DePuy Synthes
THE ORTHOPAEDICS COMPANY OF Johnson & Johnson

DePuy Synthes Products Inc.
CLINICAL RESEARCH

PROTOCOL/CLINICAL INVESTIGATION PLAN (CIP)

Multi-Center Clinical Investigation of the ATTUNE® Cementless Fixed Bearing Tibial Base and Cementless Patella Implants in Total Knee Arthroplasty

Clinical Investigation Plan (CIP) Number:	DSJ_2019_05
Countries:	Targeted Regions/Sites: United States
CIP Prepared By:	PPD
CIP Version & Date:	Rev D – 24 August 2022
Clinical Investigation Sponsor:	DePuy Synthes Products, Inc. 325 Paramount Drive Raynham, MA 02767 Tel: PPD

Revision	Description of Change
Rev A, 27 APR 2020	Original version.
Rev B, 18 SEP 2020	A full description of the revisions is provided in Exhibit E.
Rev C, 2 DEC 2020	A full description of the revisions is provided in Exhibit E.
Rev D, 24 AUG 2022	A full description of the revisions is provided in Exhibit E.

PROTOCOL SIGNATURE PAGE

Principal Investigator: 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 accordance with Good Clinical Practices (GCP), applicable country regulations, the Declaration of Helsinki, applicable local regulations, the signed clinical study contract with 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 Institutional Review Board (IRB) / Ethics Committee (EC), or other oversight committee, to ensure complete and continual oversight of this clinical investigation.

I will use an Informed Consent Document approved by the Sponsor and my reviewing IRB/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 events reporting requirements of my reviewing IRB/EC.

I agree to permit the Sponsor, its authorized representatives, my reviewing IRB/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.

PRINTED OR TYPED NAME	SIGNATURE	DATE
Principal Investigator		

Table of Contents

The Sponsor maintains an updated list of Principal Investigators, Sites and Institutions within the Medidata RAVE system. The definitive list shall be integrated into the study report.

1 SUMMARY

Title:	Multi-Center Clinical Investigation of the ATTUNE Cementless Fixed Bearing Tibial Base and Cementless Patella Implants in Total Knee Arthroplasty
Short Title:	ATTUNE Cementless FB Tibial Base Clinical Study
Protocol Number:	DSJ_2019_05
Treatment Devices:	ATTUNE® Cementless Fixed Bearing (FB) Knee: • *ATTUNE Cementless Femoral Component (Cruciate Retaining (CR) or Posterior Stabilizing (PS))* • *ATTUNE Cementless Fixed Bearing (FB) Tibial Base* • *ATTUNE Fixed Bearing Tibial Insert (CR, Medial Stabilized (MS) or PS)* • *ATTUNE Cemented Patella* • *ATTUNE Cementless Patella*
Control Device:	N/A
Intended Use for the Device:	Total knee arthroplasty is intended to provide increased patient mobility and reduced pain by replacing the damaged knee joint articulation in patients where there is evidence of sufficient sound bone to seat and support the components. Total knee replacement may be considered for younger patients if, in the opinion of the surgeon, an unequivocal indication for total knee replacement outweighs the risks associated with the age of the patient, and if limited demands regarding activity and knee joint loading can be assured. This includes severely crippled patients with multiple joint involvement for whom a gain in knee mobility may lead to an expectation of significant improvement in the quality of their lives.
Primary Objective:	The primary objective of this clinical investigation is to evaluate functional responder rates with an objective performance criteria (OPC) of 85% as measured by the KOOS questionnaire for the first 225 tibia (CR FB and PS FB combined) implanted with the ATTUNE Cementless FB tray (primary and revision procedures) and will be analyzed when these patients have passed the 1 year preferred post-op window.
Secondary Objectives:	To establish the surgical effectiveness of the ATTUNE Cementless Fixed Bearing Tibial Base by evaluating: • *Type and frequency of Adverse Events and Device Deficiencies.* • *Functional responder rates with an objective performance criteria (OPC) of 85% as measured by the KOOS questionnaire for all subjects (CR FB and PS FB combined) at the 1-year timepoint.* • *The change from preoperative baseline to the 6-week, 6-month, 1-year, 2-year and 5-year timepoints in functional outcomes and quality of life*

Title:	Multi-Center Clinical Investigation of the ATTUNE Cementless Fixed Bearing Tibial Base and Cementless Patella Implants in Total Knee Arthroplasty
Short Title:	ATTUNE Cementless FB Tibial Base Clinical Study
Protocol Number:	DSJ_2019_05
	assessments, as measured using additional patient reported outcomes measures (PROMS): ○ *AKS (2011)* ○ *KOOS (all subscores)* ○ *FJS-12 (post-op only)* ○ *EQ-5D-5L* • *Implant survivorship of the ATTUNE Cementless FB Tibial base using Kaplan-Meier survival analysis at 1, 2 and 5 year timepoints.* • *Investigator-conducted radiographic analysis of the tibial and patellar components at 6 weeks/6 months, 1, 2 and 5 years after surgery.*
Tertiary Objectives	• *Implant survivorship of the ATTUNE Cementless FB Tibial base using Kaplan-Meier survival analysis at 3 and 4 year timepoints.*
Study Design:	Prospective, multi-center, non-randomized, single arm observational study. Level of evidence: Level III
Device Approvals	All devices allowed in this clinical study have FDA 510(k) clearance in the United States.
Number of Sites:	Up to 25 sites in the United States are anticipated to participate in this study. This may include both English and Non-English speaking (if validated translations are available) populations.
Study Subject Population	Male and female subjects, (age 22-80 years, inclusive) with a severely painful knee and/or, severely disabled knee function resulting from osteoarthritis, post-traumatic arthritis, or a failed previous implant provided that adequate bone is present
Sample Size	The sample size for this study is anticipated to be a minimum of 600 subjects. A minimum of each of the following variants must be included: • *300 ATTUNE Cementless Cruciate Retaining Fixed Bearings* • *300 ATTUNE Cementless Posterior Stabilizing Fixed Bearings* • *Up to 300 ATTUNE Cementless Patellae (if available in United States market during the clinical study)*

Title:	Multi-Center Clinical Investigation of the ATTUNE Cementless Fixed Bearing Tibial Base and Cementless Patella Implants in Total Knee Arthroplasty
Short Title:	ATTUNE Cementless FB Tibial Base Clinical Study
Protocol Number:	DSJ_2019_05
Inclusion Criteria	Subjects meeting all of the following specific criteria will be considered for participation in the study: a) Subject is male or female and between the ages of 22 and 80 years at the time of consent, inclusive. b) Subject has a severely painful knee and/or severely disabled knee function resulting from osteoarthritis, post-traumatic arthritis, or a failed previous implant provided that adequate bone is present. c) The subject requires total knee arthroplasty and would receive the study implant independent of this research protocol d) Subject that is willing to give voluntary, written informed consent to participate in this clinical investigation and authorize the transfer of his/her information to the Sponsor. e) Subject is currently not bedridden. f) Subject, in the opinion of the Investigator, is able to understand this clinical investigation and is willing and able to perform all study procedures and follow-up visits and co-operate with investigational procedures. g) Subject is able to read and comprehend the Informed Consent Document as well as complete the required PROMs in either English or one of the available translations.
Exclusion Criteria	Subjects will be excluded from participation in the study if they meet any of the following criteria: a) The Subject is a woman who is pregnant or lactating. b) Contralateral knee has already been enrolled in this study[1]. c) Revision knee that was previously enrolled in the study as a primary knee (ipsilateral). d) Subject has participated in a clinical study with an investigational product (drug or device) in the last two (2) years. e) Subject has had surgery on their contralateral knee within six (6) months of study enrolment or has surgery planned on their contralateral knee less than six (6) months of the study surgery. f) Subject is suffering from inflammatory arthritis in any joint (e.g., rheumatoid arthritis, juvenile rheumatoid arthritis, psoriatic arthritis, systemic lupus erythematosus, etc.). g) Active local or systemic infection.

[1] This study does not permit enrolment of any subject undergoing simultaneous bilateral knee surgery. If the subject plans staged bilateral knee surgery, the surgeries must be 6 months apart with the "first" knee enrolled into this study.

Title:	Multi-Center Clinical Investigation of the ATTUNE Cementless Fixed Bearing Tibial Base and Cementless Patella Implants in Total Knee Arthroplasty
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	h) Loss of bone or musculature, inadequate bone quality (e.g. severe osteoporosis), neuromuscular compromise or vascular deficiency at the bone site in the affected limb in sufficient degree to render the procedure unjustifiable (e.g. absence of musculoligamentous supporting structures that could lead to implant instability, joint neuropathy). i) Severe instability secondary to advanced loss of osteochondral structure or the absence of collateral ligament integrity. j) The inability to make bone cuts (e.g. inadequate bone stock) so as to assure correct component position, a firm press fit, and intimate apposition of the cut bone and prosthetic surfaces. k) Subject is currently involved in any personal injury litigation, medical-legal or worker's compensation claims. l) Subject, in the opinion of the Investigator, is a drug or alcohol abuser (in the last five 5 years) or has a psychological disorder that could affect their ability to complete patient reported questionnaires or be compliant with follow-up requirements.
Study Duration:	It is anticipated that recruitment for each configuration will be completed study-wide in 2.5 years. Follow-up is five (5) years. Therefore, the total planned study duration for each configuration is approximately seven and a half (7.5) years.
Procedure Schedule	Subjects included in the investigation will be evaluated pre-operatively, at 6 weeks, 6 months, 1 year, 2 years and 5 years postoperatively. Subjects will also be contacted at 3 years and 4 years, but no detailed clinical assessments will be done at that time. **See Table 1-1 Time & Events Table for details.**
Safety	Type and frequency of Adverse Events will be collected. Site Ethics Committees (EC), Institutional Review Boards (IRB), and Regulatory Authorities will provide oversight for study Subject safety. A Data and Safety Monitoring board (DSMB) / Data Monitoring Committee (DMC) / Critical Events Committee (CEC) will not be used for this trial. Routine safety review of Adverse Events and Serious Adverse Events will be conducted during the study.

Table 1-1: Time and Events Table

	Pre-op	Operative	6wk	6mo	1yr	2yr	3yr Contact	4yr Contact	5yr
Required	-180 to -1d	Day 0	1d to 90d	**91d** to **303d**	**304d** to 669d	670d to 1033d	1034d to 1398d	1399d to 1763d	1764d to **2044d**
Preferred	-90d to -1d		28d to 56d	166d to 194d	335d to 395d	670d to 790d	1065d to 1125d	1430d to 1490d	1795d to 1855d
Screening/Enrolment Log	S*								
Informed Consent	S								
eCRF: Subject	E								
eCRF: Inclusion/Exclusion	E								
eCRF: Demographics	E								
eCRF: Medical and Surgical History	E								
eCRF: Study Visit	E	E	E	E	E	E	E	E	E
eCRF: 2011 AKS (Pre-op Patient Eval'n)	P								
eCRF: 2011 AKS (Post-op Patient Eval'n)			P	P	P	P			P
eCRF: 2011 AKS (Surgeon Eval'n)	E		E♦	E♦	E♦	E♦			E♦
eCRF: KOOS	P		P	P	P	P			P
eCRF: FJS-12			P	P	P	P			P
eCRF: EQ-5D-5L	P		P	P	P	P			P
eCRF: Study Procedure		E							
eCRF: Device Log		E							
eCRF: Image / Scan	X		X		X	X			X
eCRF: Radiographic Eval'n			X		X	X			X
eCRF: Adverse Event Summary		E*	E*	E*	E*	E*	E*	E*	E*
eCRF: Adverse Event		E*	E*	E*	E*	E*	E*	E*	E*
eCRF: Device Deficiency Summary		E*	E*	E*	E*	E*	E*	E*	E*
eCRF: Device Deficiency		E*	E*	E*	E*	E*	E*	E*	E*
eCRF: Protocol Deviation Summary	E*	E*	E*	E*	E*	E*	E*	E*	E*
eCRF: Protocol Deviation	E*	E*	E*	E*	E*	E*	E*	E*	E*
eCRF: Subject Completion/ Discontinuation	E*	E*	E*	E*	E*	E*	E*	E*	**E**

LEGEND:
S = Remains on site as source document
S* = Original remains on site as source document with copies regularly submitted to sponsor
E = Source data transcribed onto electronic Case Report Form (eCRF) and submitted to sponsor
E♦ = Source data transcribed onto electronic Case Report Form (eCRF) and submitted to sponsor if In Clinic Visit completed.
E* = Source data transcribed onto eCRF and submitted to sponsor if In Clinic Visit, Alternative Visit, or Phone/Mail Contact Visit completed.
P = Patient Recorded Outcome Measures (PROMs), completed by Subject, data entered on eCRF & submitted to sponsor
X = X-ray image to be taken & submitted to core imaging lab for storage/analysis. Optional at Postoperative visits performed outside of clinic

2 INTRODUCTION

Primary total knee arthroplasty (TKA) is a common, elective surgical procedure performed frequently to alleviate pain most frequently due to osteoarthritis, with factors such as age (older being more frequently replaced) and gender (females being more frequent sufferers of knee OA) influencing the patient demographics[1]. The clinical demand for TKA use is increasing, with demand for primary total knee replacement in the United States alone being forecast to rise by over 600% to 3.48M from 2005 to 2030[2].

TKA components can be fixed to the bone with or without cement. Whilst cemented fixation remains the gold standard [3-8], the optimal implant fixation remains a debate. Aside from the choice of implant system, the clinical decision relating to implant fixation is heavily influenced by surgeon training and regional preferences. For example, comparing the results of 2 national joint registries of all the primary TKAs performed in 2018, in Australia 9.9% of these procedures used fully cementless fixation[9] whilst in the UK 3.8% of TKAs were fully cementless[10]. Lastly, even if a given surgeon utilizes cementless TKA routinely, patient to patient differences may cause a surgeon to deviate from their standard of care based on the needs of the patient. Surgeons' fixation choice can also vary treatment from patient to patient due to factors such as intraoperatively observed bone quality and patient expectations. According to Fricka et. al.[11] "the potential benefits of cementless fixation include preservation of bone stock, shorter operating room time, ease of revision, and the elimination of complications associated with cemented fixation, including third body wear and retained loose fragment." Designs using cementless fixation are also preferred by some surgeons often in their treatment of younger patients due to the fact that the procedure preserves more of the bone stock than cemented fixation designs and the fixation achieved is physiologic and can respond to stresses in a physiologic manner[12]. It has been shown that the survivorship of cemented TKA in younger patients is not as good as in the older population[13] and the younger patients (<50) have a 4.7 times higher likelihood of revision due to aseptic loosening in the first year compared to patients over the age of 65[14]. Despite the excellent long term survivorship of cemented TKA[3-7], several authors have also raised concerns about the long term durability of bone cement, particularly for younger patients[15,16].

Cementless knee prostheses have been on the market for 30 years, with designs evolving over that time period. Cementless TKA that achieves a good initial fixation, sufficient to allow good bone ingrowth, has the ability to deliver a reliable long term fixation, as evidenced by a number of publications on long term follow-up of cementless TKAs[17-20].

As knee arthroplasty overall has evolved (both by implant design and surgical technique), patients have become more demanding and the mean age at which patients are receiving a primary knee replacement is decreasing with the proportion of patients younger than 65 increasing[2,9]. Younger patients generally want to live a more active lifestyle and to meet this demand; prostheses that enable higher flexion are now available on the market.

In 2011, DePuy Synthes Joint Reconstruction introduced the ATTUNE Knee System with a goal of addressing the unmet needs of patients, surgeons, and hospital providers. The initial offering was only

available for cemented fixation. The high-level system goals were to improve function through motion with stability, improve patient fit, improve patellofemoral function, improve design/materials for durability, and advance surgical process for implant positioning and OR efficiency. In order to bring the ATTUNE Knee System design principles to those surgeons who prefer to treat their patients with cementless fixation, the 3-D printed ATTUNE Cementless Fixed Bearing (FB) Tibial Base has been developed and is the focus of this study. These components are to be used in conjunction with the ATTUNE Cementless Cruciate Retaining (CR) and Posterior Stabilized (PS) femoral components (already commercially available in the markets to be included in this clinical study) and ATTUNE FB CR, MS and PS Tibial Inserts.

All implant components are commercially available for use in the United States.

2.1 Summary of Preclinical Experience

There are numerous in vitro publications available regarding the design of the ATTUNE knee system. The key areas of research included: anthropometrics and kinematics[21-29]. The in vitro results are encouraging and reflect the design goal of improving patient satisfaction. The ATTUNE Cementless FB Tibial Base has been designed to incorporate 3D printed technology and a titanium porous surface structure, which have been shown to increase pull-out force and optimize bone ingrowth[30,31].

3 RATIONALE

3.1 Study Rationale

The ATTUNE Cementless Knee System includes both a rotating platform (RP) and fixed bearing (FB) option. Currently, the RP configuration is on the market and being used worldwide. Data on the RP configuration is being gathered through a post-market clinical study of 498 enrolled subjects with over half of the subjects past their 2-year follow-up visit. The early signs from that study support the system delivers good clinical outcomes in terms of Patient Reported Outcome Measures (PROMs) and survivorship. The ATTUNE Cementless FB Tibial Base will be investigated through this protocol with the aim of demonstrating their safety and effectiveness in the population that they are designed to treat. The resultant study data will be used for CE mark registration of the Cementless FB Tibial Base device in Europe and other regions.

3.2 Study Design Rationale

The study is designed as a non-comparative, multi-center study with each site initially having a cohort of approximately 30 Subjects to recruit (maximum of 50 per site). The follow-up period of 5 years was selected to assess the early period (the first year) when any initial problems may become evident with initial fixation and stability associated with cementless fixation, as well as the medium-term period (out to five years) which is a good indicator of longer-term survivorship. Longer-term survivorship will become available as the product is captured in National Joint Registries in various markets in the absence of any other studies being planned at this point in time.

3.3 Rationale of Endpoints

The primary endpoint of the Knee Osteoarthritis and Outcomes Score – (KOOS-Activities of Daily Living (ADL), Pain and Quality of Life) at 1 year was selected as it is a good benchmark by which the outcomes of Total Knee Arthroplasty (TKA) can be measured with the KOOS being one of the three most commonly referenced questionnaires in the TKA literature[32]. The KOOS scores listed above will be used to find the Functional Responder Rate (FRR) at 1 year (further defined in Section 9.8.4.1). KOOS is collected as a standard of care in many centers, contains sub-scores that encompass symptoms, routine functional activities to more advanced activities, can be reported as a WOMAC score for comparisons with published literature, it is a measure of function which is a relevant manner for assessing recovery and there are numerous publications supporting its use[33-38].

3.4 Rationale of Study Population

The population described in the Instruction for Use (IFU) is limited. Candidates for this study include patients with a severely painful and/or severely disabled knee function resulting from osteoarthritis, post-traumatic arthritis, or a failed previous implant provided that bone quality is adequate and there is no presence of inflammatory joint disease. The rationale for these inclusion criteria is to enhance the ability to pool data across patients recognizing bone defects and/or issues with poor bone quality that render a cementless procedure unjustifiable and recognizing that inflammatory disease may introduce differences in recovery.

4 STUDY RISK / BENEFIT ANALYSIS

4.1 Potential Risks to the Subject

Any surgical procedure poses a potential risk and the procedures undertaken as part of this clinical investigation are no exception. There are known risks associated with the method of anesthesia (general, epidural, local). In addition, there are risks associated with implantation of a device. The risks associated with the study devices are similar to those of any primary, cementless total knee replacement. A full description of the potential risks related to the ATTUNE Cementless FB is included in the Instructions for Use. In addition to the risks provided in the product IFU, bleeding or excessive blood loss, transfusion reaction, or death may occur. These risks may occur with any total knee arthroplasty procedure.

