an email alert describing the AE.

7.2 Serious Adverse Events

Serious Adverse Events (SAEs) are defined as any adverse event that:

1. Led to a death,
2. Led to a serious deterioration in the health of the subject that,
   a. Resulted in life-threatening illness or injury,
   b. Resulted in permanent impairment of a body structure or a body function,
   c. Required in-patient hospitalization or prolongation of existing hospitalization
   d. resulted in medical or surgical intervention to prevent life threatening illness or injury or permanent impairment to a body structure or a body function,
3. Led to fetal distress, fetal death or a congenital abnormality or birth defect

A planned hospitalization and/or medical intervention for pre-existing conditions documented in the study records that have not changed in severity, or a procedure required by the protocol, without serious deterioration in health, is not considered to be a serious adverse event.

Investigator must submit to DePuy Synthes any SAEs occurring during the study as soon as possible, but within 72 hours, after becoming aware of the event and provide additional information if required by DePuy Synthes. All SAEs need to be followed until the event is resolved (with or without sequelae), additional information is located in Section 7.3. The Study Safety Lead of this study will decide if more follow-up information is needed (via electronic queries) in case the event is not resolved at study completion.

The Investigator notifies his/her REB of all SAEs as required by REB policy (and any additional information as required by REB). All SAEs are to be reported to the Sponsor.

7.3 Duration of Follow-up After Adverse Events

The Investigator should ensure that adequate medical care is provided to any subject for any adverse events related to the study.

Only SAE, device and/or procedure related Adverse Events will be collected for the purposes of this study. All device or procedure adverse events should be followed until the condition has resolved, or in the case of permanent impairment until the condition stabilizes and clinical outcome has been ascertained, or the study has been completed.

7.4 Reporting an Adverse Event

Adverse events are reported from the time of surgery until the subject's study participation has ended (i.e. completion of study or withdrawal of consent). All reported AEs must be followed until the AE has resolved, stabilized, or the study has been completed. Any medical event, that if it had occurred post-operatively would be considered a Serious adverse event, that occurs prior to surgery is to be reported as history on the Medical History eCRF.

The Investigator will record the nature, severity, treatment and outcome of the AE, and will determine its relationship to the investigational products or any protocol mandated procedures involved in the clinical study.

The determination whether the AE is related to the device and/or procedure will be based upon whether a causal relationship between the device and/or procedure and the AE is at least a

reasonable possibility, i.e. the relationship cannot be ruled out. A causal relationship cannot be ruled out if, in the medical judgment of the Investigator, the effect follows a reasonable temporal association with the use of the device and/or is confirmed by the improvement of the effect upon discontinuation of the clinical use of the device, and/or the effect is not reasonably explained by the Subject's clinical state.

Relationship to study device or procedure should be rated as follows:

1) Not related (definitely not related): there is no relationship between study device and/or procedure and the event.

2) Possibly related (remote possibility, possibly, or probably related): the relationship between study device and/or procedure could exist if there is no contradicting evidence that can reasonably explain the Subject's condition.

3) Definitely related (definitely related): the relationship between study device and/or procedure and event does exist and is confirmed upon further investigation by the Investigator.

The following categories of adverse event severity are to be used:

Mild	Awareness of sign or symptom that does not interfere with the subject's usual activity or is transient, resolved without treatment and with no sequelae,
Moderate	Interferes, but does not hinder, the subject's usual activity and may require treatment,
Severe	Symptom(s) causing severe discomfort and significant impact on the subject's usual activity and requires treatment or intervention.

Adverse events will be reported by the Investigator to DePuy Synthes via the Adverse Events eCRF.

NOTE: Please refer to Appendix B (Anticipated Adverse Events) where a listing of common surgical adverse events is listed. These adverse events are anticipated and assuming the events are consistent with the normal postoperative course, then they do not have to be reported as adverse events.

