# T2 Alpha Tibia Clinical Investigation Plan

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| **CLINICAL INVESTIGATION TITLE:** | A Post-Market Clinical Evaluation of the Treatment of Tibia Fractures with the T2 Alpha Tibia Nailing System |
| **ABBREVIATED CLINICAL INVESTIGATION TITLE:** | T2 Alpha Tibia |
| **DEVICE NAME:** | T2 Alpha Tibia Nailing System |
| **CLINICAL INVESTIGATION DESIGN:** | • Post-Market,<br>• Multicenter,<br>• Prospective,<br>• Non-Randomized |
| **INDICATIONS:** | This clinical investigation will adhere to the indications and contraindications for the T2 Alpha Tibia Nailing System as are detailed in the device's Instructions For Use. |
| **REGULATORY STATUS** | K180436 - 510(k) clearance received on 06Jun2018 |
| **CLINCIAL INVESTIGATION PLAN PHASE:** | Post-Approval Clinical Investigation |
| **SPONSOR:** | Stryker Orthopaedics<br>325 Corporate Drive<br>Mahwah, NJ 07430 |
| **INVESTIGATORS:** | Investigators' information is on file at the Sponsor |
| **MEDICAL EXPERT:** | Dr. Thomas Demuth, M.D. |
| **SPONSOR'S RESPONSIBLE CLINICAL RESEARCH HEAD:** | Rebecca Gibson |
| **COMPLIANCE STATEMENT:** | This clinical investigation will be conducted in compliance with the Clinical Investigation Plan, International Conference of Harmonisation Good Clinical Practice (ICH-GCP), and all other applicable regulatory requirements, including the retention of essential documents. Investigators will be trained on the clinical investigation devices and surgical techniques prior to implanting clinical investigation subjects. |
| **CONFIDENTIALITY STATEMENT:** | This Clinical Investigation Plan contains confidential information and its' use is limited to investigational staff intending to conduct the clinical investigation, Institutional Review Boards (IRBs)/Ethics Committees (ECs) and any others charged with reviewing the clinical investigation. |
| **VERSION:** | 3 |
| **DATE:** | 23Nov2020 |

## Approval Page

| APPROVERS | | | |
|---|---|---|---|
| **Role** | **Name** | **Signature** | **Date** |
| *Medical Expert* | Dr. Thomas Demuth | DocuSigned by:<br>Name des Unterzeichners: Thomas Demuth<br>Signiergrund: Ich genehmige dieses Dokument<br>Signierzeit: 26-Nov-2020 \| 1:55 AM PST<br>AF4A3F4855F64F08909D5CB4B21EFC36 | 26-Nov-2020 \| 1:55 AM PST |
| *Clinical Research Head (CRH)* | Rebecca Gibson | DocuSigned by:<br>Signer Name: Rebecca Gibson<br>Signing Reason: I approve this document<br>Signing Time: 24-Nov-2020 \| 7:42 PM EST<br>B69B71B0C1FA437DB21659BFBEB69FE2 | 24-Nov-2020 \| 7:42 PM EST |
| *Regulatory Affairs (RA)* | Cindy Leon | DocuSigned by:<br>Signer Name: Cindy Leon<br>Signing Reason: I approve this document<br>Signing Time: 01-Dec-2020 \| 8:23 AM PST<br>35D1D8D3DF5D4AC29231DB98BF0249AD | 01-Dec-2020 \| 8:23 AM PST |
| *Statistician* | Claudia Beimel | DocuSigned by:<br>Signer Name: Claudia Beimel<br>Signing Reason: I approve this document<br>Signing Time: 25-Nov-2020 \| 12:47 AM PST<br>6A460663AAD14348AC5448B30B90F068 | 25-Nov-2020 \| 12:47 AM PST |