Since it is anticipated that study subjects would be undergoing total knee replacement with a Cementless total knee system whether or not they enroll in the study, there are no foreseeable study-related risks involved with study participation except for the possibility of additional radiation exposure and / or unintentional disclosure of protected health information. Participation in this study may require study subjects to have between 1 and 3 additional X-ray examination(s) that they otherwise would not receive if they did not take part.

4.2 Minimization of Risk

Risks have been minimized by designing the device under evaluation (ATTUNE Cementless FB Tibial Base) to be similar to commercially available total knee arthroplasty implants used for the same indication. The ATTUNE Cementless FB implants have been functionally tested to verify performance characteristics and biocompatibility. In addition, only trained Orthopaedic Surgeons with expertise in treating this condition will implant the study device within this protocol.

Investigators should refer to the *ATTUNE® Porous Fixed Bearing Tibial Base, Medialized Dome Patella and Medialized Anatomic Patella with AFFIXIUM™ 3DP Technology* Instructions For Use, and the *ATTUNE® Knee System Surgical Technique Featuring the ATTUNE® Fixed Bearing Porous Knee* for additional information.

The Sponsor will further minimize the identified and/or emergent risks throughout the study by reviewing the reported complications and Adverse Effects. Any reported Adverse Events and Device Deficiencies will be reviewed and evaluated by the Study Safety Lead assigned to this project.

4.3 Benefit Analysis

The main benefit of this Clinical Study is that the data will enable the introduction of new implants to the market that will enable more surgeons to access the ATTUNE Cementless system (those who prefer a FB construct). Subjects involved in this Clinical Study may also have more follow-up visits than they otherwise would, which then increases the chance of earlier detection of any problems that may arise. The knowledge gained from this investigation may also help future TKA patients.

5 SUBJECT DEFINITION

Male and female subjects, age 22-80 years, inclusive, with a severely painful and/or severely disabled knee function resulting from osteoarthritis, post-traumatic arthritis, or a failed previous implant provided that adequate bone is present and are determined suitable to receive the ATTUNE Cementless FB Tibial Base and the ATTUNE cemented/Cementless Patella (if the patella is resurfaced) implants are eligible for enrolment in this study.

Subjects who do not meet all inclusion criteria and/or who meet any of the exclusion criteria are automatically excluded from study consideration and participation.

5.1 Inclusion Criteria

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

a) Subject is male or female and between the ages of 22 and 80 years at the time of consent, inclusive.

b) Subject has a severely painful knee and/or severely disabled knee function resulting from osteoarthritis, post-traumatic arthritis, or a failed previous implant provided that adequate bone is present.

c) The subject requires total knee arthroplasty and would receive the study implant independent of this research protocol.

d) Subject that is willing to give voluntary, written informed consent to participate in this clinical investigation and authorize the transfer of his/her information to the Sponsor

e) Subject is currently not bedridden.

f) Subject, in the opinion of the Investigator, is able to understand this clinical investigation and is willing and able to perform all study procedures and follow-up visits and co-operate with investigational procedures.

g) Subject is able to read and comprehend the Informed Consent Document as well as complete the required PROMs in either English or one of the available translations[2].

5.2 Exclusion Criteria

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

a) The Subject is a woman who is pregnant or lactating.

b) Contralateral knee has already been enrolled in this study[3].

c) Revision knee that was previously enrolled in the study as a primary knee (ipsilateral).

d) Subject has participated in a clinical study with an investigational product (drug or device) in the last two (2) years.

e) Subject has had surgery on their contralateral knee within six (6) months of study enrolment or has surgery planned on their contralateral knee less than six (6) months of the study surgery.

f) Subject is suffering from inflammatory arthritis in any joint (e.g., rheumatoid arthritis, juvenile rheumatoid arthritis, psoriatic arthritis, systemic lupus erythematosus, etc.).

g) Active local or systemic infection.

h) Loss of bone or musculature, inadequate bone quality (e.g. severe osteoporosis), neuromuscular compromise or vascular deficiency at the bone site in the affected limb in sufficient degree to render the procedure unjustifiable (e.g. absence of musculoligamentous supporting structures that could lead to implant instability, joint neuropathy).

i) Severe instability secondary to advanced loss of osteochondral structure or the absence of collateral ligament integrity.

j) The inability to make bone cuts (e.g. inadequate bone stock) so as to assure correct component position, a firm press fit, and intimate apposition of the cut bone and prosthetic surfaces.

k) Subject is currently involved in any personal injury litigation, medical-legal or worker's compensation claims.

l) Subject, in the opinion of the Investigator, is a drug or alcohol abuser (in the last five 5 years) or has a psychological disorder that could affect their ability to complete patient reported questionnaires or be compliant with follow-up requirements.

5.3 Definition of Subject Enrolment

A patient will be considered enrolled when they have provided written informed consent to participate in this Investigation, which includes authorization of the release of their Personal Health Information (PHI).

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[2] Note the AKS may not be available in all required languages – if there is no translation available for the Subject's primary language then that Subject need not complete that particular eCRF.

[4] This study does not permit enrolment of any subject undergoing simultaneous bilateral knee surgery. If the subject plans staged bilateral knee surgery, the surgeries must be 6 months apart and first knee will be enrolled into this study.

6 OBJECTIVES

6.1 Primary Objective

The primary objective of this clinical investigation is to evaluate functional responder rates with an objective performance criteria (OPC) of 85% as measured by the KOOS questionnaire for the first 225 tibia (CR FB and PS FB combined) implanted with the ATTUNE Cementless FB tray (primary and revision procedures) and will be analyzed when these patients have passed the 1 year preferred post-op window. Study success will be determined using the primary TKA (CR FB and PS FB combined) analysis group.

6.2 Secondary Objectives

The secondary objectives of this study are to establish the surgical effectiveness of the ATTUNE Cementless Tibial Base by evaluating:

- *Type and frequency of Adverse Events and Device Deficiencies.*
- *Functional responder rates with an objective performance criteria (OPC) of 85% as measured by the KOOS questionnaire for all subjects at the 1-year timepoint.*
- *The change from preoperative baseline to the 6-week, 6-month, 1-year, 2-year and 5-year timepoints in functional outcomes and quality of life assessments, as measured using additional patient reported outcomes measures (PROMS):*
    - *AKS (2011)*
    - *KOOS (all subscores)*
    - *FJS-12 (post-op only)*
    - *EQ-5D-5L*
- *Implant survivorship of the ATTUNE Cementless FB Tibial Base using Kaplan-Meier survival analysis at 1, 2 and 5-year timepoints.*
- *Investigator-conducted radiographic analysis of the tibial and patellar components at 6 weeks/6 months 1, 2 and 5 years after surgery.*

6.3 Tertiary Objectives

- *Implant survivorship of the ATTUNE Cementless FB Tibial Base using Kaplan-Meier survival analysis at 3 and 4-year timepoints.*

The primary and secondary clinical endpoints and the relevant statistical analyses are described in detail in **Section 9**.

Table 6-1: Summary of Primary and Secondary Objectives with Respective Endpoints

	Outcome	Endpoint Timing
Primary Endpoint	Functional Responder rates are expected to be between 91%-94% where subject shows 20% improvement from baseline and 10 points improvement from baseline in at least 2 of the following categories: • *KOOS (ADL)* • *KOOS (Pain)* • *KOOS (Quality of Life)* The Objective performance criteria is expected to be 85%. The primary endpoint will be performed for 225 tibia (CR FB and PS FB combined) implanted as primary TKA procedures. Study success will be determined using the primary TKA (CR FB and PS FB combined) analysis group.	1 year
Secondary Endpoints	Type and frequency of Adverse Events and Device Deficiencies for non-screen failed subjects.	Intraoperative through to end of study
	Functional responder rates with an objective performance criteria (OPC) of 85% as measured by the KOOS questionnaire for all subjects.	1 year
	Change from pre-op baseline in AKS (2011), KOOS (all subscores), and EQ-5D-5L and change from first post-operative visit to all other post-operative visits for FSJ-12.	6 week, 6 months, 1, 2 and 5 years
	Survivorship	1, 2 and 5 years
	Radiographic Interface Analysis	1, 2 and 5 years

7 STUDY DESIGN

This study is designed as a post-market, prospective, multi-center, non-randomized, non-comparative, single arm observational study. Level of evidence: III. The sample size for this study is anticipated to be a minimum of 600 subjects. A minimum of each of the following variants must be included:

- *300 ATTUNE Cementless Cruciate Retaining Fixed Bearings*
- *300 ATTUNE Cementless Posterior Stabilizing Fixed Bearings*
- *Up to 300 ATTUNE Cementless Patellae (if available in United States market during the clinical study)*

There will be a maximum of 25 sites in the United States. The study will allow for a minimum of 600 subjects to be implanted: 300 ATTUNE Cementless Cruciate Retaining Fixed Bearing (CR Femoral with CR or MS Tibial Insert) TKAs, 300 ATTUNE Cementless Posterior Stabilizing Fixed Bearing (PS Femoral with PS Tibial Insert) TKAs, and up to 300 ATTUNE Cementless Patellae (if market available) will be included in the

total sample. It is expected that each site will implant approximately 30 subjects (maximum of 50 per site). Treatment assignment in this study is not randomized. Sites are able to enroll subjects with the required variants, any allowed configuration until the minimum of 300 cases for that variant (CR FB or PS FB) is met. Once the cases for any particular variant are met, sites will continue to enroll the remaining variants until their site maximum of 50 subjects is met. Details regarding sample size are presented in Section 9.7.

The Sponsor will monitor overall project enrollment. The Sponsor can authorize a shift of a group of Subjects from one site to another to maintain project timelines. For example, the Sponsor can reduce the cohort of a slow-enrolling site to a faster-enrolling site and the faster-enrolling site will assume responsibility for the reallocated cohort.

Primary Endpoint analyses will be conducted after 225 patients who have undergone TKA have passed the 1 year preferred window for submission to regulatory authorities. The remaining follow-up through 5 years will further evaluate mid-term outcomes and support post-market clinical follow-up commitments.

The Investigator should follow their current standard of care with respect to patellar resurfacing. Specifically, the Investigator can choose to:

- resurface the patella with a cemented ATTUNE patella.
- leave the patella unresurfaced.

When the ATTUNE Cementless Patella becomes available to the Sites, the Investigator can choose to:

- resurface the patella with an ATTUNE Cementless Patella.
- resurface the patella with a cemented ATTUNE Patella.
- Leave the patella unresurfaced.

8 PROTOCOL

8.1 Subject Enrolment

No study-specific procedure, eCRF or form associated with this study can be completed using a patient's personal and/or medical information until written Informed Consent is obtained for that Subject (see Section 5.3. Definition of Subject Enrolment).

8.1.1 Subject Screening

All patients who present with osteoarthritis, post-traumatic arthritis, or a failed previous implant affecting the knee, and are candidates for cementless TKA, and who generally meet the study requirements, will be screened for eligibility and will be listed on the Screening and Enrolment Log in order to document that the Subject selection was unbiased. The date of screening, the results of screening (included or not) and if applicable, the primary reason for not including the patient (*e.g.*, does not satisfy eligibility criteria, not interested in participating) will be recorded on this log. The original log is to be retained at the Site and a copy sent to the Sponsor regularly during enrolment.

Eligible patients who agree to participate in the study will be required to sign an Informed Consent Document prior to any study-specific procedures being done. ***After signing the Informed Consent, study Subjects are defined as "enrolled" and site will complete the non-standard of care pre-operative data collection.***

It is expected that complete data collection will be obtained for all enrolled Subjects, with the only exceptions being a Subject who is subsequently withdrawn (see section 8.4 Discontinuation of Subject Participation for details).

8.1.2 Subject Informed Consent

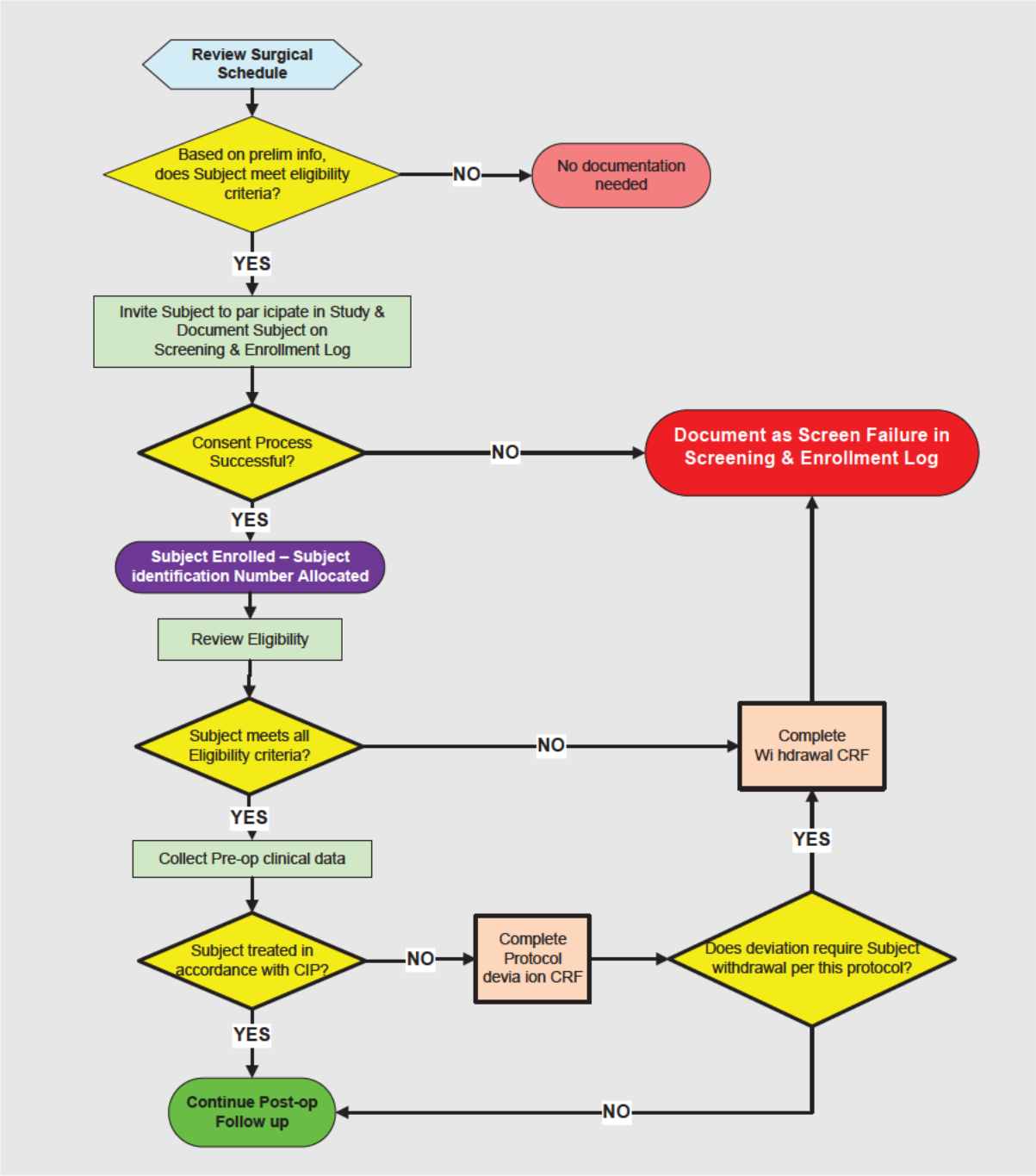
The Principal Investigator is responsible for ensuring that no Subject is included in the study without adequate informed consent being provided. Failure to obtain and properly document this process is in violation of ISO 14155, the Declaration of Helsinki, and this study protocol.

All Informed Consent Documents (ICD) must have favorable opinion of the responsible IRB/EC and reviewing Regulatory Authority, as applicable (Section 12.1). Consent of a Subject needs to be from the Subject themselves and documented on an ICD in the primary language of the Subject as well as the process of consent documented in the Subject's source medical records. Each Subject will be allowed sufficient time to decide whether they wish to participate in this clinical investigation. **Written informed consent from the Subject MUST be obtained before any of the study-specific procedures are performed and PRIOR TO the Day of Surgery. Acquiring consent on the day of surgery will be considered a Protocol Deviation. Note: On review and approval by Sponsor, a CRF completed as part of an investigator's standard of care (e.g. KOOS) can be used as a source document for study required PROMs after the study informed consent has been signed.**

Screening, consenting and enrolment are illustrated in Figure 8-1. The Investigator or trained designee preliminarily screens to determine if a patient generally meets the eligibility criteria for the study. If so, the Investigator or trained designee shall offer study participation to those patients. Having explained the study intent to the Patient, the Investigator or trained designee shall offer to answer any of the Patient's questions. If the Patient then agrees to participate, his or her willingness must be documented via a signature and date on the IRB/EC's approved ICD and this document subsequently countersigned and dated by the person taking consent with a copy of the signed consent document being provided to the study Subject. This full consent process must be documented by the Investigator or trained designee.

Upon successful completion of the consent process, the Patient is enrolled and is identified as a Study Subject.

Figure 8-1: Screening and Enrolment Process



8.1.3 Subject Identification Numbering

The **database assigns Subject ID numbers** after consent is obtained and data are entered into the Electronic Data Capture system.

Each site is identified uniquely, e.g., PPD - followed by PPD for the first Subject at the site, PPD for the second Subject and so on. Together the Site number and the Subject number will then become the unique identifier of the Subject and will be recorded on each page of the eCRF and on the Subject Screening & Enrolment Log. For example, the first three enrolled patients at site #PPD would be: PPD .

In the instance of a Subject being enrolled, a number assigned and subsequently the Subject is deemed ineligible prior to receiving the ATTUNE Cementless FB knee, a Subject Completion/Discontinuation eCRF should be completed and the Subject will be recorded as a screen failure on the Screening & Enrolment log. In the case of pre-operative withdrawals, a further Subject will be enrolled to replace the withdrawn Subject in order to ensure a minimum of 600 Subjects are implanted: a minimum of 300 CR FB (CR or MS Tibial Insert) and 300 PS FB (PS Tibial Insert) configurations with up to 300 cementless patellae combined across both configurations (if market available). Once a Subject identification number is assigned, it may not be reused. Refer to Section 8.4.1 Enrolment Replacement Rules.

8.2 Study Procedures

This section is applicable to enrolled study Subjects. The study Surgeons have selected to implant a total knee arthroplasty using cementless fixation as their standard of care. Therefore, this study does not limit the procedures involved in the treatment of the subject. The pre-operative, anesthesia, general operative procedures post-op care, and follow up are not research procedures, and therefore are not restricted by the study and are regardless of the research.

This section details the study requirements in terms of the pre-operative, operative, and post-operative management of Subjects. Visit evaluations include clinical and radiographic evaluations and Subject self-assessments. eCRFs must be submitted to DePuy Synthes Products Inc. as outlined in Section 11.7 Case Report Form Completion and Data Submission.

The patient reported outcome instruments AKS, KOOS, FJS-12, and EQ-5D-5L are compulsory at all sites. PROMs are compulsory for those Subjects whose primary language is one in which the tools are available. Sites will be advised during training whether validated translations are available in the local language(s) applicable to the Site.

8.2.1 Detailed Instructions on Data Collection

The following evaluation tools are to be used to collect and evaluate study subject outcomes pre-operatively, intra-operatively and post-operatively as outlined in Table 8-1. Patient reported outcomes (in italics) will be provided in hard copy printed sets for **completion by the study subject during a clinic type visit.**

The PROM assessments should be the first assessments administered on the visit day. Pre-operative PROMs should be performed within the preferred visit window (-90d to -1d prior to surgery). **Note: The required window allows the preoperative assessment to be completed 180 days to 1 day prior to surgery.** Each of the questionnaires are to be completed ONLY by the Subject, and usually takes 2-3

minutes per questionnaire to complete. The research team member will provide an official copy of the PROMs to the Subject. The Subject is then to read and complete the form themselves. The research team member is not permitted to read out any of the questions or mark Subject answers on the form. Subjects that are not able to read and complete the questionnaires themselves should not be included in the study (as per Inclusion Criteria F). Subjects should be encouraged to answer all questions.