8 EARLY DISCONTINUATION

8.1 Reasons for Early Discontinuation

Possible reasons for early discontinuation may include, but are not limited to the following:

- Withdrawal of consent: Subject decides to withdraw from the study. This decision must be an "independent decision" that is documented in the patient study files;
- Adverse event: Adverse event or serious adverse event may not lead to subject discontinuation from the study. If the Investigator decides to discontinue further study related procedures, the subject must still be followed until the adverse event resolves or until a stable clinical endpoint is reached, or the subject withdraws consent (i.e. the subject will continue to be followed for safety);
- If the surgeon deems that screw fixation or any component other than those listed in the protocol is required for that subject;
- Revision of any component;
- Death, and/or
- Early study termination: DePuy Synthes can decide to discontinue the study prematurely for various reasons.

8.2 Subject Early Discontinuation

Every subject should be encouraged to remain in the study until they have completed the protocol-required 2-year follow-up period. If the subject discontinues prematurely from the study, the reason for discontinuation must be documented in the source documents and site files and submitted via eCRF.

Data which have been received on subjects who discontinue prematurely will be included in the analysis of results. Subjects who discontinue prematurely, excluding those withdrawn pre-operatively, intra-operatively or those subjects who were unable to complete their 6 week visit due to the COVID-19 Pandemic, will not be replaced.

8.3 Study Early Discontinuation

DePuy Synthes reserves the right to temporarily suspend or prematurely discontinue this study either at a single site, multiple sites, or at all sites at any time for reasons including, but not limited to, safety or ethical issues, inaccurate or incomplete data recording, non-compliance, or unsatisfactory enrollment with respect to quality or quantity.

If the study is prematurely terminated or suspended, DePuy Synthes or its representatives will inform the Investigators/institutions of the termination or suspension and the reason(s) for the termination or suspension, in accordance with applicable regulatory requirement(s). The REB should also be informed and provided with reason(s) for the termination or suspension by DePuy Synthes or by the Investigator/institution, as specified by the applicable regulatory requirement(s). In addition, arrangements will be made for the return of all study material in accordance with Sponsor procedure for the study.

9 STATISTICAL METHODOLOGY

The following sections provide a general description of the statistical plan for the analysis of study data. A separate Statistical Analysis Plan (SAP) document that provides greater detail on data derivations and the analyses to be performed will be finalized prior to database lock. The SAP will reflect the protocol and any amendments that have been implemented at the time the SAP is finalized. Any deviations from the final SAP will be noted in the final clinical summary report.

9.1 Study Design

This is a prospective, multi-center, non-randomized, non-controlled study designed to establish the 2-year migration profile of the Pinnacle Acetabular Shell when implanted using 3 different surgical approaches: posterior, anterior, and lateral.

9.2 Treatment Assignment

Subjects enrolled will undergo THA using the study devices listed in Section 3.5 and one of the surgical approaches under study: posterior, anterior, and lateral. Centers will be selected for their expertise in one or more of the surgical approaches. Each surgeon will perform the approach they are most comfortable with and have the greatest expertise. In general, subjects enrolled at the Winnipeg site will undergo a posterior approach or direct lateral approach. Subjects enrolled at the London site will undergo a direct anterior approach, direct lateral approach or posterior approach. Enrollment will be closely monitored to ensure a minimum of 30 subjects are enrolled in each surgical approach group. Once a group has reached 30 implantations, Investigators of that approach group will be informed to halt enrollment of further subjects.

9.3 Randomization and Blinding Procedures

Not applicable.

9.4 Interval Windows

Data collected throughout the study will be assessed for compliance with the protocol-specified visit schedule. **Error! Reference source not found.**Six windows are defined based on the number of days prior to or after surgery, Day 0. Visits conducted within the intervals shown in Table 9-1 will be assessed for compliance with the protocol. If multiple visits fall into the pre-operative window, or into the 6 Week post-operative window, the result collected most proximate to surgery will be utilized. If multiple measurements fall into the 3 Month, 6 Month, 1 Year, or 2 Year window, the last value (furthest from surgery) will be utilized for the analysis. All safety data will be included in the Safety analysis.