# Table of Contents

# 1. List of Abbreviations

| Acronym | Definition |
|---|---|
| ADE | Adverse Device Effect |
| AE | Adverse Event |
| CI | Confidence Interval |
| CIP | Clinical Investigation Plan |
| CRF | Case Report Form |
| eCRF | Electronic Case Report Form |
| EC | Ethics Committee |
| EDC | Electronic Data Capture |
| EUDAMED | European Database on Medical Device |
| ICF | Informed Consent Form |
| ICH-GCP | International Conference of Harmonisation Good Clinical Practice |
| IFU | Instructions for Use |
| ITT | Intent-to-Treat |
| Intra-Op | Intra-Operative |
| IRB | Institutional Review Board |
| LTFU | Lost to Follow-Up |
| MCS | SF-36 Mental Component Summary |
| MDD | Medical Device Directive |
| MDR | Medical Device Regulation |
| PCS | SF-36 Physical Component Summary |
| PP | Per Protocol |
| Pre-Op | Pre-Operative |
| SADE | Serious Adverse Device Effect |
| SAE | Serious Adverse Event |
| SAP | Statistical Analysis Plan |
| SF-36v2 | 36-Item Short Form Health Survey |
| UADE | Unanticipated Adverse Device Effect |

# 2. Synopsis

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|---|---|
| Title | A Post-Market Clinical Evaluation of the Treatment of Tibia Fractures with the T2 Alpha Tibia Nailing System |
| Treatment | T2 Alpha Tibia Nailing System |
| Design | • Post-Market<br>• Multicenter<br>• Prospective<br>• Non-Randomized |
| Objective | The objective of this clinical investigation is to demonstrate the safety and efficacy/performance of the T2 Alpha Tibia Nailing System.<br><br>Efficacy/performance of the procedure will be measured by an equal or higher (non-inferior) SF-36 Physical Component Summary (PCS) score result of the T2 Alpha Tibia Nailing System compared to the T2 Tibia benchmark literature (Wang, et al. 2017; Sanders, et al. 2014; Sun, et al. 2016; Chan, et al. 2016) at 12 months.<br><br>In addition, demonstration of bone consolidation in correct alignment will be measured by Investigator assessment by 12 months.<br><br>Safety of the T2 Alpha Tibia Nailing System will be demonstrated through reporting of device related intra-operative and post-operative Adverse Events/incidents by 12 months. |
| Target Population | Approximately 80 subjects are to be enrolled in this clinical investigation at up to 5 sites. Enrolled subjects will be assessed at Operative/Discharge, and at 3 Months, 6 Months and 12 Months after the index procedure. |
| Inclusion Criteria | a. Subject is a male or non-pregnant female age 18 years or older at the time of surgery;<br><br>b. Subject is willing and able to give written informed consent and comply with the requirements of this Clinical Investigation Plan;<br><br>c. Subject is intended to be treated with the Tibial Nail of the T2 Alpha Tibia Nailing System in accordance with the following legally cleared/ approved Indications for Use:<br><br>Indications for Use approved **In United States and Canada** include:<br><br>• Open and closed tibial fractures<br>• Pseudoarthrosis and correction osteotomy<br>• Pathologic fractures, impending pathologic fractures and tumor resections<br>• Fractures involving osteopenic and osteoporotic bone<br>• Nonunions and malunions<br><br>Indications for Use approved **In Europe and Other Countries** include:<br><br>• Open and closed tibial fractures<br>• Nonunions and malunions |