It is best practice to administer PROMs in reverse recall order (longest to shortest recall duration) and general outcomes to specific outcomes, e.g., in order of subject completion by Subject: AKS, FJS-12, KOOS, and EQ-5D-5L.

Sponsor Approved PROMs by Mail Method (postoperative follow-up only): The packets should be set up with the order of PROM completion as would be done in clinic and should include only those PROMs translated in the Subjects' language (i.e. the Subject portion only of the AKS, KOOS, FSJ-12, & EQ-5D-5L). The packets will be mailed to the Subject along with a cover letter approved by reviewing IRB/ECs. At a minimum, the cover letter should include instructions on how to complete the PROMs and how to mail them back to the site. NOTE: The surgeon portion of the AKS and radiographs are not required with this option and will not result in a protocol deviation if Sponsor approved.

Table 8-1: Data collection, with Subject Completed forms in italics

Case Report Form	Details of Evaluation	Pre-Op/ Intra-op/Post—Op
Subject	System generated Subject ID Number	Pre-Op Only
Inclusion/Exclusion	Verification of Subject as per Inclusion / Exclusion Criteria	Pre-Op Only
Demographics	Record of relevant Subject demographic information	Pre-Op Only
Medical and Surgical History	Authorized medical personnel will collect Subject's relevant medical and surgical history relating to any previous cardiovascular, neurologic, general medical history and previous surgeries on the affected knee.	Pre-Op Only
Study Visit	Assists study site to verify that study visit occurred in the appropriate interval and by the appropriate means (at clinic, by mail or by phone). Prior approval from Sponsor required for Site to exercise mail or phone options.	Pre-op & Post-op
Pre-operative AKS 2011[39] Patient reported section	*A member of the research team will administer each of these PROMs as detailed in Section 8.2.3, below. The total time for completion per study Subject is approximately 20-25 minutes.*	*Pre-op Only*
Post-operative AKS 2011 – Patient reported section		*Post-op Only*

Case Report Form	Details of Evaluation	Pre-Op/ Intra-op/Post—Op
Knee injury and Osteoarthritis Outcomes Score (KOOS)		*Pre-op & Post-op*
Forgotten Joint Score (FJS-12)		*Post-op*
EQ-5D-5L		*Pre-op & Post-op*
AKS 2011 – Surgeon reported section	The Investigator or appropriately trained designee must complete the OBJECTIVE KNEE INDICATORS section that assesses the Subject's alignment, instability, and joint motion.	Pre-op & Post-op
Image/Scan	Date and details of Radiographs collected at each required timepoint. AP/PA, Lateral and Skyline (as applicable) radiographs will be obtained post-operatively (Section 8.2.7) Pre-operative radiographs (taken as per the Sites standard of care) can be taken up to -180 days prior to the surgical event (or older at the discretion of the PI). Pre-operative Radiographs provide background information only, and do not constitute either a primary or secondary endpoint. Post-operative radiographs must be taken as per study-required Image Acquisition Protocol (IAP).	Pre-Op & Post-Op
Radiographic Evaluation	Surgeon evaluation of post-op radiographs	Post-Op
Study Procedure	Description of Subject's surgical procedure including such items as configuration used, surgery time, tourniquet time, surgical technique details etc.	Intra-Op
Device Log	Identification of devices implanted, including product codes, lot numbers and Universal ID code/device identifier (if available).	Intra-Op
Adverse Event Summary	Summary of all recorded AEs for each subject	As required (Intra-Op and/or Post-Op)
Adverse Event	Includes diagnosis, date of onset, treatment and classification of the AE.	As required (Intra-Op and/or Post-Op)

Case Report Form	Details of Evaluation	Pre-Op/ Intra-op/Post—Op
Device Deficiency Summary	Notes whether there were any device deficiencies	As required (Intra-op or Post-Op)
Device Deficiency	Nature of device deficiency and implications of that deficiency (both implant and instrument related)	As required (Intra-op or Post-Op)
Protocol Deviation Summary	Summary of all recorded Protocol Deviations for each subject	As required (Preop, Intra-Op and/or Post-Op)
Protocol Deviation	Nature of deviation that has occurred and reason why	As required (Pre-op - Post-Op)
Subject Completion / Discontinuation	Reason for follow-up being concluded (e.g., completed study requirements, consent withdrawn)	As required (Pre-op - Post-Op)

8.2.2 Pre-operative Management

Prior to surgery, the data in Table 1-1 (the Time & Events Table) must be collected for each enrolled Subject. The interval for obtaining the Informed Consent and pre-op assessments is from -90 days through day -1 (1 day prior to surgery) as designated on the Time & Events Table (Table 1-1). The -90 day time frame is important to support PROMs being collected closer to the time of surgery since it is anticipated that there may be deterioration in function as the patient awaits surgery.

The interval for obtaining preoperative radiographs is extended to -180 days (or older at discretion of PI*) to day -1 (day prior to surgery) so that study Subjects would not need to have repeat radiographs if any radiographs that had been taken as standard of care prior to the Subject being enrolled were the required views. This will be allowed to minimize the study Subject's unnecessary exposure to radiation.

*Note: it would be preferred if the radiographs were taken from -90 days through -1 day, however, if radiographs are available that exceed the 180 day maximum timepoint, they can still be used if they are thought to be acceptable for preoperative surgical planning (per the surgeon's standard of care) at the discretion of the Principal Investigator (PI). If the preoperative x-rays are not able to be uploaded to the MMI system, submitted to MMI via CD, available via hard copy for courier to MMI, or are not de-identifiable, they should be repeated.

Once written informed consent is given, the below will be followed:

- *Pre-operative Patient Reported Outcome questionnaires, Inclusion/Exclusion, Demographics, Medical and Surgical History, 2011 American Knee Society Score surgeon (AKS) and Image/Scan CRFs are to be completed.*
- *The TKA surgical details and all intra-operative complications, regardless of their relationship to the procedure or device, are captured on eCRFs for subsequent analysis.*
- ***In clinic** follow-up intervals include 6 weeks, 6 months, 1 year, 2 years and 5 years post-operative. Post-operative radiographs will be taken at either the **6-week OR the 6-month** follow-up (if x-rays are taken as standard of care at both visits then the 6-week x-rays should be used) and again at 1 year, 2 years and 5 years.*
- *Subjects will be contacted by phone or by mail at 3 and 4 years post-op to optimize accuracy of the survivorship data, enable timely capture of AEs and maximize the chance of good long term follow-up.*

8.2.2.1 Subject History

At the pre-operative visit, the Subject's relevant medical and surgical history, relating to any previous neurological, cardiovascular or general substantive issues and prior ipsilateral knee surgical history should be collected and recorded in the respective eCRF. Any changes relating to the issues listed in the medical or surgical history that occur during the clinical study (i.e. during study surgical event and later) should be recorded as an Adverse Event or Serious Adverse Event, as appropriate.

8.2.3 Operative Management

The preparation of the subject for a total knee arthroplasty should follow the Surgeon's standard of care. Once the patient is ready for the first incision the surgical workflow should follow the *ATTUNE® Knee System Surgical Technique Featuring the ATTUNE® Fixed Bearing Porous Knee* for the devices to be implanted (hereinafter known as "Surgical Technique"). The Surgical Technique will be provided to all study Sites prior to the start of the study. Deviation from the relevant Surgical Technique must be reported as a Protocol Deviation.

Table 8.2: Protocol Requirements During Surgery

Surgical Process Detail	Protocol Instructions
Instrumentation	Surgeons are permitted to use any instrumentation specified in the current Surgical Technique for the region in which the surgery is completed.
Femur and Tibia Treatment	ATTUNE Cementless Cruciate Retaining (CR) or Posterior Stabilized (PS) Femoral Implants are to be used in combination with the ATTUNE Cementless Fixed Bearing (FB) Tibial Base implant and appropriate ATTUNE Tibial Insert.

<table>
<tr><td></td><td>NOTE: If a subject is enrolled in the clinical study prior to implementation of this protocol amendment and receives the ATTUNE Medial Stabilized Tibial Insert as part of the investigator's standard of care, that subject will remain in the study, but must be reconsented with the updated IRB approved ICF which includes the Medial Stabilized insert. A Protocol Deviation must be completed for use of a non-study device with the ATTUNE Cementless Tibia. Once this protocol is IRB approved, no further Protocol Deviations are required for use of the Medial Stabilized Insert from the date of IRB approval forward as long as the subject signs the consent including the Medial Stabilized Tibial Insert as an option.

In this study, bone cement must not be used with the ATTUNE Cementless Femoral or Tibial Base components. If bone cement is used on either of these components, a Protocol Deviation CRF must be recorded and the patient will continue in the study as part of the Safety Population. However, if the site is located in the US and uses DePuy Synthes Antibiotic Impregnated Bone Cement (off-label use), a Protocol Deviation CRF must be recorded and the patient will be discontinued from the study (Study Completion/Discontinuation eCRF). The subject will be replaced with another enrolled subject.</td></tr>
<tr><td>Patellar Treatment</td><td>Study subjects may be implanted with the ATTUNE Cemented Patella, ATTUNE Cementless Patella (after product availability), or not undergo patella resurfacing as part of their study procedure.

<table>
<tr><th>If</th><th>Then</th></tr>
<tr><td>the site is located in the US and the patella is resurfaced using an ATTUNE Cemented Patella</td><td>The site is not permitted to use DePuy Synthes Antibiotic Impregnated Bone Cement (off-label use). If this occurs, a Protocol Deviation CRF must be completed and the patient will be discontinued from the study (Study Completion/Discontinuation eCRF). The subject will be replaced with another enrolled subject.</td></tr>
<tr><td>the patella is resurfaced using an ATTUNE Cementless Patella</td><td>In this study, bone cement must not be used with the ATTUNE Cementless Patella. If bone cement is used, a Protocol Deviation CRF must be recorded and the patient will continue in the study as part of the Safety Population.</td></tr>
</table>
</td></tr>
</table>

8.2.4 Post-operative Management

Immediate post-operative management including physical therapy protocol is at the discretion of the Surgeon and support staff and should follow each Surgeon's standard of care. Rehabilitation programs are often individualized.

The methods of data collection and follow-up windows have been selected to achieve the primary objective of evaluating functional responder rates from baseline to one year as measured from the KOOS questionnaire, as well as providing further data to include survivorship and performance measures out to five years. Every effort should be made to schedule the post-operative follow-up within these windows to enhance follow-up compliance. While required interval windows have been designed to be continuous to improve follow-up compliance and accommodate various standards of care across sites, this study includes preferred windows as well to increase the consistency with respect to the timing of data collection, since function is changing with time, particularly in the early recovery phase.

All follow-up visits will be conducted according to the Time and Events Table (Table 1-1), and applicable eCRFs must be submitted to DePuy Synthes Products Inc. Data collected during the post-operative management of the Subject is listed in Table 8-1.

8.2.4.1 Postoperative Data Collection Methods:

A postoperative follow-up is to be done ONLY by a clinic visit at the 6 week, 6 month, 1 year, 2 year and 5 year follow-up windows. The phone contact visit is to be done only at postoperative years 3 and 4:

The definition of a **Clinic visit** as defined by this protocol is either of the below:

- *The Preferred In Clinic Method: Subject is seen in clinic, receives an assessment of the study knee including study required radiographs, the Subject completes the source document PROMs and the required data is submitted to the Sponsor as per protocol (See Time and Events Table 1-1).*
- ***An Alternative PROMS by Mail Method + Phone Contact**** *(postoperative follow-up only): This method is to be done in the event the Subject is either unable or unwilling to be seen in the clinic office and agrees to complete and return the study required PROMs by mail AND attend a follow-up phone contact visit*. Upon completion of both methods of data collection (in the same interval window), an alternative clinic visit will be considered completed. This type of visit allows for the surgeon portion of the AKS and radiographs to be optional. The details associated with administration of PROMs are described in Section 8.2.1 and apply for this method of data collection A sample cover letter, Contact Form, and Phone Script are provided in Exhibit F.*

The definition of a ***Phone Contact** visit is defined as:

- *A telephone call with the Study Subject (See Time and Events Table 1-1). In order to optimize the accuracy of survivorship data, enable timely capture of AEs and maximize the chance of good long- term follow-up, contact will be made with each Subject at **3 and 4 years post-operatively**. These telephone contact visits will occur in between the 2yr and 5yr clinic visits and will ideally occur within the preferred window. **No PROMs are to be completed.***

Phone Contact visits will take the form of a telephone call where a member of the study team, typically a Research Coordinator, speaks with the study Subject. The topics to be covered and information to be collected during the call will include: confirmation of the Subject's contact information; assessment of whether there has been a revision or any adverse events to the Subject's implanted knee for the study; reminder to the Subject of their next scheduled visit and the importance of their continued study participation. As an alternative approach if in keeping with sites' standard of care, the data collected via a phone contact visit can be collected face to face (in clinic or virtual) or via mail in lieu of being done over the phone.

Note: If a full clinic visit data set is collected at the phone contact intervals (3 & 4 yrs postoperatively), the site will only be compensated for a phone contact type visit.

8.2.5 Radiographic Procedures

Radiographs are to be obtained pre-operatively and at either the 6 week or 6 month visit (1st follow-up/baseline evaluation, timeline as per the Site's standard of care) and again 1, 2 and 5 years post-operatively (within the respective windows specified in this protocol). Pre-operative radiographs are to be collected as per the Site's standard of care. AP/PA and Lateral views are required for all Subjects at the above post-operative timepoints. Skyline views should also be collected post-operatively for Subjects with an implanted patellar component. Investigators will complete questions within the eCRF regarding interpretation of the radiographs for each required set of radiographs.

Radiographic guidelines regarding image collection will be provided to Sites. Sites are also required to send all radiographs collected during the course of the study to an external image analysis facility; training on the process to transfer images will be provided prior to study start.

8.2.6 Protocol Deviations

Any deviations from the procedure outlined in this Protocol should be recorded as Protocol Deviations in the eCRF (see Section 11.8 for further detail).

8.3 Adverse Events

For this study, all SAEs, all Device and/or Procedure-Related AEs and all Device Deficiencies must be reported for all Subjects.

8.3.1 Adverse Event Determination

Adverse Event determination will be done by the Principal Investigator, or appropriate designee. The Investigator will record the nature, severity, treatment and outcome of the AE, and will determine the level of association to the device and/or the study procedure.

8.3.2 Adverse Events Not Required to be Reported to the Sponsor

There are particular immediate post-operative events that are changes from the baseline condition of the Subject but are expected events resulting from surgery, in general. For the purposes of this protocol these are referred to as Non-Reportable Adverse Events and are listed in Exhibit A and are not included in the product IFU. If these events occur, they should be recorded in the Subject's medical record, but these should NOT be reported as AEs in the eCRF or to the Sponsor.

8.3.3 Adverse Event Definitions

The definitions of various type of Adverse Events are provided below:

Table 8-3 Adverse Event Definitions

Term	Details
Adverse Event (AE)	Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to a medical device. Note: This definition includes a) events that are anticipated as well as unanticipated events. b) events related to the medical device under study and c) events related to the procedures involved. See Table 8.5 for definitions of expectedness and Section 8.3.4 for AE reporting requirements. Adverse Event is synonymous with complication or medical event.
Serious Adverse Event (SAE)	An Adverse Event that: leads to death, leads to a serious deterioration in the health of the subject, that either resulted in: ○ *a life-threatening illness or injury,* ○ *a permanent impairment of a body structure or a body function,* ○ *in-patient hospitalization or prolongation of existing hospitalization,* ○ *medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to body structure or a body function,* leads to fetal distress, fetal death or a congenital abnormality or birth defect. Note: Planned hospitalization for a pre-existing condition, or a procedure required by the CIP, without serious deterioration in health, is not considered a serious adverse event.

Term	Details
Adverse Device Effect (ADE)	An adverse event related to the use of the medical device under study. Note: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation or operation, or any malfunction of the medical device under study. This definition includes any event resulting from use error or from intentional misuse of the medical device under study.
Unanticipated Adverse Device Effect (UADE)	An adverse device effect which by its nature, incidence, severity or outcome has not been previously identified in the current version of the risk analysis report. Note: Event will also not be listed in the Instructions for Use.
Serious Adverse Device Effect (SADE)	An adverse event related to the use of a medical device that has resulted in any of the consequences characteristic of a serious adverse event.
Unanticipated Serious Adverse Device Effect (USADE)	A **serious** adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis. This definition includes any event resulting from insufficiencies or inadequacies in the instructions for use or the deployment of the device. This definition includes any event that is a result of a user error. Note: Event will also not be listed in the Instructions for Use.
Expected/ Anticipated Serious Adverse Device Effect (ASADE)	A **serious** adverse device effect which by its nature, incidence, severity or outcome has previously been identified in the current version of the risk analysis report. Note: Event will also be listed in the Instructions for Use.
Device Deficiency (DD)	Inadequacy of a medical device related to its identity, quality, durability, reliability, safety or performance, such as malfunction, misuse, use error or inadequacy in information supplied by the manufacturer.
Awareness (Date of AE Awareness)	The day, month and year that the study site becomes aware of information from any source that reasonably suggests that an Adverse Event has occurred. Note: This date may or may not correspond to the date of onset. The date of awareness is critical to reporting timelines (see Section 8.3.4).

8.3.3.1 Determination of Anticipated / Unanticipated

For the purpose of this protocol, the term "expected" will be synonymous with the term "anticipated" and "unexpected" will be synonymous with "unanticipated".

The PI is responsible for determining whether an AE is **anticipated** or **unanticipated**. This determination is based on whether the severity, type and frequency of the AE is consistent with the Instructions for Use (IFU) in the opinion of the PI. Note that since TKA is a routine elective procedure, the majority of adverse events are anticipated and included in the IFU.

When a PI classifies an AE as unanticipated, the Sponsor will also review and classify anticipated/ unanticipated based on the reported event and in consideration of the IFU and internal risk reports. In the event that the Sponsor has a different opinion on anticipated/unanticipated, a query will be generated. When there is a discrepancy between the site and the Sponsor, both opinions will be recorded and reported as required to the relevant IRB/EC/Regulatory Authority.

8.3.3.2 Determination of AE Severity

Severity refers to the intensity of the symptoms experienced by the study subject and can be used with any event, without regard to whether or not the AE is classified as Serious. Definitions are provided below.

Table 8-4: Definitions of Severity of AEs

Term	Description
Severe Symptoms	The intensity of the symptoms is severe and poorly tolerated, requiring intervention, and significantly affect activities of daily life; or place the Subject at immediate risk or harm.
Moderate Symptoms	The intensity of the symptoms is moderate. Intervention is either noninvasive or not indicated. Activities of daily living can be sustained.
Mild Symptoms	The intensity of the symptoms is mild, transient or asymptomatic. Intervention is not indicated. Clinical or diagnostic observations only and no impairment of normal activity.

8.3.3.3 Determination of Relationship to Device and/or Procedure

The determination whether the AE is related to the device and/or procedure will be based upon whether a causal relationship between the device 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. The Investigator must document all AEs which occur in the Subject's medical record along with the determination of relationship to device and/or procedure to ensure it is clearly documented which AEs will or will not be reported to the Sponsor based on this relationship. Definitions for Device and Procedure Relatedness of AEs are provided below.

Table 8-5: Definitions of Device Relatedness and Procedure Relatedness for AEs

Caused By	Term	Description
Study Device	**Not Related**	Relationship to the study device can be excluded.
	Possible	The relationship with the use of the study device is weak but cannot be ruled out completely.
	Probable	The relationship with the use of the study device seems relevant and/or the event cannot be reasonably explained by another cause, but additional information may be obtained.