Table 9-1 Study Visit Interval Windows per Time and Events Table

Study Visit	Study Interval Window (days)
Pre-Op	-90 to DOS*
Operative	0
Prior to Discharge	Day 1 to Discharge
6 Weeks	28 to 56
3 Months	60 to 120

6 Months	135 to 225
1 Year	275 to 455
2 Years	640 to 820

* For radiographs Pre-Op study film window is from -270 days to DOS.

9.5 Analysis Sets

Safety Analysis Set

The Safety Analysis Set consists of all enrolled subjects who receive THA surgery. Subjects will be analyzed according to the surgical approach applied during of the study.

Per Protocol (PP) Analysis Set

The Per Protocol (PP) Analysis Set will be a subset of Safety Set subjects who have no major inclusion/exclusion protocol violations, and who have a baseline RSA exam and at least one post-baseline RSA exam. Subjects will be analyzed according to the actual treatment (surgical approach) received during of the study.

9.6 Primary and Secondary Endpoints and Associated Hypotheses

There are no hypotheses associated with the primary or secondary endpoints; endpoints appear below.

9.6.1 Primary Endpoint

The primary endpoint is the RSA measured mean superior cup migration (Y translation subsidence in mm) at 2 years.

9.6.2 Secondary Endpoints

The secondary endpoints are the following:

- RSA measured subsidence (superior cup migration) at 3 months, 6 months and 1 year.
- Other RSA measurements (X and Z translations in mm, X, Y, and Z rotations in degrees, and maximal total point motion in mm) at all time points
- Linear head penetration at, 1 year and 2 years;
- Harris Hip Score at 6 weeks, 3 months, 6 months, 1 year and 2 years;
- HOOS Jr. at 6 weeks, 3 months, 6 months, 1 year and 2 years;
- Forgotten Joint Score (FJS-12) at 6 weeks, 3 months, 6 months, 1 year and 2 years.

9.6.3 Exploratory Endpoints

The following will be summarized as exploratory analyses:

- Correlation of functional and health status outcomes (Harris Hip Score, HOOS Jr, and FJS-12) vs. RSA observations may be explored.

9.7 Levels of Significance

There are no specific hypotheses being tested in this study. To facilitate clinical interpretation, confidence intervals will accompany primary and secondary endpoint estimates and will be 2-sided 95% confidence intervals; these confidence intervals are considered to be exploratory.

9.8 Sample Size Justification

This study sample size was established to provide adequate precision on the mean subsidence estimate at 2 years for each surgical approach. A common standard deviation of 0.2 mm is anticipated. Based upon this standard deviation and a sample size of N=30, a 2-sided 95% confidence interval for each respective surgical approach is anticipated to have a margin of error equal to approximately $2\text{SE} = 2 \times \frac{\text{SD}}{\sqrt{n}} = 2 \times \frac{0.2}{\sqrt{30}} = 0.073$ mm. This margin of error was deemed to be an adequate level of precision by the Sponsor.

9.9 General Conventions

All statistical analysis will be performed using SAS® Version 9.3 or higher, unless otherwise noted. A separate Statistical Analysis Plan (SAP) will provide detail on data derivations and the analyses to be performed for the final study report. It will be approved prior to database lock.

Descriptive statistics for continuous variables will include the number of subjects with an observation, mean, standard deviation (SD), median, minimum, and maximum. Descriptive statistics for dichotomous/categorical variables will include the count and percentage of subjects in each category.

Unless specifically stated otherwise, all endpoints will be analyzed by surgical approach and overall, pooling all surgical approaches.

9.10 Disposition of Study Subjects

An overall summary of the number of subjects in each analysis set (Safety and Per Protocol) who had major protocol deviations, who withdrew before study completion, and who completed the study will be tabulated for all surgical approaches combined.

A patient accounting table to present the number of subjects in the Safety Analysis Set at each visit interval will be summarized: theoretical due, deaths, withdrawn, and expected due in the interval.

9.11 Demographic and Baseline Characteristics

Descriptive statistics summarizing demographics and baseline characteristics will be displayed for both the Safety Analysis Set and the Per Protocol Analysis Set. These summaries will include, but are not limited to, age, gender, BMI, general medical conditions, Harris Hip Score, Hoos Jr. and Forgotten Joint Score.