| | |
|---|---|
| Exclusion Criteria | a. Subject has an active or suspected latent infection or marked local inflammation in or about the affected area<br>b. Subject has compromised vascularity that would inhibit adequate blood supply to the fracture or the operative site<br>c. Subject has documented bone stock compromised by disease, infection or prior implantation which cannot provide adequate support and / or fixation of the device<br>d. Subject has documented or suspected sensitivity to materials<br>e. Subject is obese such that he / she produces a load on the implant which can lead to failure of fixation of the device or to failure of the device itself<br>f. Subject has inadequate tissue coverage over the operative site.<br>g. Subject has implant utilization that would interfere with anatomical structures or physiological performance<br>h. Subject has mental or neuromuscular disorder which would create an unacceptable risk of fixation failure or complications in post-operative care<br>i. Subject has any other medical or surgical condition which would preclude the potential benefit of surgery |
| Endpoints | **Primary Endpoint**<br>The primary endpoint of this clinical investigation is to confirm efficacy/performance at 12 months, as measured by the SF-36 Physical Component Summary (PCS). Confirmation of efficacy/performance at 12 months will be based on an equal or higher (non-inferior) SF-36 Physical Component Summary (PCS) result of the T2 Alpha Tibia Nailing System compared to the T2 Tibia benchmark literature (Wang, et al. 2017; Sanders, et al. 2014; Sun, et al. 2016; Chan, et al. 2016).<br>**Secondary Endpoints**<br>• Safety: Incidence of device-related adverse events will be monitored by 12 months through data collection and analyses.<br>• Efficacy/Performance: Bone consolidation will be assessed by 12 months as measured by Investigator assessment. |

# 3. General Information and Administrative Structure

3.1. SPONSOR

Stryker Orthopaedics
325 Corporate Drive
Mahwah, NJ 07430

3.2. KEY SPONSOR PERSONNEL

Susanne Höfer
Clinical Study Manager
Role: Author and Clinical Investigation Manager
Email: Susanne.hoefer@stryker.com
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Rebecca Gibson
Manager, Clinical Research
Role: Clinical Research Head

Dr. Thomas Demuth, M.D.
Medical Affairs Director
Role: Medical Expert

3.3. EDC SYSTEM

Name: IBM Clinical Development
Email: icdhelp@us.ibm.com
Phone: +1 888 500 4247

# 4. Product Information

All components of the T2 Alpha Tibia Nailing System were cleared and approved for sale and use prior to starting the clinical investigation. 510(k) clearance was received on 06Jun2018. This system is to be used only for indications for which it has been approved. Please see the approved Instructions for Use and Operative Technique manuals for a detailed description of the medical device(s) and instrumentation, and intended use information.

Medical device product traceability will be achieved by capturing the implant lot number.

# 5. Risks and Benefits

This prospective, multi-center, clinical investigation is designed to examine the safety and efficacy/performance of the T2 Alpha Tibia Nailing System, in accordance with the approved instructions for use, labeling and instrumentation. The potential risks to subjects are described in the approved Instructions for Use and Operative Technique manuals.

Potential benefits resulting from the T2 Alpha Tibia Nailing System over other devices and procedures, as demonstrated by superior scoring on outcome surveys and positive results on other clinical evaluation measurements (outlined in section 8), would also suggest affirmative clinical efficacy.

# 6. Introduction

The T2 Tibia Nailing System represented the latest and most comprehensive development of the original intramedullary principles presented by Professor Gerhard Kuentscher in 1940. As an addition to the T2 Nailing System, Stryker has created a new generation tibial implant that offers an efficient treatment option for multiple indications. The T2 Alpha Tibia Nail includes new locking options and the ability to utilize the advanced locking screw which creates an axial and angular stable construct. New instrumentation offers a combination of innovation, simplicity and efficiency that is designed to suit the various needs of surgeons and OR staff.

# 7. Clinical Investigation Design

This investigation is a prospective, multicenter clinical investigation. It is anticipated that a total of 80 subjects will be enrolled at up to 5 sites. Enrollment is estimated to commence in Q4 of 2018. Neither

subjects nor investigators are blinded to treatment and the clinical investigation includes a historical control which will be compared to the T2 Alpha Tibia Nailing System.

The enrollment period is expected to occur over32 months. Total duration of enrollment, 12 month follow-up and analysis is expected to take 47 months. The clinical investigation has been designed to follow the surgeon's standard of care for tibia fractured subjects, in addition to a 12 month follow-up visit.