Caused By	Term	Description
	Causal Relationship	The event is associated with the study device beyond reasonable doubt.
Study Procedure	Not Related	Relationship to the procedure can be excluded
	Possible	The relationship with the study procedure is weak but cannot be ruled out completely.
	Probable	The relationship with the study procedure seems relevant and/or the event cannot be reasonably explained by another cause, but additional information may be obtained.
	Causal Relationship	The event is associated with the study procedure beyond reasonable doubt.

8.3.3.4 Outcome

The outcome of each AE must be assessed according to the classifications below.

In the event of a previously reported AE which has worsened significantly, the original AE is to be listed as Recovered/Resolved and a new AE reported for the worsened AE. The worsened AE will then be linked to the original AE in the eCRF.

Table 8-6: Adverse Event Outcome Classifications

Classification	Definition
Recovered/Resolved	Subject fully recovered with no observable residual effects
Recovered/Resolved with sequelae	Subject recovered with observable residual effects
Recovering/Resolving	Subject's condition improved, but residual effects remain
Not recovered/Not resolved	AE is ongoing without changes in the overall condition
Fatal	Subject died as a result of the AE (whether or not the AE is related to the device or procedure)
Unknown	Information is not available

8.3.4 Adverse Event Reporting Guidelines

8.3.4.1 AE Reporting by Site to Sponsor

Subjects should be encouraged to report AEs spontaneously or in response to general, non-directed questioning (e.g. "How has your health been since your last visit?"). The Subject may volunteer information relating to AEs at any time during the Study. If an event occurs at an outside institution, the Investigator should attempt to obtain, if possible, required AE information.

All SAEs and all Device and/or Procedure-Related AEs must be reported to the Sponsor, regardless of classification, severity or outcome. The Investigator is responsible for ensuring that all protocol reportable

AEs observed by the Investigator (or designee), or reported by the Subject, that occur from the intraoperative time frame through to the end of the Study (either study completion or withdrawal of consent) are properly assessed, recorded and reported. All protocol reportable AEs must be documented in the study Subject's medical records (source documents) and reported in the database on the Adverse Event eCRFs. All AEs will be monitored until they are adequately resolved or explained. When a Subject ends participation in the study (either through study completion or consent withdrawal) an AE must be designated either as "resolved" (end date must be provided), or as "ongoing."

Table 8-7: Adverse Event Reporting Requirements to Sponsor

Type of Adverse Event	Reporting Requirements
SAEs (including SADEs, USADEs and ASADEs)	Report to Sponsor by completing an AE eCRF or by direct contact to Sponsor (i.e. via phone or e-mail) immediately upon awareness of event but no later than 72 hours. If related to an Implant/Instrument Device Deficiency, also complete a Device Deficiency eCRF as soon as possible but no later than 72 hours.
All Implant Device Deficiencies (including those that potentially could have led to an AE/SAE*)	
AE (Device and Procedure Related, including ADEs and UADEs). See Table 8.5 for further definition of AE relatedness	Report to Sponsor by completing an AE eCRF or by direct contact to Sponsor (i.e. via phone or e-mail) immediately upon awareness of event but no later than 72 hours.
AEs related to a Device Deficiency	Report to Sponsor immediately upon awareness of event but no later than 72hrs, in line with Device Deficiency reporting requirement above.
All other AEs not listed above	Report to Sponsor within 2 weeks of awareness.

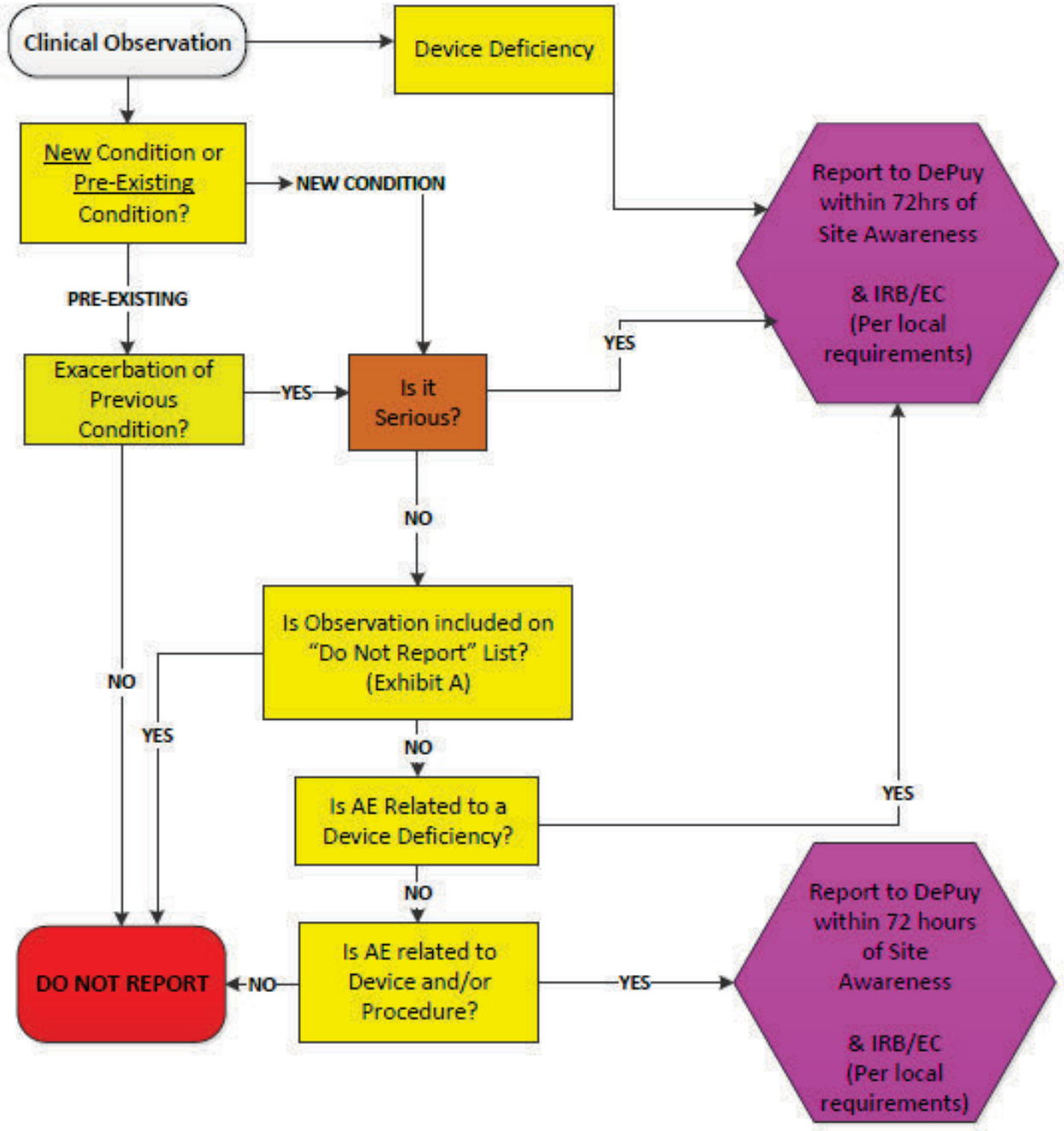
* if a) suitable action had not been taken, or b) intervention had not been made or, c) if circumstances had been less fortunate.

***NOTE: Not meeting the above reporting timelines to the Sponsor will result in a Protocol Deviation.**

Pre-existing medical conditions or symptoms reported prior to the surgical event are to be recorded as part of the medical history and not to be recorded/reported as AEs[5]. The only exception would be in the event there is an exacerbation of a pre-existing medical condition or symptom(s) in the post-operative time frame, then an AE must be reported.

[5] An example could be pre-existing contralateral knee osteoarthritis with a planned TKA intervention after the index knee surgery.

Figure 8.2 AE Reporting Flowchart



8.3.4.2 Institutional Review Board (IRB) / Ethics Committee (EC) Reporting

In any instances of Serious Adverse Events, Serious Adverse Device Effects, Unanticipated Adverse Device Effects, Unanticipated Serious Adverse Device Effect, the Clinical Investigator is responsible for informing the IRB/EC in accordance with their local procedures. The Clinical Investigator should institute appropriate therapeutic and follow-up measures in accordance with good medical practice and record them in the subject's source documentation.

8.3.4.3 Regulatory Reporting Requirements

All reported protocol-required AEs will be reviewed by DePuy Synthes and reported if applicable to the appropriate regulatory bodies.

8.3.5 Safety Oversight

Safety oversight will be conducted by the study Safety Lead. Study data will be reviewed periodically throughout the Study in order to promptly identify new issues or trends which may have an impact on the conduct of the study and/or Subject safety.

8.4 Discontinuation of Subject Participation

Study participation may be discontinued through screen failure, not receiving the tibial base implant, revision of the femoral and/or tibial component(s), withdrawal of consent, or death. Table 8-8 describes how data will be captured on Subjects that are discontinued prior to receiving the study device while Table 8-9 describes post-op withdrawal scenarios. In all cases, once a subject is enrolled (per Figure 8-1), if they discontinue study participation, the Subject Completion/Discontinuation eCRF must then be completed.

8.4.1 Enrolment Replacement Rules

Since Subjects are enrolled at the time of consent, any Subject that is withdrawn pre-operatively and or does not receive the study required tibial / femoral implants will be replaced with a subsequent Subject. Overall, the number of Subjects who receive a TKA procedure with the study required tibial / femoral components across all sites must meet the minimum sample size of 300 patients per configuration (CR Femoral with CR or MS Tibial Insert or PS Femoral with PS Tibial Insert) and up to 300 cementless patellae (across both configurations). Intra-operative withdrawals will also be replaced with a subsequent Subject and will be assessed to understand reasons why the implant was not appropriate for use in that subset of Subjects.

Table 8-8: Data Collection for Enrolled Subjects Who are Subsequently Found to be Pre-operative and Intra-operative Screen Failures

Screen Failure Type	Screening/ Enrolment Log?	Data submitted on eCRF?	Enrolled Subject?	Example	Action
Pre-operative screen failure (discovered post-consent but pre-op)	Yes	Yes	Yes	*Subject withdrew consent or the Subject no longer met inclusion/ exclusion criteria.*	• Complete Subject Completion/Discontinuation eCRF • Recruit an additional subject
Pre-operative screen failure (Discovered post-op)	Yes	Yes	Yes	*Age criteria not met*	• Keep as Subject – continue to follow as per Safety population • Complete Protocol Deviation eCRF
Intra-operative screen failure	Yes	Yes	Yes	*Did not implant ATTUNE Cementless Tibial / Femoral device*	• Complete Subject Completion/Discontinuation eCRF • Recruit an additional subject

8.5 Post-operative Withdrawal of Enrolled Subjects

A post-operative withdrawal is a Subject who has signed the Informed Consent Document (ICD), has been implanted with a study device, and is later withdrawn from study participation (i.e., withdrawal of consent, revision of any study TKA component, death, etc.). Table 8-9 describes post-operative withdrawal scenarios and the eCRF to be completed. Further description of revision is provided in Section 8.6 Revisions. No data after the date of withdrawal will be included in the clinical analysis.

Table 8-9: Post-operative Withdrawal Scenarios

Example	Action	Follow Up
Subject withdraws consent	• *Study site documents Subjects' request for withdrawal from study.* • *Complete Study Completion/Discontinuation eCRF*	Do not continue
Surgeon preference / medical opinion	• *Study site documents Surgeons' reason for patient withdrawal from study (should occur under very limited conditions, in order to avoid investigator bias).* • *Complete Study Completion/Discontinuation eCRF*	Do not continue
Death	• *Complete Adverse Event eCRF* • *Complete Study Completion/Discontinuation eCRF*	Do not continue
Revision	See Section 8.6 and Table 8-10 Revision Examples	

8.6 Revisions

A "**revision**" is defined as a surgical procedure of the affected knee where one or more of the TKA components (metal femoral component and/or metal tibial base, polyethylene insert, or patella polyethylene resurfacing component) are removed. Should it be necessary for the Subject to undergo a revision of any ATTUNE Cementless Femoral and/or Tibial Base component between the time of enrolment and completion of the study data acquisition, the Subject is to be withdrawn from study participation. Thus, both an Adverse Event (AE) eCRF and the Subject Completion/Discontinuation eCRF must be completed (see Table 8-9). Note that if a tibial insert is exchanged and/or a resurfaced patella is revised, but both the femoral and tibial base components remain, then an AE eCRF must be completed, but the subject is not to be withdrawn from the study.

A "re-operation" is defined as any surgical procedure of the affected knee in which none of the TKA components are removed. Examples include irrigation & debridement without tibial insert exchange or the resurfacing of a previously unresurfaced patella. These subjects are not to be withdrawn. An Adverse Event (AE) eCRF must be completed.

Table 8-10: Revision and Reoperation Examples

Example	Actions	Follow Up
Removal / revision of metal Tibial Base and/or Femoral component	• *Complete Adverse Event eCRF* • *Complete Revision/Reoperation eCRF* • *Complete Study Completion/Discontinuation eCRF*	Do not continue
Tibial Insert polyethylene exchange	• *Complete Adverse Event eCRF* • *Complete Revision/Reoperation eCRF*	Continue
Revision of a previously resurfaced patella	• *Complete Adverse Event eCRF* • *Complete Revision/Reoperation eCRF*	Continue
Resurfacing of a previously unresurfaced patella in combination with a Tibial polyethylene exchange	• *Complete Adverse Event eCRF* • *Complete Revision/Reoperation eCRF*	Continue

8.7 Lost to Follow-up

Although follow-up compliance is essential to study quality, some Subjects may not be able to return for follow-up evaluations. Sites should make every effort to ensure complete follow-up including phone calls and/or written requests to a Subject. If these approaches are not successful, then the site may document a Subject as lost-to-follow-up on the Subject Completion/Discontinuation eCRF. Contact attempts (minimum of 3 attempts) should be documented in the Subject's medical notes.

8.8 Medical Care Following Study End

In the event that a study subject is withdrawn from the study for any reason, their follow-up care will continue per their surgeon's standard of care.

9 STATISTICAL METHODOLOGY

This section describes the statistical methods for the study design and planned analysis of study data.

9.1 Study Design

This is a prospective, multi-center, non-randomized, single arm observational study. A minimum of 600 subjects will be enrolled at a maximum of 25 sites in the United States. Two (2) implant configurations will be studied: 300 CR FB knees (CR or MS Tibial Inserts) and 300 PS FB knees (PS Tibial Inserts) and up to 300 Cementless Patellae (if available in United States market during the clinical study).

9.2 Treatment Assignment

This is a non-randomized, non-comparative, unblinded study; all subjects will receive an ATTUNE® Cementless FB Tibial Base. Each surgeon will use their standard of care configuration for enrolled subjects. This includes either the CR FB (CR or MS Tibial Inserts), PS FB, or both. In addition, surgeons will select to resurface the patella with the ATTUNE Cemented Patella or the ATTUNE Cementless Patella once available or leave the patella unresurfaced.

9.3 Interval Windows

The pre-operative assessment is to be done between 180 days prior to the procedure up to day -1 (day zero defined as the day of the index procedure for this study); radiographs for this study may be from 180 days prior to day -1 (or longer if the PI determines they are acceptable for surgical planning). The required window intervals are defined as follows for analysis purposes:

Table 9-1: Interval Windows

Required* Follow-up Intervals (days)								
Pre-op**	Day 0	6 Week	6 Months	1 Year	2 Year	3 Year Contact	4 Year Contact	5 Year
-180 to -1d	0 (Defined as the Day of TKA)	1-90	91-303	304-669	670-1033	1034-1398	1399-1763	1764-2044
Preferred* Follow-up Intervals (days)								
Pre-op**	Day 0	6 Week	6 Months	1 Year	2 Year	3 Year Contact	4 Year Contact	5 Year
-90 to -1d	0 (Defined as the Day of TKA)	28-56	166-194	355-395	670-790	1065-1125	1430-1490	1795-1855

* Although these are the windows for analysis purposes, narrower "preferred" interval windows have also been included in this protocol

** Pre-operative radiographs may be in the window -180 to -1 days (or longer if the PI determines they are acceptable for surgical planning)

Multiple visits within these defined windows for a single subject may occasionally occur. If this occurs, then for both the pre-op interval the visit closest to the date of surgery will be considered the study visit. Individual pre-op data (i.e. radiographs, PROMs, etc.) may be collected at different pre-op visits and each type of data will be considered separately when considering multiple visits. For post-op intervals the later of the visits will be considered the study visit for analysis purposes.

9.4 Levels of Significance

Where estimated, all confidence intervals will be 95% confidence intervals. For the primary endpoint hypothesis test an alpha = 0.05 will be used to determine statistical significance. No adjustments will be made for multiplicity as this is the only hypothesis in the study.

9.5 Handling of Missing Data

Only actual data will be analyzed; there will be no imputation of missing data.

9.6 Analysis Sets

The following analysis sets are defined for the purpose of analysis: an Intent to Treat (ITT) analysis set, a Safety analysis set, and a Per Protocol (PP) analysis set. The analyses of adverse events and the Kaplan-Meier analysis of revisions will be carried out on the Safety analysis set. The primary endpoint analysis and all secondary endpoint analyses will be carried out on the Per Protocol analysis set. The analysis of the tertiary endpoints will be carried out on the PP analysis set unless otherwise stated in the final clinical summary report.

9.6.1 ITT Analysis Set

The ITT analysis set consists of all subjects who are consented and enrolled into the study. Subjects in the ITT analysis set who do not undergo surgery to implant the ATTUNE Cementless FB tibial base will be withdrawn from the study without any further data collection. The purpose of this analysis set is to provide accountability for these subjects who do not receive the ATTUNE Cementless FB tibial base system. There are no other analyses which are planned for this dataset.

9.6.2 Safety Analysis Set

The Safety analysis set consists of all ITT subjects who undergo surgery to implant the ATTUNE Cementless FB tibial base. Subjects who withdraw from the study prior to surgery will not be included in the Safety analysis set.

9.6.3 PP Analysis Set

The Per Protocol (PP) analysis set is a subset of the Safety analysis set that includes all subjects who meet the following criteria:

- There are no clinically meaningful deviations from the protocol eligibility criteria, and
- The subject receives an ATTUNE Cementless FB tibial base,
- The subject has at least one post-operative evaluation in the 6 week or later time window.

9.7 Sample Size Justification

The primary endpoint in this study will be to estimate the Functional Responder (defined below in Section 9.8.4.1) rate at 1 year and demonstrate superiority to the 85% objective performance criteria. Functional Responder rates are anticipated to be between 91-94% in primary TKA based on a previous study of ATTUNE Cemented and ATTUNE Cementless CR RP knees. Using the lowest anticipated rate of 91%, a sample size of 191 knees will provide at least 80% power to show superiority of the Functional Responder rate compared to the objective performance criteria of 85%, with 95% confidence using a one-sided, normal approximation, one-proportion test and associated confidence interval. Accounting for up to 15%

attrition at 1 year, the sample size population for analysis of the primary endpoint was increased to the first N=225 knees enrolled.

Due to various global requirements and anticipated regulatory submissions the sample size is increased to N=300 per configuration.