9.12 Primary, Secondary, and Safety Endpoint Analyses

9.12.1 Primary Endpoint Analysis

RSA Measured Subsidence at 2 years

The primary endpoint of RSA measured subsidence (Y translation, also known as superior cup migration) results in the 2-year visit window will be summarized on the subset of subjects in the Per Protocol Analysis Set (primary analysis) who have 6 week and 2 year data for the analysis. The analysis will also be conducted on the subset of subjects in the Safety Analysis Set (supportive analysis) who have 6 week and 2 year data for the analysis. Standard continuous summaries will be provided along with 95% confidence intervals. These summaries will be provided for each surgical approach, as well as combined.

9.12.2 Secondary Endpoint Analysis

RSA Measured Subsidence at 3 months, 6 months and 1 year

The analysis for this secondary endpoint will be identical to the analyses described for the primary endpoint except conducted on the results in the 3 month, 6 month, and 1 year visit windows, respectively, using the Per Protocol Analysis Set and the Safety Set.

Linear Head Penetration at 1 year and 2 years

Linear head penetration will be assessed at 6 weeks, 1 year and 2 years. Results within each visit window will be summarized and changes from baseline will be provided using the Per Protocol Analysis Set.

Harris Hip Score at 6 weeks, 3 months, 6 months, 1 year and 2 years

Harris hip scores are assessed at the Pre-Op visit and at 6 weeks, 3 months, 6 months, 1 year and 2 years. Results within each visit window will be summarized and changes from baseline will be provided using the Per Protocol Analysis Set. Standard continuous summaries will be supplemented with 95% confidence intervals. The ROM at 6 weeks is considered optional; the score will be missing for subjects for whom ROM was not performed.

HOOS Jr. Score at 6 weeks, 3 months, 6 months, 1 year and 2 years

HOOS Jr. Score are assessed at the Pre-Op visit and at 6 weeks, 3 months, 6 months, 1 year and 2 years. Results within each visit window will be summarized and changes from baseline will be provided using the Per Protocol Analysis Set. Standard continuous summaries will be supplemented with 95% confidence intervals.

Forgotten Joint Score (FJS-12)

FJS-12 are assessed at the 6 week visit and at 3 months, 6 months, 1 year and 2 years. Results within each visit window will be summarized and changes from baseline will be provided using the Per Protocol Analysis Set. Standard continuous summaries will be supplemented with 95% confidence intervals.

9.12.3 Exploratory Endpoint Analysis

Exploratory analyses will include the following:

- Correlation of functional and health status outcomes (Harris Hip Score, HOOS Jr, and FJS-12) vs. RSA observations may be explored.

9.13 Safety Endpoint Analysis

Adverse Events will be coded according to the Medical Dictionary for Regulatory Activities (MedDRA) version 21.1. Analyses will be conducted for all subjects in the Safety Analysis Set.

An overall summary of the AE incidence within each surgical approach group will be presented and will include the number and percentage of subjects having one or more:

- Serious adverse event (SAE)
- Device related AEs
- Procedure related AEs
- Withdrawals due to AE
- Deaths

The number (%) of subjects with adverse events will be presented by MedDRA system organ class (SOC) and preferred term (PT) for all device related AEs, procedure related AEs and SAEs. A subject-level listing will be provided to display details of all reported AEs.

9.14 Plans for Interim Analysis

There are no formal interim analyses that are designed to potentially stop or change the study design. A planned interim summary analysis will take place after all subjects have completed the 1 year visit in order to give product development an understanding of acetabular cup subsidence that might be expected for future product development purposes. There is no intention to utilize this interim analysis as a means to justify stopping the study early.

9.15 Handling of Missing Data

Only subject data which is collected in the study will be utilized in analyses; there will be no imputation of missing data.

10 STUDY MANAGEMENT AND ADMINISTRATION

10.1 Investigator Responsibilities

In conducting this clinical study, the Investigator is responsible for:

- Ensuring that the clinical study is conducted according to the Declaration of Helsinki, applicable local regulations, the clinical study agreement and the protocol;
- Protecting the rights, safety and welfare of subjects under the Investigator's care; and
- Ensuring the integrity of the data.