### 7.1. CLINICAL INVESTIGATION RATIONALE

The T2 Alpha Tibia Nailing System is fully integrated into the T2 Alpha Platform. The system includes two approaches: infrapatellar approach and suprapatellar approach and allows for multiple locking configurations for stable fixation. This clinical investigation will evaluate the safety and efficacy/performance of the T2 Alpha Tibia Nailing System.

## 8. Objective

### 8.1. PRIMARY ENDPOINT

The primary endpoint of this clinical investigation is to confirm efficacy/performance at 12 months, as measured by the SF-36 Physical Component Summary (PCS). Confirmation of efficacy/performance at 12 months will be based on an equal or higher (non-inferior) SF-36 Physical Component Summary (PCS) result of the T2 Alpha Tibia Nailing System compared to the benchmark literature (Wang, et al. 2017; Sanders, et al. 2014; Sun, et al. 2016; Chan, et al. 2016).

### 8.2. SECONDARY ENDPOINTS

- Safety: Incidence of device-related adverse events by 12 months will be monitored through collection and analyses.
- Efficacy/Performance: Bone consolidation will be assessed by 12 months as measured by Investigator assessment.

## 9. Selection of Clinical Investigation Population

Subjects participating in this clinical investigation will be recruited from the investigator's standard subject population, where all subjects presenting for treatment of tibial fractures will be evaluated for clinical investigation participation based on the eligibility criteria listed below.

### 9.1. INCLUSION CRITERIA

a. Subject is a male or non-pregnant female age 18 years or older at the time of surgery;

b. Subject is willing and able to give written informed consent and comply with the requirements of this Clinical Investigation Plan;

c. Subject is intended to be, treated with the Tibial Nail of the T2 Alpha Tibia Nailing System in accordance with the following legally cleared/ approved Indications for Use:

Indications for Use approved **In United States and Canada** include:

- Open and closed tibial fractures
- Pseudoarthrosis and correction osteotomy
- Pathologic fractures, impending pathologic fractures and tumor resections
- Fractures involving osteopenic and osteoporotic bone

- Nonunions and malunions

Indications for Use approved **In Europe and Other Countries** include:

- Open and closed tibial fractures
- Nonunions and malunions

9.2. EXCLUSION CRITERIA

a. Subject has an active or suspected latent infection or marked local inflammation in or about the affected area

b. Subject has compromised vascularity that would inhibit adequate blood supply to the fracture or the operative site

c. Subject has documented bone stock compromised by disease, infection or prior implantation which cannot provide adequate support and / or fixation of the device

d. Subject has documented or suspected sensitivity to materials

e. Subject is obese such that he / she produces a load on the implant which can lead to failure of fixation of the device or to failure of the device itself

f. Subject has inadequate tissue coverage over the operative site.

g. Subject has implant utilization that would interfere with anatomical structures or physiological performance

h. Subject has mental or neuromuscular disorder which would create an unacceptable risk of fixation failure or complications in post-operative care

i. Subject has any other medical or surgical condition which would preclude the potential benefit of surgery

9.3. WITHDRAWAL CRITERIA

If, during the clinical investigation, a subject must be prematurely withdrawn, the procedures outlined in this section must be followed. These procedures should not interfere with the initiation of any new treatments that are necessary to treat a subject's condition. Information on all withdrawn subjects will be documented.

Subjects may be withdrawn from the clinical investigation for any of the following reasons:

a. Subject Withdrawal: A subject may voluntarily withdraw from the clinical investigation at any time and for any reason. The subject should be asked when possible, and without any form of coercion, the reason for his/her decision. If the participant withdraws from the clinical investigation completely, then data collected up until the point of withdrawal will be included in the final analysis. Subjects who decline to continue to take part will be given the opportunity to discuss/inform the research team of the reasoning behind their decision not to take part.