9.8 Analyses to be Conducted

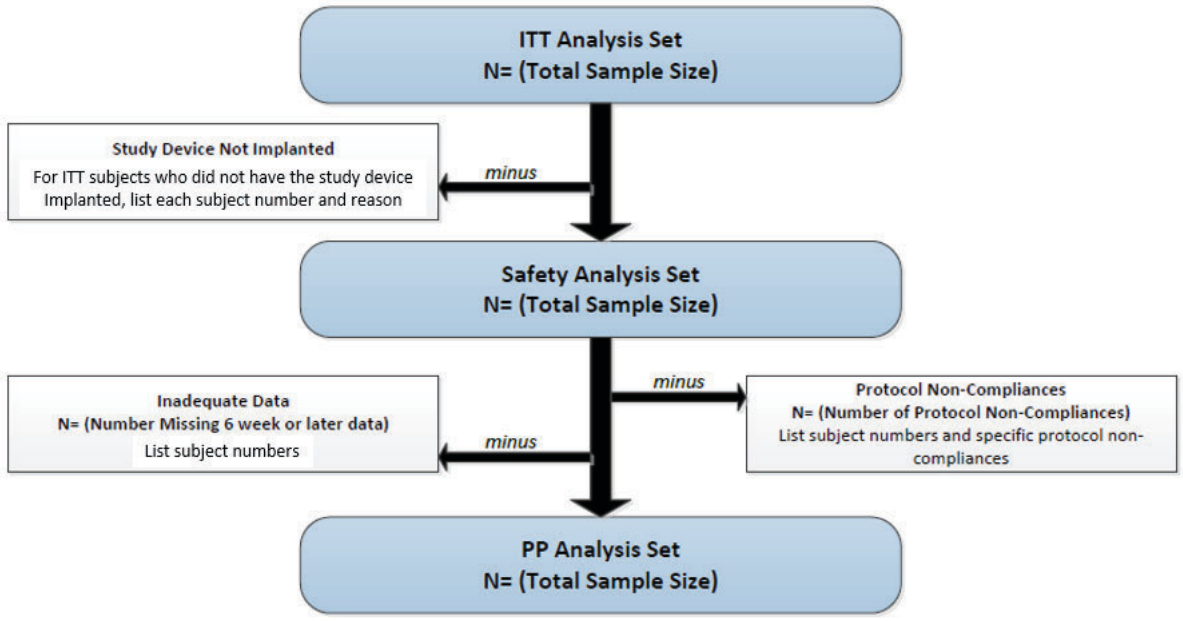
9.8.1 General Conventions

All analysis will be performed using SAS v9.4 or higher. Statistical summaries (tallies and percentages for categorical variables, and sample size, mean, standard deviation, minimum and maximum (and others as needed) for continuous variables) at each respective time point, or cumulatively for safety endpoints.

9.8.2 Disposition of Study Subjects

A detailed account of all enrolled subjects will be presented in a dataset flow diagram to display the analysis datasets, beginning with the set of ITT subjects and explicitly listing the subjects with distinguishing reasons for exclusion from the other datasets. A template of this dataset flow diagram is given in Figure 8-1 below.

Figure 9-1: Analysis Set Flow Diagram



9.8.3 Demographics and Baseline Characteristics

Demographic and baseline characteristics will be summarized overall and by configuration. The demographics characteristics will not be compared statistically.

9.8.4 Primary and Secondary Endpoints and Associated Hypotheses

Each endpoint below will be analyzed for all knees and separately for primary and revision procedures and CR FB (CR or MS Tibial Inserts) and PS FB configurations, unless otherwise specified.

9.8.4.1 Primary Endpoint and Associated Hypotheses

The primary endpoint is the Functional Responder Rate (FRR) at 1 year. A Functional Responder is defined as:

- A subject that shows at least 20% improvement from baseline and at least a 10-point improvement from baseline in at least 2 of the following categories:
    - KOOS (ADL)
    - KOOS (Pain)
    - KOOS (Quality of Life)

Functional Responder rates are expected to be between 91%-94%. The objective performance criteria for study success is 85%.

$$H_0: FRR \leq 85\%$$

$$H_A: FRR > 85\%$$

The primary endpoint will be performed on the first 225 tibia implanted with the ATTUNE Cementless FB tray (primary and revision procedures, CR FB and PS FB combined) and will be analyzed when these patients have passed the 1 year preferred post-op window (395 days). This analysis will be done on the Per Protocol (PP) population. Study success will be determined using the primary TKA (CR FB and PS FB combined) analysis group.

9.8.4.2 Secondary Endpoints and Associated Hypotheses

The secondary endpoints in this study are:

- *Type and frequency of Adverse Events and Device Deficiencies.*
    - *Functional responder rates with an objective performance criteria (OPC) of 85% as measured by the KOOS questionnaire for all subjects (CR FB and PS FB combined) at the 1 year timepoint.*
- *The change from preoperative baseline to the 6 week, 6 month, 1 year, 2 year and 5 year timepoints in functional outcomes and quality of life assessments, as measured using additional patient reported outcomes measures (PROMS):*
    - *AKS 2011*
    - *KOOS (all subscores)*
    - *FJS-12 (changes post-operatively only)*
    - *EQ-5D-5L*
- *Implant survivorship of the ATTUNE Cementless FB Tibial Base using Kaplan-Meier survival analysis at 1, 2 and 5 year timepoints.*
- *Investigator-conducted radiographic analysis of the tibial and patellar components at 6 weeks/6 months, 1, 2 and 5 years after surgery.*

All secondary endpoint analyses may be conducted after all patients have passed the recommended study window (ex. with a 2-year follow-up analysis conducted after all subjects have passed 790 days post-op). All analyses at these time points will be conducted again with final data, along with endpoints which have a 5-year follow-up time point, with locked data at the close of the study.

A Kaplan-Meier survivorship model will be used to estimate survivorship rates (where a revision is defined in Section 8.6) along with a two-sided, log-log based 95% confidence intervals; this analysis will be conducted on the Safety analysis set.

The types and frequencies of adverse events that occur throughout the study will be tabulated by MedDRA system organ class (SOC) and preferred term (PT) for all Subjects in the Safety analysis set. The proportion of Subjects experiencing each complication (PT within SOC) will be presented, and a 95% confidence interval will be estimated with the binomial exact method.

All other specified secondary endpoints will be presented with statistical summaries at each respective time point; these secondary endpoint analyses will be carried out with all data on subjects in the Per Protocol analysis set.

9.8.4.3 Additional Endpoints

Additional endpoints include:

- *Implant survivorship of the ATTUNE Cementless FB Tibial Base using Kaplan-Meier survival analysis at 3 and 4 year timepoints.*
- *To evaluate the duration of surgery ("skin-to-skin" time) for all surgeries, with analysis stratified by cemented/Cementless patella usage.*

Duration of surgery ("skin to skin" time) may be analyzed any time after all subjects have been enrolled and undergone surgery. All other post-operative tertiary endpoints may be conducted after all subjects have passed the preferred post-op window. All analyses at these time points will be conducted again with final data, along with endpoints which have a 5-year follow-up time point, with locked data at the close of the study.

9.8.5 Plans for Interim Analysis

There are no formal interim analyses planned with the intent of early trial closure.

Interim summaries may be performed as required, for example to provide information to Regulatory Authorities or Notified Bodies.

10 DEVICE DESCRIPTION

All implant components are commercially available for use in the United States. The intended purpose, indications, contraindications and population are described in the Instructions for Use (IFU), which is contained in the packaging of all products marketed in the United States.

10.1 Fixation

ATTUNE Cementless Cruciate Retaining (CR) or Posterior Stabilized (PS) Femoral implants are to be used in combination with the ATTUNE Cementless Fixed Bearing (FB) Tibial Base implant and appropriate Tibial Insert and must be used without bone cement. If any Cementless components are cemented, a Protocol Deviation eCRF must be completed and the subject will continue to be followed as part of the Safety Population. See Table 8-2 Protocol Requirements During Surgery for additional details regarding fixation requirements.

10.2 Devices

A list of devices permitted for Subjects enrolled in the study is presented in Table 10-1. All Investigators will be trained on the use of these devices prior to their first enrolment. The components permitted for each of the two (2) constructs is defined in Table 10-1. The details of the individual components are provided in Table 10-2. Additional, detailed information regarding component product codes are provided in Exhibit B.

Table 10-1: Components of the Construct

Configuration	Components Needed for Construct			
	Femoral (Cementless)	Tibial Base (Cementless)	Insert	Cemented Patella*
• Cruciate Retaining fixed bearing (ATTUNE® CR FB)	CR	FB	Cruciate Retaining or Medial Stabilized	Medial Offset OR Anatomic
• Posterior Stabilized fixed bearing (ATTUNE® PS FB)	PS	FB	Posterior Stabilized	
*** Patella resurfacing shall follow site standard of care (unresurfaced or cemented patella). For Subjects where the patella will be resurfaced, 2 patella implant designs are permitted.**				

Table 10-2: Knee Configurations

Regulatory Status	Device Component	Component Offerings	Details	
CE mark & 510(k) clearance	Cementless Femoral Components	Cruciate Retaining (CR)	ATTUNE femoral components are available in **cruciate retaining (CR)** and **posterior stabilized (PS) configurations**. The femoral components are manufactured from cast Co-Cr-Mo alloy conforming to ASTM standard F-75 and the bone opposing surfaces are coated with Co-Cr-Mo POROCOAT, a proprietary porous coating technology. They are available in lefts and rights. Fourteen sizes are available including standard sizes 1-10 and narrow sizes: 3N, 4N, 5N, 6N. Femoral components are sterilized using gamma irradiation. **They are available for cementless use only.** The PS femoral components have a cam mechanism that articulates with a corresponding spine on the PS tibial insert.	
		Posterior Stabilized (PS)		
510(k) clearance	Cementless Tibial Base	Fixed Bearing (FB)	ATTUNE tibial components are manufactured from wrought and 3D printed titanium conforming to ASTM standard F-3001 and the bone opposing surfaces are comprised of 3D printed porous coating technology and fixation geometry features. The proximal surface is designed to work with currently available ATTUNE FB tibial inserts, CR and PS. The cementless FB tibial bases are available in sizes 1-10. Tibial components are sterilized using gamma irradiation.	
CE mark & 510(k) clearance	Tibial Inserts	Fixed Bearing (FB)	Cruciate Retaining (CR)	The CR and PS tibial inserts are symmetrical tibial inserts manufactured from AOX Antioxidant UHMWPE and are available in sizes 1-10 and thicknesses from 5, 6, 7, 8, 10, 12, 14, 16, 18mm. Additional thicknesses 20 & 22mm are available for the PS inserts. The distal surface has features that secure the insert to the FB tibial base. Tibial inserts are sterilized using gamma irradiation.
			Posterior Stabilized (PS)	
510(k) clearance	Tibial Inserts	Fixed Bearing (FB)	Medial Stabilized (MS)	The ATTUNE Medial Stabilized tibial inserts are asymmetrical fixed bearing tibial inserts that will form part of the ATTUNE Knee system. They are designed to work with the ATTUNE CR femur and any of the ATTUNE Fixed Bearing Tibial Base options. They are manufactured from AOX Antioxidant

				UHMWPE and are available in right and left sizes 1-10 and thickness from 5, 6, 7, 8, 10, 12, 14 and 16. Tibial inserts are sterilized using gamma irradiation.
CE mark & 510(k) clearance	Cemented Patellaes	Medial Offset	The patellar components are manufactured from UHMWPE and are available in two styles, medialized dome and medialized anatomic. They are available in 5 sizes with proportionally increasing thicknesses from 8.5 to 10.5 mm. Patellar components are sterilized using gamma irradiation. **They are available for cemented use only.**	
		Anatomic		
510(k) clearance	Cementless Patellaes	Medial Offset	The cementless patellar components are manufactured from UHMWPE overmolded onto 3D printed titanium conforming to ASTM standard F-3001 and the bone opposing surfaces are comprised of 3D printed porous coating technology. The anterior surface is designed to work with currently available ATTUNE CR and PS femoral components. They are available in 4 sizes with proportionally increasing thicknesses from 9.0 to 10.5 mm. Patellar components are sterilized using gamma irradiation.	
		Anatomic (if available during enrolment)		

10.3 Use of the Study Devices

In addition to the CIP training provided, all Investigators will receive training with the Study Devices, to be arranged by the Sponsor, prior to implanting the ATTUNE FB Tibial Base as part of this clinical investigation.

10.4 Device Management

Device Deficiency reporting for this clinical study includes both the implantable components and the instrumentation. Specific device accountability is not required for this study as it is entirely post-market. Implant catalog and lot numbers will be collected.

10.4.1 Reporting on Deficient Devices

All study Sites (regardless of Site location) are required to report Device Deficiencies relating to ANY of the implantable ATTUNE components, component packaging, and instrumentation to the Sponsor via the Device Deficiency eCRF (see Section 8.3). In the event a device deficiency is associated with a Study Subject experiencing an adverse event, the Adverse Event eCRF is also required to be submitted to the Sponsor.

11 INVESTIGATOR RESPONSIBILITES AND GOOD CLINICAL PRACTICES

In conducting this medical device clinical investigation the Investigator is responsible for:

- Ensuring that a clinical investigation is conducted according to the Declaration of Helsinki, applicable local regulations, the signed Clinical Trial Agreement, and the Clinical Investigation Plan.
- 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 investigation at each site, the responsible Principal Investigator will acknowledge their understanding of this Clinical Investigation Plan (CIP) by signing the signature page. This signature confirms that the clinical investigation will be performed in compliance with the CIP.

11.1 Qualification of Principal Investigator and Investigational Site

The PI shall:

- *be qualified by education, training and experience to assume responsibility for the proper conduct of the clinical investigation in accordance with ISO14155. Evidence of such qualifications of the PI and key members of the investigative site team shall be provided to the Sponsor through up-to-date CVs or other relevant documentation.*
- *be experienced in the field of orthopaedics and total knee replacement and trained in the use of the investigational device under consideration.*
- *disclose potential conflicts of interest, including financial, that interfere with the conduct of the clinical investigation and/or interpretation of results.*
- *be knowledgeable with the method of obtaining informed consent.*

The PI shall be able to demonstrate that the proposed investigational site:

- *has the required number of eligible subjects needed within the agreed recruitment period.*
- *has one or more qualified investigators, a qualified investigational site team and adequate facilities for the foreseen duration of the clinical investigation.*

11.2 Institutional Review Board (IRB)/Ethics Committee (EC) Approval

All Principal Investigators must submit to their institution's IRB/EC for initial review a copy of the clinical investigational plan (CIP), a sample Informed Consent Document (ICD) provided by the Sponsor. Many institutions request modification of the ICD to satisfy specific institutional requirements. The use of a modified or unique Informed Consent Document is permitted provided that the document is reviewed and approved by the Sponsor. Additionally, all translated consent forms require IRB/EC approval.

All Principal Investigators must submit the Clinical Investigation for continuing review and any other additional required submissions to their IRB/EC according to their IRB/EC's policies and procedures.

Initial approval/favorable opinion and all continuing review approvals must be documented; originals of correspondence and approvals are to be filed by the Investigator and copies forwarded to the Sponsor.

11.3 Informed Consent

The Principal Investigator is responsible for maintaining source documents evidencing informed consent was obtained from study Subjects prior to participation in the study and the process followed to obtain consent.

If an Investigator performs any study-specific procedures and/or data collection without obtaining informed consent, the Investigator will report such action(s) to the Sponsor and the reviewing IRB/EC.

For further details and a description of the Informed Consent process, please refer to Section 8.1.2, Subject Informed Consent.

11.4 Protected Health Information

The Principal Investigator is responsible to inform study Subjects their personal data will be collected, processed, and confidentially maintained in accordance with local data privacy regulation and law.

United States: The Principal Investigator is responsible for taking the necessary steps to collect, process and maintain confidentiality of the Subject's personal data in accordance with data protection legislation including the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Subjects will be asked to sign an Authorization for Release of Protected Health Information (PHI) for the purpose of this investigation. The authorization may be combined with the ICD, depending on local IRB preference.

Results from the Clinical Investigation may be published. However, Subject confidentiality will be maintained at all times and it will not be possible to identify individual Subjects from any data presented.

11.5 Subject Completion/Discontinuation from the Clinical Investigation

Any Subject is entitled to discontinue/withdraw from this clinical investigation for any reason without obligation and/or prejudice to further treatment. In addition, the Investigator may decide, for reasons of medical prudence, to withdraw a Subject.

The Investigator will clearly document the date and reason(s) for the Subject's discontinuation from this clinical investigation in the Subject Completion/Discontinuation eCRF and submit to DePuy Synthes Products Inc.

Please refer to Section 8.4 Discontinuation of Subject Participation for further details.

11.6 Source Documentation

The Investigator will maintain a complete, current and accurate case history (Source Documentation records) on each study Subject according to the usual procedure at the investigational site. Case histories, medical records, including progress notes, hospital charts, nurses' notes etc. Additional documents to be retained include:

- Signed original Informed Consent Document
- Completed Source worksheets (if used)
- Results of relevant diagnostic and laboratory tests

- Intraoperative and post-operative complications and treatment, and
- Any other relevant information or documentation pertaining to the condition of the Subject.

Monitors may verify data reported in the electronic data capture (EDC) system against Subject source documents. The Investigator agrees that the Sponsor's employees or designees will have the right to audit and review pertinent medical records relating to this clinical investigation and the Subject will grant approval for such access to their medical records via the Informed Consent process.

11.7 Case Report Form Completion and Data Submission

Data will be captured within an electronic data capture system provided by DePuy Synthes Products Inc.

Electronic Case Report Forms (eCRFs) will be used to collect and submit all Subject data once a Subject is enrolled in the study. **Investigative study sites are asked to transfer Subject data from the source PROMs into the eCRFs preferably within 2 weeks from the time the Subject was seen for their scheduled study visit.**

Role-specific training on eCRF completion is required to be completed by the Investigator(s) and study support staff prior to initiating Subject enrolment.

The personal data recorded on all documents, including copy documents, and within the EDC system, will be regarded as confidential. The Investigator will be responsible for the timing, completeness and accuracy of the details entered within the electronic data capture system. All data entered in the database must have source documents in the Subject's medical records or source worksheets.

The respective eCRFs must be fully completed for each Subject. The Investigator's electronic signature will be obtained within the EDC system once all study data has been entered, cleaned and coded (and at interim analysis if applicable). Sign off can occur on a per form or per casebook level. Any changes to the data will break the Investigator's signature and sign off will need to be obtained again on the relevant data.

The patient-reported outcome measures (AKS, KOOS, EQ5D-5L, and FJS-12) will be recorded on paper-based or other validated electronic questionnaires. The data will then be transferred into the respective eCRF within the electronic data capture system by the Investigator or designee. The patient-reported outcomes measures captured on paper-based questionnaires must be stored in the Subject's binder as these will be considered to be the source document. Any errors on paper forms should be crossed out with a single stroke, initialed and dated. Typing correction fluid must not be used. The Investigator will retain one copy of each completed paper CRF in the medical notes.

The Investigator must record the Subject's participation in this clinical investigation in the Subject's medical notes. In addition, the Investigator must keep a separate list of all Subjects entered into this clinical investigation showing each Subject's name, date of birth and assigned Subject number (for identification purposes). A Patient Information log will be provided in the Investigator Site File for this purpose and remain at the site.

The Investigator should retain copies of all documents pertaining to this clinical investigation (including source documentation, the informed consent document and any other documents to identify the

Subjects) per the applicable retention period in your region[4] or per your IRB/EC/RA after this clinical investigation is completed. In addition, if the Investigator moves/retires, etc., he should provide the Sponsor with the name and address of the person who will be responsible for the Subjects' clinical investigation related records.

Data queries will be generated by the system at the time of data entry, if applicable. Resolution of the queries will be the responsibility of the Investigator and investigation team members. Following completion of all data queries on each eCRF, the Investigator will be responsible for reviewing and confirming agreement to the data within the system.

The platform software has been validated in accordance with 21 CFR Part 11, European Commission's Directive on Data Protection and EU General Data Protection Regulation. Prior to being released for data entry, validation of the study level components (i.e., data entry screens, associated edit checks and workflow) will be conducted in accordance with approved user acceptance testing procedures. Access to this system will be controlled so that only authorized users will have the ability to enter into the system. The system is considered a closed system according to 21 CFR Part 11 Electronic Records; Electronic Signatures.