Prior to the initiation of this clinical study at each site, the responsible Principal Investigator will approve this protocol by signing the signature page. This signature confirms that the clinical study will be performed in compliance with the protocol.

10.2 Good Clinical Practice

The study will be conducted in accordance with the GCP and the appropriate regulatory requirement(s). The Investigator will be thoroughly familiar with the appropriate use of the study device as described in the Instructions for Use. Essential clinical documents will be maintained to demonstrate the validity of the study and the integrity of the data collected. Master files should be established at the beginning of the study, maintained for the duration of the study and retained according to the appropriate regulations.

10.3 Ethical Considerations

The study will be conducted in accordance with ethical principles founded in the Declaration of Helsinki. The REB will review all appropriate study documentation in order to safeguard the rights, safety, and well-being of the subjects. The study will only be conducted at sites where initial and annual REB approval has been obtained. In addition, a copy of the REB approval letter must be filed on site in the Investigator's study files.

The protocol, Instructions for Use, informed consent form, advertisements (if applicable), written information given to the subjects, safety updates, annual progress reports, and any revisions to these documents will be provided to the REB by the Investigator. When applicable, amendments to the protocol will be submitted for REB review before implementation.

10.4 Subject Information and Informed Consent

After the study has been fully explained, written informed consent will be obtained from either the subject or his/her guardian or legal representative prior to study participation. The method of obtaining and documenting the informed consent and the contents of the consent will comply with GCP and all applicable regulatory requirement(s), which at a minimum include:

- The most current, approved ICF is completed by the subject prior to the start of study specific procedures;
- The subject personally signed and dated the ICF;
- The investigator or designated study personnel has also signed and dated the ICF;
- The subject's source describes the consent process, including date, by whom, that the subject had an opportunity to ask questions, and that they were offered a copy of their signed ICF; and
- The signed ICF(s) are retained by the investigator and are available for inspection.

10.5 Subject Confidentiality

In order to maintain subject privacy, all eCRFs, study device accountability records, study reports and communications will identify the subject by the assigned subject number. The Investigator will grant monitor(s) and auditor(s) from the Sponsor or its designee and regulatory authority(ies) access to the subject's original medical records for verification of data gathered on the eCRFs and to audit

the data collection process. The subject's confidentiality will be maintained and will not be made publicly available to the extent permitted by the applicable laws and regulations.

10.6 Direct Access to Source Data

The study will be monitored by DePuy Synthes or its designee. Monitoring will be done by personal visits from a representative of DePuy Synthes (site monitor) and will include on-site review of the eCRFs for completeness and clarity, cross-checking with source documents, and clarification of administrative matters will be performed. The review of medical records will be performed in a manner to ensure that subject confidentiality is maintained.

The site monitor will ensure that the investigation is conducted according to protocol design and regulatory requirements by frequent communications (letter, telephone, e-mail and/or fax). Regulatory authorities, the REB, and/or DePuy Synthes quality assurance group may request access to all source documents, eCRFs and other study documentation for on-site audit or inspection. Direct access to these documents must be guaranteed by the Investigator, who must provide support at all times for these activities.

10.7 Case Report Form Completion

An electronic data capture system, compliant to 21 CFR Part 11, will be used to collect data from this study.

eCRFs will be completed for each study subject. It is the Investigator's responsibility to ensure the accuracy, completeness, and timeliness of the data reported in the subject's eCRF. Source documentation supporting the eCRF data should indicate the subject's participation in the study and should document the dates and details of study procedures, adverse events, and subject status. The Investigator, or designated representative, should complete the eCRF pages as soon as possible after information is collected, preferably on the same day that a study subject is seen for an examination, treatment, or any other study procedure. Any outstanding entries must be completed immediately after the final examination. An explanation should be given for all missing data.