b. Lost to Follow-Up (LTFU): A subject will be considered LTFU after all reasonable efforts have been made to contact the subject and request his/her continued participation in the clinical investigation. All attempts to contact the subject must be documented and should include at least two attempts to contact the subject by phone and one attempt via a certified letter. Data collected up until the point where the subject is LTFU will be included in the final analysis.

c. Removal of Device or Adverse Event/Incident: The discontinuation of a subject's participation in the clinical investigation due to the removal of the Tibial Nail of the T2 Alpha Tibia Nailing System or Adverse Event/incident that prohibits his/her continued participation must be fully explained. All available information concerning the removal of the device or Adverse

Event/incident should be provided. Data collected up until the point of removal or Adverse Event/incident will be included in the final analysis.

d. Death: The discontinuation of a subject's participation in the clinical investigation due to death must be fully explained. All available information concerning the death should be provided. Removal of a subject from continued follow-up in the clinical investigation due to death will not be considered a device failure unless the death is directly caused by, or attributable to, the T2 Tibia Nailing System. Data collected up until the point of death will be included in the final analysis.

e. Other: A subject may be withdrawn by the Investigator if he/she believes that it is in the best interest of the subject or the IRB/EC may determine that a subject's continued participation in the clinical investigation represents an unacceptable risk to the subject. The Sponsor must be notified immediately if this occurs. All data collected up until the point of withdrawal or IRB/EC determination will be included in the final analysis.

   A subject may also be withdrawn if the subject is non-compliant with the clinical investigation procedures or visits, or if a selection criteria violation is noted after the subject received the clinical investigation treatment and it is determined that the subject should be discontinued. All data collected up until the point of withdrawal will be included in the final analysis.

# 10. Clinical Investigation Evaluations, Procedures and Assessments

## 10.1. METHODS OF ASSIGNING SUBJECTS

No specific methods (e.g. randomization, blinding, or stratification) for assigning subjects are used in this Clinical Investigation Plan. Consecutive subjects at each site meeting all the eligibility criteria will be enrolled in this clinical investigation.

## 10.2. PROCEDURES

Subjects recruited to this clinical investigation have received the Tibial Nail of the T2 Alpha Tibia Nailing System. Please see the approved Instructions for Use and Operative Technique Manuals for a detailed description of the medical device(s) and instrumentation, intended use information and associated risk. Any additional clinically indicated procedures are permitted as deemed necessary by the clinical investigation investigator.

## 10.3. INITIAL ASSESSMENT

All subjects presenting for treatment of femoral fractures at the investigative sites will be evaluated for clinical investigation participation based on the eligibility criteria listed in Section 9. Informed consent will be obtained from each subject before any study procedures are performed. Details on obtaining informed consent and related documentation are provided in Section 15.2.

The initial assessment may occur prior to the index surgery, during the subject's hospital stay, or within the 3 months post-surgery. Should the initial assessment occur after the subject's index surgery, data from the subject's medical history, surgical procedure, and the SF-36 PCS and MCS will be collected retrospectively in order to record the subject's pre-operative health status.

## 10.4. FOLLOW-UP EVALUATIONS

The follow-up evaluations will occur at 3 Months, 6 Months and 12 Months after the index procedure and include an assessment of device-related adverse events/incidents, evaluation using the SF-36 PCS and MCS scores, as well as clinical assessment of bone consolidation. Investigators should consider weight-bearing, pain and imaging when assessing bone consolidation. See the section below for visit windows and a list of assessments to be performed at each visit.

Investigative site personnel will contact subjects prior to their scheduled follow-up evaluations to encourage compliance with clinical investigation visits and participation.

If a subject misses a visit and is outside of the visit window, every effort should be made to collect data instead of noting the visit as missed.