11.8 Protocol Adherence

The Investigator(s) agrees to conduct the study in accordance with this protocol. An Investigator must not make any changes in a study without first receiving approval from the Sponsor and IRB/EC, except when necessary to eliminate apparent immediate hazards to a Subject.

With the exception of emergency situations, no deviations to this CIP will be permitted. In the event of an emergency situation, the Investigator must notify the Sponsor immediately. The Site will be responsible for completing a Protocol Deviation eCRF within the EDC system, which will serve as Sponsor notification. IRB/EC/RA notification will be the responsibility of the Investigator.

If serious or repeated protocol deviations are found at a Site, either through study monitoring, data review or audit (internal or external), the Sponsor is able to take one, or more of the following actions:

- *Issue Site retraining.*
- *Issue Corrective and Preventative Actions.*
- *Temporary Site suspension (see Section 12.4).*
- *Site termination (see Section 12.4).*

11.9 CIP Amendments

If it becomes necessary to amend the Clinical Investigation, the nature of the amendment will be agreed between the Sponsor and the Principal Investigator(s) and this will be recorded with a justification for the amendment. The appropriate IRBs/ECs will be informed of any amendments.

[4] for at least 5 years in the UK and for at least 3 years in the United States

11.10 Reports

In fulfillment of study related requirements, the Investigator is responsible for preparing and submitting complete, accurate, and timely reports as described below.

Table 11-1: Investigator Reporting Responsibilities

Report	Description	Action
Withdrawal of IRB/EC approval	The Investigator will promptly notify the Sponsor of a withdrawal of approval by the reviewing IRB/EC or of the Investigator's part in an investigation within 2 weeks.	Preferably within 2 weeks (or less if required by local regulations)
Progress Report	If required by your IRB/EC, the Investigator is responsible for submitting progress reports on the investigation to the reviewing IRB/EC.	As required per your IRB/EC
Reports of deviations from the investigational plan	The Investigator will notify the Sponsor of any deviation from the Investigational Plan as soon as able. The Investigator will notify the IRB/EC of any deviation from the Investigational Plan per the IRB/EC requirements.	Per IRB/EC requirements;
Other	The Investigator will, upon request of a reviewing IRB/EC or Sponsor, provide accurate, complete, and current information about any aspect of the investigation.	As requested

The Principal Investigator 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 Informed Consent, compliance with this study plan, and the collection of all required data.

11.11 Investigator Site File

Each Investigator and all personnel from the investigational site must maintain accurate, complete, and current information about all aspects of this Clinical Investigation. This includes documentation relating to the Investigator's participation, Subject information and correspondence: electronic, written, and verbal, relating to any aspect of the clinical investigation. The records are maintained in the Investigator Site File consisting of, but not limited to, correspondence with other participating Investigators, the reviewing IRB/EC, and the Sponsor.

Upon receipt of copies of changes or revision updates to the Clinical Investigation Plan (otherwise known as the Study Protocol) from the Sponsor, the Investigator will add the updated document and Revision Log to the Investigator Site File. The outdated version will be filed.

11.12 Investigator Study Termination

The Investigator may prematurely terminate the clinical investigation at any time. Should this be necessary, the procedures will be arranged on an individual clinical investigation basis after review and consultation by both parties. In terminating the clinical investigation, the Sponsor and the Investigator will assure that adequate consideration is given to the protection of the Subject's interests, all documentation is archived per Section 11.7 and the appropriate bodies such as the IRB/EC/RA are informed as appropriate.

12 SPONSOR OBLIGATIONS

12.1 IRB/EC Approval

The Sponsor requires this Clinical Investigation Plan to be submitted to the IRB/EC for initial review and approval before implementation at each site. Additionally, all protocol amendments must be submitted to the IRB/EC for review and approval before implementation.

Each site is required to submit a copy of the IRB/EC initial approval, and any subsequent renewals to the Sponsor for filing in the study's Trial Master File. The site is to maintain the original documentation of the initial approval and renewals in the site's Investigator Site File.

12.2 Investigator Training, Study Initiation

Prior to enrolling Subjects in this study, the Investigator(s) and/or appropriate Site personnel will be trained on this Clinical Investigation Plan to include:

- All general aspects of study administration,
- Content and manner of administration of the questionnaires,
- All procedures in the protocol, and
- The procedure for e-data acquisition and transmission.

The Sponsor will provide hands on training to supplement the professional education and experience of the surgeon regarding the implant and surgical instruments when deemed necessary by the Sponsor.

12.3 Study Monitoring

Monitoring activities will follow the Sponsor standard operating procedures (SOPs), Clinical Monitoring Plan, applicable regulations and good clinical practices (GCPs). Monitoring will include onsite monitoring visits unless prevented by a global pandemic (e.g. COVID-19) or other unforeseen crisis. Remote monitoring may be conducted if deemed appropriate by the Sponsor (*e.g.*, global pandemic).

During the visit, the Sponsor and authorized Sponsor representatives shall be given access to all study records, including study Subject medical records to ensure proper monitoring of this clinical investigation. The monitor's duties are to verify that:

a) compliance with the CIP, any subsequent amendment(s) and regulatory requirements is maintained; deviations shall be discussed with the Principal Investigator(s) or authorized designee, documented and reported to the Sponsor.

b) only authorized individuals, as detailed on the Delegation Log, are participating in the Clinical Investigation.

c) the study device is being used according to the CIP or IFU.

d) investigational site resources and the investigation site team remain adequate throughout the duration of the Clinical Investigation.

e) the Principal Investigator continues to have access to an adequate number of subjects and study devices.

f) signed and dated informed consent forms have been obtained from each subject at the point of enrolment or before any Clinical Investigation-related procedures are undertaken.

g) source documents and other Clinical Investigation records are accurate, complete, up to date, stored and maintained appropriately.

h) CRFs and queries are complete, recorded in a timely manner, and consistent with source documents.

i) appropriate corrections, additions or deletions are made to the CRFs, dated, explained if necessary and initialed by the Principal Investigator or by his/her authorized designee; the monitor shall not make corrections, additions or deletions to the CRFs.

j) all device- and procedure-related AEs, SAEs and Device Deficiencies are reported to the Sponsor, and all SAEs and Device Deficiencies that could have led to a SADE are reported to the sponsor without unjustified delay.

k) all SAEs and deviations are reported to the EC, if required.

l) all other required reports, notifications, applications, submissions and correspondence are maintained in the investigator's files and are accurate, complete, timely, legible, dated and identify the Clinical Investigation.

m) subject withdrawal has been documented; the monitor shall discuss this with the Principal Investigator or his/her authorized designee.

n) subject non-compliance with the requirements stated in the informed consent has been documented; the monitor shall discuss this with the Principal Investigator or his/her authorized designee.

o) the Principal Investigator and investigation site team are informed and knowledgeable of all relevant document updates concerning the clinical investigation.

p) any corrective and preventive actions, as needed, have been implemented and are effective.

The Monitor, or representatives from the Sponsor, will be responsible for establishing the schedule and procedures to be followed for monitoring this clinical investigation and may also include the monitoring of the surgical procedure. The Clinical Investigator will receive reasonable notification prior to each monitoring visit during the course of this clinical investigation. At each visit, the Clinical Investigator will be expected to co-operate with the Monitor (and occasionally other Sponsor personnel) for the review and verification of all eCRFs and any additional records as may have been previously arranged between the Clinical Investigator and the Monitor. At each visit the Clinical Investigator will also be expected to co-operate with the Monitor for the review and verification of the device supply and device returns.

If under certain circumstances (i.e. limited access for sponsor study personnel to hospitals due to Covid-19 pandemic) on site monitoring is not possible, Sponsor may plan for remote monitoring and source data review or verification, where applicable. Details will be described in the study specific documents, such as monitoring plan, project operations manual etc.

12.4 Sponsor Study Termination

The Sponsor may prematurely terminate or suspend the clinical study as a whole or at an individual investigational site for significant and documented reasons. Reasons for premature termination or suspension include, but are not limited to safety, inadequate recruitment, Principal Investigator compliance, device-related problems, alignment with business strategy or administrative issues.

In the event of the study being terminated, any enrolled Subjects that have not yet had the surgical procedure would be treated as per their surgeon's standard practice using implants and instruments of the surgeon's choice. All enrolled Subjects would continue to be cared for by their surgeon according to his/her standard of care. No further study-related procedures or data collection would occur.

12.5 Insurance

12.5.1 Sites

The Sponsor will secure and maintain in full force and effect, throughout the duration of the Clinical Investigation, clinical trial insurance in line with national regulations. The type of insurance for each

participating site is detailed within the respective Clinical Trial Agreement or equivalent which will be executed before the start of Subject recruitment at that site.

12.5.2 Financial Agreement

Funding of this clinical investigation will be detailed in a separate agreement between the Sponsor and the Institution where the clinical investigation is being conducted and the Principal Investigator (where permitted by the Institution).

13 INVESTIGATIONAL PLAN EXHIBITS

Exhibit	Description of Exhibit
A	Listing of Non-Reportable Adverse Events
B	Preferred Terms for Select TKA Related Adverse Events
C	Component Product Codes
D	Glossary of Terms
E	Summary of CIP Versions/Revisions
F	Non-Clinic Contact Visit Documents

EXHIBIT A: Listing of Non-Reportable Adverse Events

In addition to the information provided in the Instructions for Use (included with the packaging for all implants), the following adverse events are anticipated. **Assuming the following events are consistent with the normal postoperative course, then they do NOT have to be reported on the Adverse Event eCRF or to the Sponsor, but should be recorded in the subject's medical record.**

Up to 24 Hours Postoperative	
Genitourinary	• Urinary retention
Cardiovascular	• Hypotension, not requiring treatment • Hypertension, not requiring treatment • Dysrhythmia (resolving within 36 hrs post-op)
Central Nervous System	• Incisional pain • Post-op consequences of narcotics use • Fatigue
Integumentary	• Surgical site ecchymosis • Sanguinous / sero-sanguinous drainage from incision • Venous congestion without thrombosis (foot swelling alleviated when lower limb is raised)
Constitutional	• Elevated temperature (no greater than 101°F)
Prior to Discharge	
Haematological	• 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 • Incisional /operative site pain
Respiratory	• Atelectasis not requiring treatment
Integumentary	• Foot Swelling not requiring intervention • Surgical site ecchymosis • Sanguinous / sero-sanguinous drainage from incision • Skin blisters secondary to tape • 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 adverse event reporting, then please contact DePuy Clinical Research.

EXHIBIT B: Preferred Terms for Select TKA Related Adverse Events

Preferred Term	Definition
Patellofemoral Pain	Pain or discomfort perceived by the Subject as residing in the ventral / anterior ("front") portion of the knee. Other common synonyms = anterior knee pain.
Pain (general, residual)	Pain or discomfort perceived by the Subject that is not patellofemoral pain – location is not as specific.
Symptomatic Clunk	This clinical observation is typically seen when evaluating a patient as they rise from a full squat. A phenomenon observed at a discrete point in the flexion arc occurs when the fibrosynovial hyperplasia becomes transiently entrapped within the intercondylar box, limiting patellar excursion until the fibrosynovial hyperplasia escapes the intercondylar box, resulting in a sudden superior motion (clunk) of the patellar component, which may be audible in some cases[40].
Symptomatic Crepitus	Noise or vibration produced by rubbing tissue surfaces together; manifested in the knee as a grating, grinding, crunching sound, often in the anterior aspect that causes discomfort or pain.
Instability	Anteroposterior >5mm, mediolateral >5mm or mid-flexion >5mm.
Extensor Mechanism Insufficiency	Extensor lag >10° that is not solved with routine physical therapy.
Incorrect Sizing	Based on radiographic review, any one of the components is incorrectly sized and causes symptoms.
Implant Fracture	Implant failure resulting in a break in the implant or it's component.
Polyethylene Wear	Tibial insert or patella wear observed radiographically or at time of revision.
Osteolysis	Observed radiographically or at time of revision.
Component Disassociation	Tibial insert is observed to have dislodged from tibial base.
Dislocation / Subluxation	Visually apparent patellar dislocation / subluxation.
Joint Stiffness	Mild lack of motion in flexion, extension or both. Explainable cause such as effusion/infection. Joint capsule is not contracted and no dystrophic changes. Patella mobile
Arthrofibrosis / Joint Contracture	Severe motion loss and/or contracture of the joint capsule. Joint stiffness is global and not limited to one direction. Possible dystrophic changes of the skin.
Reasons for Revision	Any revision would need to include additional details regarding the reason(s) for revision, components removed, etc.

EXHIBIT C: Component Product Codes

Table 13-1: ATTUNE Cementless Femoral Components

These components have CE mark and 510(k) clearance.

Product Code	Description
150401101	ATTUNE CR FEM LT SZ 1 POR
150401102	ATTUNE CR FEM LT SZ 2 POR
150401103	ATTUNE CR FEM LT SZ 3 POR
150401104	ATTUNE CR FEM LT SZ 4 POR
150401105	ATTUNE CR FEM LT SZ 5 POR
150401106	ATTUNE CR FEM LT SZ 6 POR
150401107	ATTUNE CR FEM LT SZ 7 POR
150401108	ATTUNE CR FEM LT SZ 8 POR
150401109	ATTUNE CR FEM LT SZ 9 POR
150401110	ATTUNE CR FEM LT SZ 10 POR
150401123	ATTUNE CR FEM LT SZ 3N POR
150401124	ATTUNE CR FEM LT SZ 4N POR
150401125	ATTUNE CR FEM LT SZ 5N POR
150401126	ATTUNE CR FEM LT SZ 6N POR
150401201	ATTUNE CR FEM RT SZ 1 POR
150401202	ATTUNE CR FEM RT SZ 2 POR
150401203	ATTUNE CR FEM RT SZ 3 POR
150401204	ATTUNE CR FEM RT SZ 4 POR
150401205	ATTUNE CR FEM RT SZ 5 POR
150401206	ATTUNE CR FEM RT SZ 6 POR
150401207	ATTUNE CR FEM RT SZ 7 POR
150401208	ATTUNE CR FEM RT SZ 8 POR
150401209	ATTUNE CR FEM RT SZ 9 POR
150401210	ATTUNE CR FEM RT SZ 10 POR
150401223	ATTUNE CR FEM RT SZ 3N POR
150401224	ATTUNE CR FEM RT SZ 4N POR
150401225	ATTUNE CR FEM RT SZ 5N POR
150401226	ATTUNE CR FEM RT SZ 6N POR
150411101	ATTUNE PS FEM LT SZ 1 POR
150411102	ATTUNE PS FEM LT SZ 2 POR
150411103	ATTUNE PS FEM LT SZ 3 POR
150411104	ATTUNE PS FEM LT SZ 4 POR
150411105	ATTUNE PS FEM LT SZ 5 POR
150411106	ATTUNE PS FEM LT SZ 6 POR
150411107	ATTUNE PS FEM LT SZ 7 POR
150411108	ATTUNE PS FEM LT SZ 8 POR
150411109	ATTUNE PS FEM LT SZ 9 POR
150411110	ATTUNE PS FEM LT SZ 10 POR

Product Code	Description
150411123	ATTUNE PS FEM LT SZ 3N POR
150411124	ATTUNE PS FEM LT SZ 4N POR
150411125	ATTUNE PS FEM LT SZ 5N POR
150411126	ATTUNE PS FEM LT SZ 6N POR
150411201	ATTUNE PS FEM RT SZ 1 POR
150411202	ATTUNE PS FEM RT SZ 2 POR
150411203	ATTUNE PS FEM RT SZ 3 POR
150411204	ATTUNE PS FEM RT SZ 4 POR
150411205	ATTUNE PS FEM RT SZ 5 POR
150411206	ATTUNE PS FEM RT SZ 6 POR
150411207	ATTUNE PS FEM RT SZ 7 POR
150411208	ATTUNE PS FEM RT SZ 8 POR
150411209	ATTUNE PS FEM RT SZ 9 POR
150411210	ATTUNE PS FEM RT SZ 10 POR
150411223	ATTUNE PS FEM RT SZ 3N POR
150411224	ATTUNE PS FEM RT SZ 4N POR
150411225	ATTUNE PS FEM RT SZ 5N POR
150411226	ATTUNE PS FEM RT SZ 6N POR

Table 13-2: ATTUNE Cementless FB Tibial Bases

These components have 510(k) clearance.

Product Code	Description
150621001	ATTUNE FB TIB BASE SZ 1 POR
150621002	ATTUNE FB TIB BASE SZ 2 POR
150621003	ATTUNE FB TIB BASE SZ 3 POR
150621004	ATTUNE FB TIB BASE SZ 4 POR
150621005	ATTUNE FB TIB BASE SZ 5 POR
150621006	ATTUNE FB TIB BASE SZ 6 POR
150621007	ATTUNE FB TIB BASE SZ 7 POR
150621008	ATTUNE FB TIB BASE SZ 8 POR
150621009	ATTUNE FB TIB BASE SZ 9 POR
150621010	ATTUNE FB TIB BASE SZ 10 POR

Table 13-3: ATTUNE Tibial Inserts – CR FB

These components have CE mark and 510(k) clearance and are commercially available for use in all Countries to be used in the Study.