10.8 Record Retention

The Investigator will maintain all study records according to GCP and applicable regulatory requirement(s). Records will be retained for at least 2 years after the completion of the clinical study, according to site procedures or according to applicable regulatory requirement(s) (whichever is longest). If the Investigator withdraws from the responsibility of keeping the study records, custody must be transferred to a person willing to accept the responsibility. The Sponsor must be notified in writing if a custodial change occurs.

Study documentation includes, but is not limited to, the following:

- Source data, informed consents and enrollment logs
- Correspondence with the REB, DePuy Synthes, the site monitor, or other Investigators
- Study protocol and any amendments issued
- Protocol and Informed Consent approvals from the REB

10.9 Investigator agreements and curricula vitae of Investigator(s), and the Site Signature and Delegation Log Investigator Reports

The Investigator(s) is required to complete the following reports:

1. Withdrawal of REB Approval – Notification must be sent to the Sponsor within 5 working days
2. Informed Consent – A report of any use of the investigational device without a signed Informed Consent form must be forwarded to the Sponsor and the REB within 5 working days of the occurrence
3. Investigational Plan Deviations – Emergent deviations must be forwarded to the REB and the Sponsor as soon as possible and within 5 working days of the event. Any departures from the protocol must be fully documented in the eCRF and source documentation
4. Progress Reports – Annual progress reports must be forwarded to the REB and the Sponsor
5. Final Report – A final report/closure submission must be filed with the REB and the Sponsor within 3 months of the Investigator's completion of study site closure.
6. Principal Investigator(s) may delegate a qualified associate(s) to complete one or more of the above functions. However, the Principal Investigator retains the overall responsibility for subject safety, proper conduct of the study including obtaining subject consent, compliance with this study plan, and the collection of all required data.

11 SPONSOR OBLIGATIONS

11.1 Investigator(s) Training

DePuy Synthes will select only Investigator(s) with extensive experience in THA. The protocol will be reviewed with the Investigator(s) and their study personnel at the Site Initiation Visit. Furthermore, they will be instructed on how to complete the study documentation.

11.2 Study Monitoring

Study monitoring will be carried out in compliance with FDA regulations (21CFR 812) and all GCP guidelines and will be consistent with the sponsor's internal monitoring procedures.

12 RESEARCH ETHICS BOARDS AND REGULATORY REQUIREMENTS

12.1 REBs

The protocol, informed consent form and other applicable study-related documents must be submitted to the appropriate REB and written approval must be obtained and submitted to DePuy Synthes prior to enrolling any subjects.

The Investigator will promptly report to the REB any change in the designation of Principal Investigator role and all unanticipated problems involving risks to human subjects and will not make any changes in the research plan without REB approval, except when necessary to eliminate immediate hazards to human subjects. Those amendments involving significant risk or change require REB approval and written documentation of this approval must be submitted to the DePuy Synthes.

The Investigator must report to the REB at least yearly on the progress of the investigation. A letter from the REB should document continuing REB review. Notification to the REB by the Investigator within 3 months after completion, termination, or discontinuation of the study at the specific site must be documented.

Other Investigator responsibilities to the REB and DePuy Synthes include the following:

- During the conduct of the study, submit progress reports to the REB and Sponsor as required (Note: the annual progress report to the REB will fulfill the Investigator's responsibility to submit progress reports to the Sponsor.
- As required, obtain approval from the REB for protocol amendments and for revisions to the informed consent or subject recruitment advertisements.
- Provide REB with any other information it requests before or during the conduct of the study.
- Maintain a file of study-related information that includes all correspondence with the REB and Sponsor.
- Notify REB within 3 months after study completion, termination or discontinuation.
- Notify DePuy Synthes, within 5 working days, of withdrawal of approval by the reviewing REB.

12.2 Protocol Amendments

As appropriate, DePuy Synthes will submit changes in the protocol to the investigators, the appropriate regulatory authorities and REBs. REB approval is required for all substantial amendments prior to implementation of any changes to study procedures.

An amendment is regarded substantial when they are likely to have a significant impact on:

- The safety or physical or mental integrity of the subjects;
- Scientific value of the trial;
- Conduct or management of the trial;
- Quality or safety of an investigational medical product used in the trial.