10.5. SCHEDULE OF EVENTS

| Assessment | Initial Assessment | 3 Months [a, b] (+/-2 weeks) | 6 Months [a, b] (+/-3 weeks) | 12 Months [b] (+/-4 weeks) |
|---|---|---|---|---|
| Informed Consent | X[c] | | | |
| Demographics & Medical History | X | | | |
| Inclusion/Exclusion | X | | | |
| Primary Diagnosis | X | | | |
| Surgical Procedure | X | | | |
| Clinical Assessment of Bone Consolidation [d, e] | | X | X | X |
| SF-36v2 (PCS & MCS) | X [f] | X | X [g] | X [g] |
| Subject Disposition [h] | | X | X | X |
| Device-Related Adverse Events/Incidents & Reoperations will be collected throughout the course of the Clinical Investigation. | | | | |

a. Follow-up visit schedule to reflect Institutions' Standard of Care practices

b. If the subject missed a visit and outside of visit window, every effort should be made to collect data instead of noting visit as missed. Visit windows are calculated from the index event, and not from the previous visit.

c. Informed consent must be obtained prior to enrollment in the study (i.e., prior to performance of any study-related activities).

d. Once bone consolidation is observed, assessment no longer needs to be conducted at the additional follow-up visits.

e. Investigators should consider weight-bearing, pain and imaging when assessing bone consolidation.

f. SF-36v2 evaluation must be collected post-informed consent.

g. If bone consolidation is previously observed at the previous follow-up visit, evaluation is to be collected via phone.

h. Subject Disposition assessment would occur at any time point for subject withdrawal prior to the completion of the clinical investigation.

# 11. Statistical Methods

The Statistical Analysis Plan (SAP) lists all variables/questions within this clinical investigation. Therefore, no additional "evaluation" chapter is required and needed for this CIP.

Data will be captured via IBM Merge EDC system and statistical analysis will be performed using IBM SPSS. All statistical hypotheses tests will be with confidence levels (1-α) of 95% and power (1-β) of 80%. The significance level (α) is 0.05 and the beta-value (β) is set to 0.20. Therefore, p-values ≤ 0.05 will indicate statistical significance.

Results will be presented using summary tables and optionally supported by graphs. For detailed information per variable, see SAP.

## 11.1. DETERMINATION OF SAMPLE SIZE

The 12 months post-operative results for subjects implanted with the Tibial Nail of the T2 Alpha Tibia Nailing System will be compared to a historical group and results reported by Wang, et al. (2017); Sanders, et al. (2014); Sun, et al. (2016); and Chan, et al. (2016) will serve as the control group for the T2 Alpha Tibia Nail subjects.

Hypotheses were developed to allow for a comparison of 12 months post-operative SF-36 Physical Component Summary (PCS) results and 12 months effectiveness/performance between these two populations.

| **Benchmark and Objectives for Planned Research** | |
|---|---|
| **Endpoint** | Non-inferiority related to the SF-36 Physical Component Summary (PCS) for subjects undergoing infrapatellar (IP) and/or suprapatellar (SP) tibia nailing at 12 months post-operative compared to the pooled literature control. |
| **Estimated drop-out rate** | 20%<br>Source: "Stannard et al: Functional Outcome Following Intramedullary Nailing of the Femur. A Prospective Randomized Comparison of Piriformis Fossa and Greater Trochanteric Entry Portals JBJS 2011"<br>Stannard et al. reported a lost to follow up rate of 19.6% (11/56).<br>Note: The source of Stannard et al. was used for T2 Alpha Tibia as well as it represents a worst-case drop-out rate. |

**Results as reported by Benchmark**

Non-inferiority related to the SF-36 Physical Component Summary (PCS) for subjects undergoing infrapatellar (IP) or suprapatellar (SP) tibia nailing at 12 months post-operative.

The results from the sources Chan et al, Sanders et al., and Sun et al. were pooled to determine overall two-sided 90% confidence intervals of the mean SF-36 PCS (physical) and mean SF-36 MCS (mental) scores.