ATTUNE Cruciate Retaining Fixed Bearing Tibial Inserts

Product Code	Description
151620105	ATTUNE CR FB Insert Size 1 5mm
151620106	ATTUNE CR FB Insert Size 1 6mm
151620107	ATTUNE CR FB Insert Size 1 7mm
151620108	ATTUNE CR FB Insert Size 1 8mm
151620110	ATTUNE CR FB Insert Size 1 10mm
151620112	ATTUNE CR FB Insert Size 1 12mm
151620114	ATTUNE CR FB Insert Size 1 14mm
151620116	ATTUNE CR FB Insert Size 1 16mm
151620205	ATTUNE CR FB Insert Size 2 5mm
151620206	ATTUNE CR FB Insert Size 2 6mm
151620207	ATTUNE CR FB Insert Size 2 7mm
151620208	ATTUNE CR FB Insert Size 2 8mm
151620210	ATTUNE CR FB Insert Size 2 10mm
151620212	ATTUNE CR FB Insert Size 2 12mm
151620214	ATTUNE CR FB Insert Size 2 14mm
151620216	ATTUNE CR FB Insert Size 2 16mm
151620305	ATTUNE CR FB Insert Size 3 5mm
151620306	ATTUNE CR FB Insert Size 3 6mm
151620307	ATTUNE CR FB Insert Size 3 7mm
151620308	ATTUNE CR FB Insert Size 3 8mm
151620310	ATTUNE CR FB Insert Size 3 10mm
151620312	ATTUNE CR FB Insert Size 3 12mm
151620314	ATTUNE CR FB Insert Size 3 14mm
151620316	ATTUNE CR FB Insert Size 3 16mm
151620405	ATTUNE CR FB Insert Size 4 5mm
151620406	ATTUNE CR FB Insert Size 4 6mm
151620407	ATTUNE CR FB Insert Size 4 7mm
151620408	ATTUNE CR FB Insert Size 4 8mm
151620410	ATTUNE CR FB Insert Size 4 10mm
151620412	ATTUNE CR FB Insert Size 4 12mm
151620414	ATTUNE CR FB Insert Size 4 14mm
151620416	ATTUNE CR FB Insert Size 4 16mm
151620505	ATTUNE CR FB Insert Size 5 5mm
151620506	ATTUNE CR FB Insert Size 5 6mm
151620507	ATTUNE CR FB Insert Size 5 7mm
151620508	ATTUNE CR FB Insert Size 5 8mm
151620510	ATTUNE CR FB Insert Size 5 10mm

Product Code	Description
151620512	ATTUNE CR FB Insert Size 5 12mm
151620514	ATTUNE CR FB Insert Size 5 14mm
151620516	ATTUNE CR FB Insert Size 5 16mm
151620605	ATTUNE CR FB Insert Size 6 5mm
151620606	ATTUNE CR FB Insert Size 6 6mm
151620607	ATTUNE CR FB Insert Size 6 7mm
151620608	ATTUNE CR FB Insert Size 6 8mm
151620610	ATTUNE CR FB Insert Size 6 10mm
151620612	ATTUNE CR FB Insert Size 6 12mm
151620614	ATTUNE CR FB Insert Size 6 14mm
151620616	ATTUNE CR FB Insert Size 6 16mm
151620705	ATTUNE CR FB Insert Size 7 5mm
151620706	ATTUNE CR FB Insert Size 7 6mm
151620707	ATTUNE CR FB Insert Size 7 7mm
151620708	ATTUNE CR FB Insert Size 7 8mm
151620710	ATTUNE CR FB Insert Size 7 10mm
151620712	ATTUNE CR FB Insert Size 7 12mm
151620714	ATTUNE CR FB Insert Size 7 14mm
151620716	ATTUNE CR FB Insert Size 7 16mm
151620805	ATTUNE CR FB Insert Size 8 5mm
151620806	ATTUNE CR FB Insert Size 8 6mm
151620807	ATTUNE CR FB Insert Size 8 7mm
151620808	ATTUNE CR FB Insert Size 8 8mm
151620810	ATTUNE CR FB Insert Size 8 10mm
151620812	ATTUNE CR FB Insert Size 8 12mm
151620814	ATTUNE CR FB Insert Size 8 14mm
151620816	ATTUNE CR FB Insert Size 8 16mm
151620905	ATTUNE CR FB Insert Size 9 5mm
151620906	ATTUNE CR FB Insert Size 9 6mm
151620907	ATTUNE CR FB Insert Size 9 7mm
151620908	ATTUNE CR FB Insert Size 9 8mm
151620910	ATTUNE CR FB Insert Size 9 10mm
151620912	ATTUNE CR FB Insert Size 9 12mm
151620914	ATTUNE CR FB Insert Size 9 14mm
151620916	ATTUNE CR FB Insert Size 9 16mm
151621005	ATTUNE CR FB Insert Size 10 5mm
151621006	ATTUNE CR FB Insert Size 10 6mm
151621007	ATTUNE CR FB Insert Size 10 7mm
151621008	ATTUNE CR FB Insert Size 10 8mm
151621010	ATTUNE CR FB Insert Size 10 10mm
151621012	ATTUNE CR FB Insert Size 10 12mm
151621014	ATTUNE CR FB Insert Size 10 14mm
151621016	ATTUNE CR FB Insert Size 10 16mm

ATTUNE Medial Stabilized Fixed Bearing Tibial Inserts

Product Code	Description
151820105	ATTUNE Left Medial Stabilized Insert Size 1 5mm
151820106	ATTUNE Left Medial Stabilized Insert Size 1 6mm
151820107	ATTUNE Left Medial Stabilized Insert Size 1 7mm
151820108	ATTUNE Left Medial Stabilized Insert Size 1 8mm
151820110	ATTUNE Left Medial Stabilized Insert Size 1 10mm
151820112	ATTUNE Left Medial Stabilized Insert Size 1 12mm
151820114	ATTUNE Left Medial Stabilized Insert Size 1 14mm
151820116	ATTUNE Left Medial Stabilized Insert Size 1 16mm
151820205	ATTUNE Left Medial Stabilized Insert Size 2 5mm
151820206	ATTUNE Left Medial Stabilized Insert Size 2 6mm
151820207	ATTUNE Left Medial Stabilized Insert Size 2 7mm
151820208	ATTUNE Left Medial Stabilized Insert Size 2 8mm
151820210	ATTUNE Left Medial Stabilized Insert Size 2 10mm
151820212	ATTUNE Left Medial Stabilized Insert Size 2 12mm
151820214	ATTUNE Left Medial Stabilized Insert Size 2 14mm
151820216	ATTUNE Left Medial Stabilized Insert Size 2 16mm
151820305	ATTUNE Left Medial Stabilized Insert Size 3 5mm
151820306	ATTUNE Left Medial Stabilized Insert Size 3 6mm
151820307	ATTUNE Left Medial Stabilized Insert Size 3 7mm
151820308	ATTUNE Left Medial Stabilized Insert Size 3 8mm
151820310	ATTUNE Left Medial Stabilized Insert Size 3 10mm
151820312	ATTUNE Left Medial Stabilized Insert Size 3 12mm
151820314	ATTUNE Left Medial Stabilized Insert Size 3 14mm
151820316	ATTUNE Left Medial Stabilized Insert Size 3 16mm
151820405	ATTUNE Left Medial Stabilized Insert Size 4 5mm
151820406	ATTUNE Left Medial Stabilized Insert Size 4 6mm
151820407	ATTUNE Left Medial Stabilized Insert Size 4 7mm
151820408	ATTUNE Left Medial Stabilized Insert Size 4 8mm
151820410	ATTUNE Left Medial Stabilized Insert Size 4 10mm
151820412	ATTUNE Left Medial Stabilized Insert Size 4 12mm
151820414	ATTUNE Left Medial Stabilized Insert Size 4 14mm
151820416	ATTUNE Left Medial Stabilized Insert Size 4 16mm
151820505	ATTUNE Left Medial Stabilized Insert Size 5 5mm
151820506	ATTUNE Left Medial Stabilized Insert Size 5 6mm
151820507	ATTUNE Left Medial Stabilized Insert Size 5 7mm
151820508	ATTUNE Left Medial Stabilized Insert Size 5 8mm
151820510	ATTUNE Left Medial Stabilized Insert Size 5 10mm
151820512	ATTUNE Left Medial Stabilized Insert Size 5 12mm
151820514	ATTUNE Left Medial Stabilized Insert Size 5 14mm

Product Code	Description
151820516	ATTUNE Left Medial Stabilized Insert Size 5 16mm
151820605	ATTUNE Left Medial Stabilized Insert Size 6 5mm
151820606	ATTUNE Left Medial Stabilized Insert Size 6 6mm
151820607	ATTUNE Left Medial Stabilized Insert Size 6 7mm
151820608	ATTUNE Left Medial Stabilized Insert Size 6 8mm
151820610	ATTUNE Left Medial Stabilized Insert Size 6 10mm
151820612	ATTUNE Left Medial Stabilized Insert Size 6 12mm
151820614	ATTUNE Left Medial Stabilized Insert Size 6 14mm
151820616	ATTUNE Left Medial Stabilized Insert Size 6 16mm
151820705	ATTUNE Left Medial Stabilized Insert Size 7 5mm
151820706	ATTUNE Left Medial Stabilized Insert Size 7 6mm
151820707	ATTUNE Left Medial Stabilized Insert Size 7 7mm
151820708	ATTUNE Left Medial Stabilized Insert Size 7 8mm
151820710	ATTUNE Left Medial Stabilized Insert Size 7 10mm
151820712	ATTUNE Left Medial Stabilized Insert Size 7 12mm
151820714	ATTUNE Left Medial Stabilized Insert Size 7 14mm
151820716	ATTUNE Left Medial Stabilized Insert Size 7 16mm
151820805	ATTUNE Left Medial Stabilized Insert Size 8 5mm
151820806	ATTUNE Left Medial Stabilized Insert Size 8 6mm
151820807	ATTUNE Left Medial Stabilized Insert Size 8 7mm
151820808	ATTUNE Left Medial Stabilized Insert Size 8 8mm
151820810	ATTUNE Left Medial Stabilized Insert Size 8 10mm
151820812	ATTUNE Left Medial Stabilized Insert Size 8 12mm
151820814	ATTUNE Left Medial Stabilized Insert Size 8 14mm
151820816	ATTUNE Left Medial Stabilized Insert Size 8 16mm
151820905	ATTUNE Left Medial Stabilized Insert Size 9 5mm
151820906	ATTUNE Left Medial Stabilized Insert Size 9 6mm
151820907	ATTUNE Left Medial Stabilized Insert Size 9 7mm
151820908	ATTUNE Left Medial Stabilized Insert Size 9 8mm
151820910	ATTUNE Left Medial Stabilized Insert Size 9 10mm
151820912	ATTUNE Left Medial Stabilized Insert Size 9 12mm
151820914	ATTUNE Left Medial Stabilized Insert Size 9 14mm
151820916	ATTUNE Left Medial Stabilized Insert Size 9 16mm
151821005	ATTUNE Left Medial Stabilized Insert Size 10 5mm
151821006	ATTUNE Left Medial Stabilized Insert Size 10 6mm
151821007	ATTUNE Left Medial Stabilized Insert Size 10 7mm
151821008	ATTUNE Left Medial Stabilized Insert Size 10 8mm
151821010	ATTUNE Left Medial Stabilized Insert Size 10 10mm
151821012	ATTUNE Left Medial Stabilized Insert Size 10 12mm
151821014	ATTUNE Left Medial Stabilized Insert Size 10 14mm
151821016	ATTUNE Left Medial Stabilized Insert Size 10 16mm

Product Code	Description
152020105	ATTUNE Right Medial Stabilized Insert Size 1 5mm
152020106	ATTUNE Right Medial Stabilized Insert Size 1 6mm
152020107	ATTUNE Right Medial Stabilized Insert Size 1 7mm
152020108	ATTUNE Right Medial Stabilized Insert Size 1 8mm
152020110	ATTUNE Right Medial Stabilized Insert Size 1 10mm
152020112	ATTUNE Right Medial Stabilized Insert Size 1 12mm
152020114	ATTUNE Right Medial Stabilized Insert Size 1 14mm
152020116	ATTUNE Right Medial Stabilized Insert Size 1 16mm
152020205	ATTUNE Right Medial Stabilized Insert Size 2 5mm
152020206	ATTUNE Right Medial Stabilized Insert Size 2 6mm
152020207	ATTUNE Right Medial Stabilized Insert Size 2 7mm
152020208	ATTUNE Right Medial Stabilized Insert Size 2 8mm
152020210	ATTUNE Right Medial Stabilized Insert Size 2 10mm
152020212	ATTUNE Right Medial Stabilized Insert Size 2 12mm
152020214	ATTUNE Right Medial Stabilized Insert Size 2 14mm
152020216	ATTUNE Right Medial Stabilized Insert Size 2 16mm
152020305	ATTUNE Right Medial Stabilized Insert Size 3 5mm
152020306	ATTUNE Right Medial Stabilized Insert Size 3 6mm
152020307	ATTUNE Right Medial Stabilized Insert Size 3 7mm
152020308	ATTUNE Right Medial Stabilized Insert Size 3 8mm
152020310	ATTUNE Right Medial Stabilized Insert Size 3 10mm
152020312	ATTUNE Right Medial Stabilized Insert Size 3 12mm
152020314	ATTUNE Right Medial Stabilized Insert Size 3 14mm
152020316	ATTUNE Right Medial Stabilized Insert Size 3 16mm
152020405	ATTUNE Right Medial Stabilized Insert Size 4 5mm
152020406	ATTUNE Right Medial Stabilized Insert Size 4 6mm
152020407	ATTUNE Right Medial Stabilized Insert Size 4 7mm
152020408	ATTUNE Right Medial Stabilized Insert Size 4 8mm
152020410	ATTUNE Right Medial Stabilized Insert Size 4 10mm
152020412	ATTUNE Right Medial Stabilized Insert Size 4 12mm
152020414	ATTUNE Right Medial Stabilized Insert Size 4 14mm
152020416	ATTUNE Right Medial Stabilized Insert Size 4 16mm
152020505	ATTUNE Right Medial Stabilized Insert Size 5 5mm
152020506	ATTUNE Right Medial Stabilized Insert Size 5 6mm
152020507	ATTUNE Right Medial Stabilized Insert Size 5 7mm
152020508	ATTUNE Right Medial Stabilized Insert Size 5 8mm
152020510	ATTUNE Right Medial Stabilized Insert Size 5 10mm
152020512	ATTUNE Right Medial Stabilized Insert Size 5 12mm
152020514	ATTUNE Right Medial Stabilized Insert Size 5 14mm
152020516	ATTUNE Right Medial Stabilized Insert Size 5 16mm
152020605	ATTUNE Right Medial Stabilized Insert Size 6 5mm

Product Code	Description
152020606	ATTUNE Right Medial Stabilized Insert Size 6 6mm
152020607	ATTUNE Right Medial Stabilized Insert Size 6 7mm
152020608	ATTUNE Right Medial Stabilized Insert Size 6 8mm
152020610	ATTUNE Right Medial Stabilized Insert Size 6 10mm
152020612	ATTUNE Right Medial Stabilized Insert Size 6 12mm
152020614	ATTUNE Right Medial Stabilized Insert Size 6 14mm
152020616	ATTUNE Right Medial Stabilized Insert Size 6 16mm
152020705	ATTUNE Right Medial Stabilized Insert Size 7 5mm
152020706	ATTUNE Right Medial Stabilized Insert Size 7 6mm
152020707	ATTUNE Right Medial Stabilized Insert Size 7 7mm
152020708	ATTUNE Right Medial Stabilized Insert Size 7 8mm
152020710	ATTUNE Right Medial Stabilized Insert Size 7 10mm
152020712	ATTUNE Right Medial Stabilized Insert Size 7 12mm
152020714	ATTUNE Right Medial Stabilized Insert Size 7 14mm
152020716	ATTUNE Right Medial Stabilized Insert Size 7 16mm
152020805	ATTUNE Right Medial Stabilized Insert Size 8 5mm
152020806	ATTUNE Right Medial Stabilized Insert Size 8 6mm
152020807	ATTUNE Right Medial Stabilized Insert Size 8 7mm
152020808	ATTUNE Right Medial Stabilized Insert Size 8 8mm
152020810	ATTUNE Right Medial Stabilized Insert Size 8 10mm
152020812	ATTUNE Right Medial Stabilized Insert Size 8 12mm
152020814	ATTUNE Right Medial Stabilized Insert Size 8 14mm
152020816	ATTUNE Right Medial Stabilized Insert Size 8 16mm
152020905	ATTUNE Right Medial Stabilized Insert Size 9 5mm
152020906	ATTUNE Right Medial Stabilized Insert Size 9 6mm
152020907	ATTUNE Right Medial Stabilized Insert Size 9 7mm
152020908	ATTUNE Right Medial Stabilized Insert Size 9 8mm
152020910	ATTUNE Right Medial Stabilized Insert Size 9 10mm
152020912	ATTUNE Right Medial Stabilized Insert Size 9 12mm
152020914	ATTUNE Right Medial Stabilized Insert Size 9 14mm
152020916	ATTUNE Right Medial Stabilized Insert Size 9 16mm
152021005	ATTUNE Right Medial Stabilized Insert Size 10 5mm
152021006	ATTUNE Right Medial Stabilized Insert Size 10 6mm
152021007	ATTUNE Right Medial Stabilized Insert Size 10 7mm
152021008	ATTUNE Right Medial Stabilized Insert Size 10 8mm
152021010	ATTUNE Right Medial Stabilized Insert Size 10 10mm
152021012	ATTUNE Right Medial Stabilized Insert Size 10 12mm
152021014	ATTUNE Right Medial Stabilized Insert Size 10 14mm
152021016	ATTUNE Right Medial Stabilized Insert Size 10 16mm

Table 13-4: ATTUNE Tibial Inserts – PS FB

These components have CE mark and 510(k) clearance and are commercially available for use in all Countries to be used in the Study.

Product Code	Description
151640105	ATTUNE PS FB Insert Size 1 5mm
151640106	ATTUNE PS FB Insert Size 1 6mm
151640107	ATTUNE PS FB Insert Size 1 7mm
151640108	ATTUNE PS FB Insert Size 1 8mm
151640110	ATTUNE PS FB Insert Size 1 10mm
151640112	ATTUNE PS FB Insert Size 1 12mm
151640114	ATTUNE PS FB Insert Size 1 14mm
151640116	ATTUNE PS FB Insert Size 1 16mm
151640205	ATTUNE PS FB Insert Size 2 5mm
151640206	ATTUNE PS FB Insert Size 2 6mm
151640207	ATTUNE PS FB Insert Size 2 7mm
151640208	ATTUNE PS FB Insert Size 2 8mm
151640210	ATTUNE PS FB Insert Size 2 10mm
151640212	ATTUNE PS FB Insert Size 2 12mm
151640214	ATTUNE PS FB Insert Size 2 14mm
151640216	ATTUNE PS FB Insert Size 2 16mm
151640305	ATTUNE PS FB Insert Size 3 5mm
151640306	ATTUNE PS FB Insert Size 3 6mm
151640307	ATTUNE PS FB Insert Size 3 7mm
151640308	ATTUNE PS FB Insert Size 3 8mm
151640310	ATTUNE PS FB Insert Size 3 10mm
151640312	ATTUNE PS FB Insert Size 3 12mm
151640314	ATTUNE PS FB Insert Size 3 14mm
151640316	ATTUNE PS FB Insert Size 3 16mm
151640405	ATTUNE PS FB Insert Size 4 5mm
151640406	ATTUNE PS FB Insert Size 4 6mm
151640407	ATTUNE PS FB Insert Size 4 7mm
151640408	ATTUNE PS FB Insert Size 4 8mm
151640410	ATTUNE PS FB Insert Size 4 10mm
151640412	ATTUNE PS FB Insert Size 4 12mm
151640414	ATTUNE PS FB Insert Size 4 14mm
151640416	ATTUNE PS FB Insert Size 4 16mm
151640505	ATTUNE PS FB Insert Size 5 5mm
151640506	ATTUNE PS FB Insert Size 5 6mm
151640507	ATTUNE PS FB Insert Size 5 7mm
151640508	ATTUNE PS FB Insert Size 5 8mm
151640510	ATTUNE PS FB Insert Size 5 10mm
151640512	ATTUNE PS FB Insert Size 5 12mm
151640514	ATTUNE PS FB Insert Size 5 14mm

Product Code	Description
151640516	ATTUNE PS FB Insert Size 5 16mm
151640605	ATTUNE PS FB Insert Size 6 5mm
151640606	ATTUNE PS FB Insert Size 6 6mm
151640607	ATTUNE PS FB Insert Size 6 7mm
151640608	ATTUNE PS FB Insert Size 6 8mm
151640610	ATTUNE PS FB Insert Size 6 10mm
151640612	ATTUNE PS FB Insert Size 6 12mm
151640614	ATTUNE PS FB Insert Size 6 14mm
151640616	ATTUNE PS FB Insert Size 6 16mm
151640705	ATTUNE PS FB Insert Size 7 5mm
151640706	ATTUNE PS FB Insert Size 7 6mm
151640707	ATTUNE PS FB Insert Size 7 7mm
151640708	ATTUNE PS FB Insert Size 7 8mm
151640710	ATTUNE PS FB Insert Size 7 10mm
151640712	ATTUNE PS FB Insert Size 7 12mm
151640714	ATTUNE PS FB Insert Size 7 14mm
151640716	ATTUNE PS FB Insert Size 7 16mm
151640805	ATTUNE PS FB Insert Size 8 5mm
151640806	ATTUNE PS FB Insert Size 8 6mm
151640807	ATTUNE PS FB Insert Size 8 7mm
151640808	ATTUNE PS FB Insert Size 8 8mm
151640810	ATTUNE PS FB Insert Size 8 10mm
151640812	ATTUNE PS FB Insert Size 8 12mm
151640814	ATTUNE PS FB Insert Size 8 14mm
151640816	ATTUNE PS FB Insert Size 8 16mm
151640905	ATTUNE PS FB Insert Size 9 5mm
151640906	ATTUNE PS FB Insert Size 9 6mm
151640907	ATTUNE PS FB Insert Size 9 7mm
151640908	ATTUNE PS FB Insert Size 9 8mm
151640910	ATTUNE PS FB Insert Size 9 10mm
151640912	ATTUNE PS FB Insert Size 9 12mm
151640914	ATTUNE PS FB Insert Size 9 14mm
151640916	ATTUNE PS FB Insert Size 9 16mm
151641005	ATTUNE PS FB Insert Size 10 5mm
151641006	ATTUNE PS FB Insert Size 10 6mm
151641007	ATTUNE PS FB Insert Size 10 7mm
151641008	ATTUNE PS FB Insert Size 10 8mm
151641010	ATTUNE PS FB Insert Size 10 10mm
151641012	ATTUNE PS FB Insert Size 10 12mm
151641014	ATTUNE PS FB Insert Size 10 14mm
151641016	ATTUNE PS FB Insert Size 10 16mm

Table 13-5: ATTUNE Cemented Patellar Components

These components have CE mark and 510(k) clearance and are commercially available for use in all Countries to be used in the Study. To be used prior to Cementless Patella availability.