12.3 Protocol Deviations

A protocol deviation is defined as a divergence from a specific element of a protocol (e.g., missed test or procedure, visit out of window, non-adherence to inclusion/exclusion criteria).

Investigators may not deviate from the protocol except where necessary to protect the life or physical well-being of a subject in an emergency.

Deviations shall be reported to DePuy Synthes regardless of whether medically justifiable or taken to protect the subject in an emergency. Subject specific deviations will be reported in the eCRFs. Investigators will also adhere to procedures for reporting study deviations to their REB in accordance with their specific REB reporting policies and procedures. Regulations require that Investigators maintain accurate, complete and current records, including documents showing the dates and reasons for each deviation from the protocol.

13 PUBLICATION POLICY

At the conclusion of the study, a multicenter manuscript will be prepared for publication in a reputable scientific journal. The publication of the principal results from any single-site experience within the study is not allowed until the preparation and publication of the multi-center results. Exceptions to this rule require the prior approval of DePuy Synthes. The analysis of other pre-specified and non-pre-specified endpoints will be performed by Data Management. Such secondary analyses, as well as other proposed investigations, will require the approval of DePuy Synthes. For purposes of timely abstract presentation and publication, secondary publications will be delegated to the appropriate principal authors, and final analyses and manuscript review for all multi-center data will require the approval of DePuy Synthes.

14 Appendix A

Part Codes

Sector Gription Acetabular Shell

Gription	
Code	Size (mm)
1217-32-048	48
1217-32-050	50
1217-32-052	52
1217-32-054	54
1217-32-056	56
1217-32-058	58
1217-32-060	60
1217-32-062	62
1217-32-064	64
1217-32-066	66

AltrX Liner

	28 mm				32 mm				36 mm			
Size (mm)	Neutral	+4 Neutral	+4 10°	Lipped	Neutral	+4 Neutral	+4 10°	Lipped	Neutral	+4 Neutral	+4 10°	Lipped
44	1221-28-044		1221-28-144									
46	1221-28-046		1221-28-146									
48	1221-28-048	1221-28-448	1221-28-148	1221-28-248	1221-32-048	1221-32-448	1221-32-148					
50	1221-28-050	1221-28-450	1221-28-150	1221-28-250	1221-32-050	1221-32-450	1221-32-150					
52	1221-28-052	1221-28-452	1221-28-152	1221-28-252	1221-32-052	1221-32-452	1221-32-152	1221-32-252	1221-36-052	1221-36-452	1221-36-152	
54	1221-28-054	1221-28-454	1221-28-154	1221-28-254	1221-32-054	1221-32-454	1221-32-154	1221-32-254	1221-36-054	1221-36-454	1221-36-154	

56	1221-28-056	1221-28-456	1221-28-156	1221-28-256	1221-32-056	1221-32-456	1221-32-156	1221-32-256	1221-36-056	1221-36-456	1221-36-156	1221-36-256
58	1221-28-058	1221-28-458	1221-28-158	1221-28-258	1221-32-058	1221-32-458	1221-32-158	1221-32-258	1221-36-058	1221-36-458	1221-36-158	1221-36-258
60	1221-28-060	1221-28-460	1221-28-160	1221-28-260	1221-32-060	1221-32-460	1221-32-160	1221-32-260	1221-36-060	1221-36-460	1221-36-160	1221-36-260
62	1221-28-062	1221-28-462	1221-28-162	1221-28-262	1221-32-062	1221-32-462	1221-32-162	1221-32-262	1221-36-062	1221-36-462	1221-36-162	1221-36-262
64	1221-28-064	1221-28-464	1221-28-164	1221-28-264	1221-32-064	1221-32-464	1221-32-164	1221-32-264	1221-36-064	1221-36-464	1221-36-164	1221-36-264
66	1221-28-066	1221-28-466	1221-28-166	1221-28-266	1221-32-066	1221-32-466	1221-32-166	1221-32-266	1221-36-066	1221-36-466	1221-36-166	1221-36-266