Anatomic Patella

Product Code	Description
151810029	ATTUNE MEDIAL ANAT PAT 29MM
151810032	ATTUNE MEDIAL ANAT PAT 32MM
151810035	ATTUNE MEDIAL ANAT PAT 35MM
151810038	ATTUNE MEDIAL ANAT PAT 38MM
151810041	ATTUNE MEDIAL ANAT PAT 41MM

Medialized Patella

Product Code	Description
151820029	ATTUNE MEDIAL DOME PAT 29MM
151820032	ATTUNE MEDIAL DOME PAT 32MM
151820035	ATTUNE MEDIAL DOME PAT 35MM
151820038	ATTUNE MEDIAL DOME PAT 38MM
151820041	ATTUNE MEDIAL DOME PAT 41MM

Table 13-6: ATTUNE Cementless Patellar Components

These components have 510(k) clearance.

Anatomic Patella

Product Code	Description
151811032	ATT MED ANAT PAT 32MM POR
151811035	ATT MED ANAT PAT 35MM POR
151811038	ATT MED ANAT PAT 38MM POR
151811041	ATT MED ANAT PAT 41MM POR

Medialized Patella

Product Code	Description
151821032	ATT MED DOME PAT 32MM POR
151821035	ATT MED DOME PAT 35MM POR
151821038	ATT MED DOME PAT 38MM POR
151821041	ATT MED DOME PAT 41MM POR

EXHIBIT D: Glossary of Terms

ADE	Adverse Device Effect
AE	Adverse Event
AKS	American Knee Society Score
AP	Anterior-Posterior
BS EN	British Standard European Norm
21 CFR	Code of Federal Regulation: Title 21
CE	Conformité Européenne
CIP	Clinical Investigational Plan
CR	Cruciate Retaining
CRF	Case Report Form (paper)
DVT	Deep Vein Thrombosis
EC	Ethics Committee
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
EQ-5D-5L	European Quality of Life 5 Dimensions – 5 Levels
EU	European Union
FB	Fixed Bearing
FDA	Food and Drug Administration
FJS-12	Forgotten Joint Score
GCP	Good Clinical Practice
ICD	Informed Consent Document
IRB	Institutional Review Board
ISO	International Organization for Standardization
ITT	Intent To Treat
KOOS-ADL	Knee Injury Osteoarthritis Outcome Score – Activities of Daily Living
MEDDEV	Medical Device Guidance Document(s)
MS	Medial Stabilized
NIDJD	Non-inflammatory Degenerative Joint Disease
OA	Osteoarthritis
OR	Operating Room
PHI	Personal Health Information
PI	Principal Investigator
PMCF	Post-Market Clinical Follow-up
Post-op	Post-operative
PP	Per Protocol
Pre-op	Pre-operative
PROs	Patient Reported Outcomes
PROM	Patient Reported Outcome Measure
PS	Posterior Stabilized
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SAS®	Statistical Analysis System
TKA	Total Knee Arthroplasty
UADE	Unanticipated Adverse Device Effect
USADE	Unanticipated Serious Adverse Device Effect
US	United States
VAS	Visual Analogue Scale

EXHIBIT E: Summary of CIP Versions/Revisions

Revision	Description of Change
Rev A, 27 APR 2020	N/A
Rev B, 18 SEP 2020	• *Sponsor changed to DePuy Synthes Products Inc.* • *Modified countries to include United States, Canada, and New Zealand* • *CIP Version updated to Revision B, 18 SEP 2020* • *Table of Contents Updated* • *Updates made throughout protocol due to study no longer including premarket regions.* • *Updates made throughout protocol to align with US IFU and intended use of product.* • *Study objectives and endpoints updated.* • *Clarification added regarding the inclusion of primary and revision cases.* • *Inclusion and Exclusion Criteria updated.* • *Case Report Form Changes include the following:* • *Combined Medical and Surgical History eCRFs* • *Removed Surgical History eCRF* • *Removed PCS eCRF* • *Added Reoperation/Revision eCRF* • *Removed Concomitant Procedure Summary eCRF* • *Removed Concomitant Procedure eCRF* • *Added Device Deficiency Summary eCRF* • *Methods of data collection updated to include phone and mail-in options.* • *Removed size 29mm Cementless Patella implants as they are no longer in scope.* • *Added Exhibit F, Non-Clinic Contact Visit Documents.*
Rev C, 2 DEC 2020	• *Revision update to Revision C, 2 DEC 2020.*

Revision	Description of Change
	• *Multiple updates made throughout document to account for recent FDA clearance of the ATTUNE Cementless FB Tibial Base and ATTUNE Cementless Patella.* • *Study population updated to include "severely disabled" to account for product indications in all ATTUNE TKA products used in this clinical study.* • *The following inclusion was added, "The subject requires total knee arthroplasty and would receive the study implant independent of this research protocol."* • *Removed Forgotten Joint Score (FSJ-12) from preoperative visit interval.* • *Multiple administrative edits made to the protocol.*
Rev D, 24 AUG 2022	• *Revised Short Title to state "ATTUNE Cementless FB Tibial Base Clinical Study".* • *Added "Medial Stabilized (MS) Tibial Inserts to Treatment Devices. Multiple additions made throughout document. MS Inserts added to CR Cohort.* • *Focus on ATTUNE Cementless Patella removed including removal from secondary and tertiary objectives.* • *Device Approvals revised to state "All devices allowed in this clinical study have 510(k) clearance in the United States."* • *References to New Zealand and Canadian sites removed. All clinical study sites will be in the United States.* • *Sample Size updated to state "Up to 300 ATTUNE Cementless Patellae (if available in United States market during the clinical study)".* • *Summary of Published Clinical Literature section removed.*

Revision	Description of Change
	• *Note added to Table 8-2, Protocol Requirements During Surgery.* • *Clarification added throughout regarding preoperative required and preferred visit windows.* • *Safety details updated to state a DSMB, DMC, CEC will not be used.* • *Removed Section 11.4, Protected Health Information statement regarding "Sites Outside of the US".*

EXHIBIT F: Non-Clinic Contact Visit Documents

SAMPLE COVER LETTER

Insert Name of Subject
Insert Street Address
Insert City, State, Zip Code

Insert Date

Dear Insert Name of Subject,

I am writing you this letter as part of your follow up to the clinical study titled, *Multi-Center Clinical Investigation of the ATTUNE® Cementless Fixed Bearing Tibial Base and Cementless Patella Implants in Total Knee Arthroplasty* in which you are taking part with Insert Name of Study Investigator.

The reason for this letter is to obtain follow up information on your ATTUNE Cementless Fixed Bearing implant in your (insert either right or left) knee since your last contact with our clinic. Please complete the enclosed questionnaire(s) about your (insert right or left) knee implant. Make sure you share any problems you may have had especially with your (insert right or left) since your last visit with Dr. Insert Name of Study Investigator. Once completed, please return the forms to my attention in the enclosed postage paid envelope.

If you have any questions regarding the information you have received, please call me at INSERT Phone Number and I would be happy to answer your questions.

As a friendly reminder, your next appointment has been scheduled for INSERT Date of next appointment.

Finally, we want to thank you again for continuing to take part in this important study.

Sincerely,

Insert Name of Clinical Research Coordinator

With signature below you confirm you have personally completed this packet.

Printed name: _____

Signature: _____

Date: _____

Contact Visit Form – Mailer to Study Participant

Multi-Center Clinical Investigation of the ATTUNE® Cementless Fixed Bearing Tibial Base and Cementless Patella Implants in Total Knee Arthroplasty

PATIENT INFORMATION

Last Name: _____ First Name:_____ Middle Initial: _____

Address: _____City:_____State: _____ ZIP:_____

Home Phone (____) _____ Work Phone (____) _____Cell Phone (_____) _____

Email: _____

INFORMATION REGARDING YOUR STUDY KNEE

Since your last visit have you had any new problems with your study knee (Right or Left knee)?

☐ **Yes** ☐ **No**

If yes, please provide details regarding the problem with your study knee, including when the problem started, description of the problem, and if you went to a doctor to treat the problem.

_____

_____

_____

Since your last visit have you had any surgery to your study knee? (Right or Left Knee)

☐ **Yes** ☐ **No**

If yes, please provide details of surgery.

_____

_____

_____

Since your last visit have you had any other hospitalizations or surgery not related to your study knee? (Right Knee)

☐ **Yes** ☐ **No**

If yes, please provide details.

_____

_____

_____

SAMPLE PHONE SCRIPT

Subject ID: _____ Date of Phone Call: _____ Time of Phone Call: _____

Hello (Name of Subject),
I am calling you today as part of your follow up for the, Multi-Center Clinical Investigation of the ATTUNE® Cementless Fixed Bearing Tibial Base and Cementless Patella Implants in Total Knee Arthroplasty Study in which you are taking part with Insert Name of Study Investigator.

The reason for this call is to obtain follow up information on your ATTUNE Cementless Fixed Bearing implant in your (insert either right or left) knee since your last contact with our clinic. I am now going to ask you a few questions:

- *Since your last visit, have you had any new problems with your study knee?* __ *No* __ *Yes*

If yes, please describe:

- *Since your last visit, have you had any surgery to your study knee?* __ No __ Yes

If yes, please describe:

- *Have you had any other new medical problems such as a recent hospitalization or surgery not involving the study knee?* __ *No* __ *Yes*

If yes, please describe:

I want to thank you for your time today, and assure you that we will keep your information confidential. Your information will not shared outside of this study team except to those groups inside and outside of this clinic who are responsible for making sure studies are conducted correctly and ethically. If you decide (now or later) to stop, you need to know that the information already collected will continue to be used.

Do you have any questions? Is there anything else I may assist you with? Thank you for your call.

14 References

1. Knutson K, Robertsson O. The Swedish Knee Arthroplasty Register (www.knee.se): The inside story. *Acta Orthop* 2010; **81**(1): 5-7.
2. Kurtz S, Ong K, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. *J Bone Joint Surg Am* 2007; **89**(4): 780-5.
3. Berger RA, Rosenberg AG, Barden RM, Sheinkop MB, Jacobs JJ, Galante JO. Long-term followup of the Miller-Galante total knee replacement. *Clin Orthop Relat Res* 2001; (388): 58-67.
4. Font-Rodriguez DE, Scuderi GR, Insall JN. Survivorship of cemented total knee arthroplasty. *Clin Orthop Relat Res* 1997; (345): 79-86.
5. Ranawat CS, Flynn WF, Jr., Saddler S, Hansraj KK, Maynard MJ. Long-term results of the total condylar knee arthroplasty. A 15-year survivorship study. *Clin Orthop Relat Res* 1993; (286): 94-102.
6. Rasquinha VJ, Ranawat CS, Cervieri CL, Rodriguez JA. The press-fit condylar modular total knee system with a posterior cruciate-substituting design. A concise follow-up of a previous report. *J Bone Joint Surg Am* 2006; **88**(5): 1006-10.
7. Ritter MA, Berend ME, Meding JB, Keating EM, Faris PM, Crites BM. Long-term followup of anatomic graduated components posterior cruciate-retaining total knee replacement. *Clin Orthop Relat Res* 2001; (388): 51-7.
8. Rodriguez JA, Bhende H, Ranawat CS. Total condylar knee replacement: a 20-year followup study. *Clin Orthop Relat Res* 2001; (388): 10-7.
9. Australian Orthopaedic Association National Joint Replacement Registy Annual Report. Adelaide: AOA, 2019.
10. NJR England, Wales & Nothern Ireland 15th Annual Report, 2019.
11. Fricka KB, Sritulanondha S, McAsey CJ. To Cement or Not? Two-Year Results of a Prospective, Randomized Study Comparing Cemented Vs. Cementless Total Knee Arthroplasty (TKA). *J Arthroplasty* 2015; **30**(9 Suppl): 55-8.
12. Brown TE, Harper BL, Bjorgul K. Comparison of cemented and uncemented fixation in total knee arthroplasty. *Orthopedics* 2013; **36**(5): 380-7.
13. McCalden RW, Robert CE, Howard JL, Naudie DD, McAuley JP, MacDonald SJ. Comparison of outcomes and survivorship between patients of different age groups following TKA. *J Arthroplasty* 2013; **28**(8 Suppl): 83-6.
14. Meehan JP, Danielsen B, Kim SH, Jamali AA, White RH. Younger age is associated with a higher risk of early periprosthetic joint infection and aseptic mechanical failure after total knee arthroplasty. *J Bone Joint Surg Am* 2014; **96**(7): 529-35.
15. Naudie DD, Ammeen DJ, Engh GA, Rorabeck CH. Wear and osteolysis around total knee arthroplasty. *J Am Acad Orthop Surg* 2007; **15**(1): 53-64.
16. O'Rourke MR, Callaghan JJ, Goetz DD, Sullivan PM, Johnston RC. Osteolysis associated with a cemented modular posterior-cruciate-substituting total knee design : five to eight-year follow-up. *J Bone Joint Surg Am* 2002; **84**(8): 1362-71.
17. Abram SG, Nicol F, Hullin MG, Spencer SJ. The long-term outcome of uncemented Low Contact Stress total knee replacement in patients with rheumatoid arthritis: results at a mean of 22 years. *The bone & joint journal* 2013; **95-b**(11): 1497-9.
18. Buechel FF, Sr. Long-term followup after mobile-bearing total knee replacement. *Clin Orthop Relat Res* 2002; (404): 40-50.
19. Efstathopoulos N, Mavrogenis AF, Lallos S, et al. 10-year evaluation of the cementless low-contact- stress rotating-platform total knee arthroplasty. *Journal of long-term effects of medical implants* 2009; **19**(4): 255-63.

20. Lass R, Kubista B, Holinka J, et al. Comparison of cementless and hybrid cemented total knee arthroplasty. *Orthopedics* 2013; **36**(4): e420-7.
21. Abo-Alhol TR, Fitzpatrick CK, Clary CW, et al. Patellar mechanics during simulated kneeling in the natural and implanted knee. *J Biomech* 2014; **47**(5): 1045-51.
22. Clary C, Aram L, Deffenbaugh D, Heldreth M. Tibial base design and patient morphology affecting tibial coverage and rotational alignment after total knee arthroplasty. *Knee Surg Sports Traumatol Arthrosc* 2014; **22**(12): 3012-8.
23. Clary CW, Fitzpatrick CK, Maletsky LP, Rullkoetter PJ. The influence of total knee arthroplasty geometry on mid-flexion stability: an experimental and finite element study. *J Biomech* 2013; **46**(7): 1351-7.
24. Fitzpatrick CK, Baldwin MA, Clary CW, Maletsky LP, Rullkoetter PJ. Evaluating knee replacement mechanics during ADL with PID-controlled dynamic finite element analysis. *Computer methods in biomechanics and biomedical engineering* 2014; **17**(4): 360-9.
25. Fitzpatrick CK, Baldwin MA, Clary CW, Wright A, Laz PJ, Rullkoetter PJ. Identifying alignment parameters affecting implanted patellofemoral mechanics. *J Orthop Res* 2012; **30**(7): 1167-75.
26. Fitzpatrick CK, Clary CW, Cyr AJ, Maletsky LP, Rullkoetter PJ. Mechanics of post-cam engagement during simulated dynamic activity. *J Orthop Res* 2013; **31**(9): 1438-46.
27. Fitzpatrick CK, Clary CW, Laz PJ, Rullkoetter PJ. Relative contributions of design, alignment, and loading variability in knee replacement mechanics. *J Orthop Res* 2012; **30**(12): 2015-24.
28. Fitzpatrick CK, Clary CW, Rullkoetter PJ. The role of patient, surgical, and implant design variation in total knee replacement performance. *J Biomech* 2012; **45**(12): 2092-102.
29. Smoger LM, Fitzpatrick CK, Clary CW, et al. Statistical modeling to characterize relationships between knee anatomy and kinematics. *J Orthop Res* 2015; **33**(11): 1620-30.
30. Kane R, Miltner, N., Smith, B., Tong. W. Initial mechanical stability of additively manufactured pegs in calcellous bone. Othropaedic Research Society Annual Meeting; 2020.
31. Tong W, Smith, B., Henninger, D., Kane, R., Muench, T. Bone ingrowth of RTT porous structure. Orthopaedic Research Society Annual Meeting; 2020.
32. Jauregui JJ, Banerjee S, Cherian JJ, Elmallah RD, Mont MA. Rating Systems to Assess the Outcomes After Total Knee Arthroplasty. *Surg Technol Int* 2015; **26**: 289-94.
33. Aveline C, Roux AL, Hetet HL, et al. Pain and recovery after total knee arthroplasty: a 12-month follow-up after a prospective randomized study evaluating Nefopam and Ketamine for early rehabilitation. *The Clinical journal of pain* 2014; **30**(9): 749-54.
34. Collins NJ, Misra D, Felson DT, Crossley KM, Roos EM. Measures of knee function: International Knee Documentation Committee (IKDC) Subjective Knee Evaluation Form, Knee Injury and Osteoarthritis Outcome Score (KOOS), Knee Injury and Osteoarthritis Outcome Score Physical Function Short Form (KOOS-PS), Knee Outcome Survey Activities of Daily Living Scale (KOS-ADL), Lysholm Knee Scoring Scale, Oxford Knee Score (OKS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Activity Rating Scale (ARS), and Tegner Activity Score (TAS). *Arthritis care & research* 2011; **63 Suppl 11**: S208-28.
35. Davis AM, Perruccio AV, Canizares M, et al. Comparative, validity and responsiveness of the HOOS-PS and KOOS-PS to the WOMAC physical function subscale in total joint replacement for osteoarthritis. *Osteoarthritis Cartilage* 2009; **17**(7): 843-7.
36. Harris KK, Dawson J, Jones LD, Beard DJ, Price AJ. Extending the use of PROMs in the NHS--using the Oxford Knee Score in patients undergoing non-operative management for knee osteoarthritis: a validation study. *BMJ open* 2013; **3**(8): e003365.

37. Ruyssen-Witrand A, Fernandez-Lopez CJ, Gossec L, Anract P, Courpied JP, Dougados M. Psychometric properties of the OARSI/OMERACT osteoarthritis pain and functional impairment scales: ICOAP, KOOS-PS and HOOS-PS. *Clinical and experimental rheumatology* 2011; **29**(2): 231-7.
38. Singh JA, Luo R, Landon GC, Suarez-Almazor M. Reliability and clinically important improvement thresholds for osteoarthritis pain and function scales: a multicenter study. *The Journal of rheumatology* 2014; **41**(3): 509-15.
39. Noble PC, Scuderi GR, Brekke AC, et al. Development of a new Knee Society scoring system. *Clin Orthop Relat Res* 2012; **470**(1): 20-32.
40. Dennis DA, Kim RH, Johnson DR, Springer BD, Fehring TK, Sharma A. The John Insall Award: control-matched evaluation of painful patellar Crepitus after total knee arthroplasty. *Clin Orthop Relat Res* 2011; **469**(1): 10-7.