	40 mm		
Size (mm)	Neutral	+4 Neutral	+4 10°
44			
46			
48			
50			
52			
54			
56	1221-40-056	1221-40-456	1221-40-156
58	1221-40-058	1221-40-458	1221-40-158
60	1221-40-060	1221-40-460	1221-40-160
62	1221-40-062	1221-40-462	1221-40-162
64	1221-40-064	1221-40-464	1221-40-164
66	1221-40-066	1221-40-466	1221-40-166

Metal Heads (Articul/Eze 12/14)

	Standard Metal		M-Spec		
	28 mm	32 mm	28 mm	36 mm	40 mm
-2				1365-50-000	1365-04-000
+1		1365-21-000			
+1.5	1365-11-000		1365-11-500	1365-51-000	1365-05-000
+5	1365-12-000	1365-22-000	1365-12-500	1365-52-000	1365-06-000
+8.5	1365-13-000		1365-13-500	1365-53-000	1365-07-000
+9		1365-23-000			
+12	1365-14-000			1365-54-000	1365-08-000
+13		1365-24-000			
+15.5	1365-15-000			1365-55-000	1365-09-000

Corail Femoral Stem

Standard Collarless		Standard Collared		High Offset Collarless		High Offset Collared		Coxa Vara Collared	
Code	Size	Code	Size	Code	Size	Code	Size	Code	Size
L20106	6								
3L92507	8	3L92498	8						
3L92509	9	3L92499	9	L20309	9	L971109	9	3L93709	9
3L92510	10	3L92500	10	L20310	10	L971110	10	3L93710	10
3L92511	11	3L92501	11	L20311	11	L971111	11	3L93711	11
3L92512	12	3L92502	12	L20312	12	L971112	12	3L93712	12
3L92513	13	3L92503	13	L20313	13	L971113	13	3L93713	13
3L92514	14	3L92504	14	L20314	14	L971114	14	3L93714	14
3L92515	15	3L92505	15	L20315	15	L971115	15	3L93715	15
3L92516	16	3L92506	16	L20316	16	L971116	16	3L93716	16
3L92518	18	3L92508	18	L20318	18	L971118	18	3L93718	18
		3L92521	20	L20320	20	L971120	20		

125° Standard Offset Collarless		125° Standard Offset Collared		135° Short Neck Collarless		135° Short Neck Collared	
Code	Size	Code	Size	Code	Size	Code	Size
L981208	8	L971208	8	L981308	8	L971308	8
L981209	9	L971209	9	L981309	9	L971309	9
L981210	10	L971210	10	L981310	10	L971310	10

15 Appendix B

Anticipated Adverse Events

In addition to the information provided in the Instructions for Use, included with the packaging for all implants, the following surgical adverse events are anticipated. **Assuming the following events are consistent with the normal postoperative course, then they do not have to be reported as Adverse Events.**

UP TO 24 HOURS POSTOPERATIVE	
Genitourinary	• Urinary retention
Cardiovascular	• Hypotension, not requiring treatment • Hypertension, not requiring treatment • Dysrhythmia (resolving within 36 hours post-op)
Central Nervous System	• Incisional pain • Post-op consequences of narcotics use • Fatigue
Integumentary	• Venous congestion without thrombosis (foot swelling alleviated with lower limb is raised)
PRIOR TO DISCHARGE	
Hematological	• Changes in lab values not resulting in clinical symptomatology (Electrolytes, CBC, BS, PT/PTT) • Anemia, not requiring treatment

Gastrointestinal	• Transitory:
	  • Nausea
	  • Vomiting
	  • Constipation
	  • Diarrhea

Central Nervous System	• Headache • Disorientation • Confusion • Dizziness • Incision/operative site pain
Respiratory	• Atelectasis, not requiring treatment
Integumentary	• Foot swelling, not requiring intervention • Surgical site ecchymosis • Sanguineous/serosanguinous drainage from incision • Skin blisters secondary to tape/adhesive • Suture granuloma not involving cellulitis or deeper infection ('spitting suture', abscess suture)
Constitutional	• Elevated temperature (no greater than 101°F)

If you have any questions about potential adverse events (or reporting), please contact DePuy Synthes Clinical Research.