Note: The results reported by Wang et al. seemed to be based on a different calculation method for the determination of the SF-36 scores and it was not possible to evaluate, what exactly was done by the authors. The score values reported by Wang et al. are much higher compared to what was normally reported in the literature and what was defined in country specific weights and coefficients. Wang et al. reported median score values whereas the other authors reported means. As summary score results usually tend to deviate from normality, means and medians might differ significantly. Therefore, the results reported by Wang et al. were not included into the pooled analysis.

| Source | Subgroup | Mean SF36-PCS | Mean SF36-MCS | Pooling |
|---|---|---|---|---|
| Chan et al. | IP | 38.00 | 47.00 | included |
| Chan et al. | SP | 46.00 | 47.00 | included |
| Sanders et al. | SP | 40.80 | 46.00 | included |
| Sun et.al. | SP | 49.41 | 44.71 | included |
| Sun et.al. | IP | 43.21 | 43.81 | included |
| *Wang et.al.* | | *79.10* | *77.00* | *excluded* |

Summary of explorative analysis is listed below:

**Descriptives**

| | | | Statistic | Std. Error |
|---|---|---|---|---|
| SF-36 PCS Physical at 12 months post-op | Mean | | 43,4840 | 1,98495 |
| | 90% Confidence Interval for Mean | Lower Bound | 39,2524 | |
| | | Upper Bound | 47,7156 | |
| | Median | | 43,2100 | |
| | Std. Deviation | | 4,43849 | |
| | Minimum | | 38,00 | |
| | Maximum | | 49,41 | |
| | Range | | 11,41 | |
| | Interquartile Range | | 8,31 | |
| SF-36 PCS Mental at 12 months post-op | Mean | | 45,7040 | ,63333 |
| | 90% Confidence Interval for Mean | Lower Bound | 44,3538 | |
| | | Upper Bound | 47,0542 | |
| | Median | | 46,0000 | |
| | Std. Deviation | | 1,41617 | |
| | Minimum | | 43,81 | |
| | Maximum | | 47,00 | |
| | Range | | 3,19 | |
| | Interquartile Range | | 2,74 | |

As the mean physical score (PCS) was slightly lower, it was used for the sample size calculation.

For the clinical investigation the one-sided 95% confidence interval will be applied.

## Acceptance Criteria for Sample Size Calculation

| | | |
|---|---|---|
| **Significance Level (α)** | 0.05 (5%) | |
| **Power (1-β)** | 0.80 (80%) | |
| **Confidence Interval (CI)** | 0.95 (95%) | |
| **Tails** | 1 | |
| **Path** | Non-inferiority<br>T2 Alpha Tibia (A) ≥ Benchmark (B, pooled benchmark results) | |
| **Hypotheses Pair** | Null ($H_0$) | $A - B < -\theta$ |
| | Alternative ($H_1$) | $A - B \geq -\theta$ |
| **Benchmark Timepoint** | 12 months post-operative | |
| **Benchmark Mean** | **43.48 points** SF-36 PCS at 12 months (IP and SP together) | |
| **Benchmark Std. Dev.** | No standard deviation results were given by Chan et al., Sanders et al. nor by Wang et al.<br>• Only Sun et al. reported standard deviations at 12 months postoperative for SF-36 PCS of 6.27 for the SP and of 6.52 for the IP subgroup<br>As a worst-case, the double standard deviation reported by Sun et al. was used for the sample size calculation (2 * 6.52 = **13.04 points**) | |
| **Benchmark 90% CI of Mean** | **Lower 90% CI: 39.25** (two-sided 90% CI equals a one-sided 95% CI) | |
| | Upper 90% CI: 47.72 | |
| **Margin (-θ)** | Lower 90% CI of Benchmark: **39.25** | |
| **Software Used** | IBM SPSS Sample Power V3.0 | |

**IBM SPSS Sample Power Output**

One goal of the proposed clinical investigation is to test the null hypothesis that the population mean is 39.25. The criterion for significance (alpha) has been set at 0.050. The test is 1-tailed, which means that only an effect in the expected direction will be interpreted.

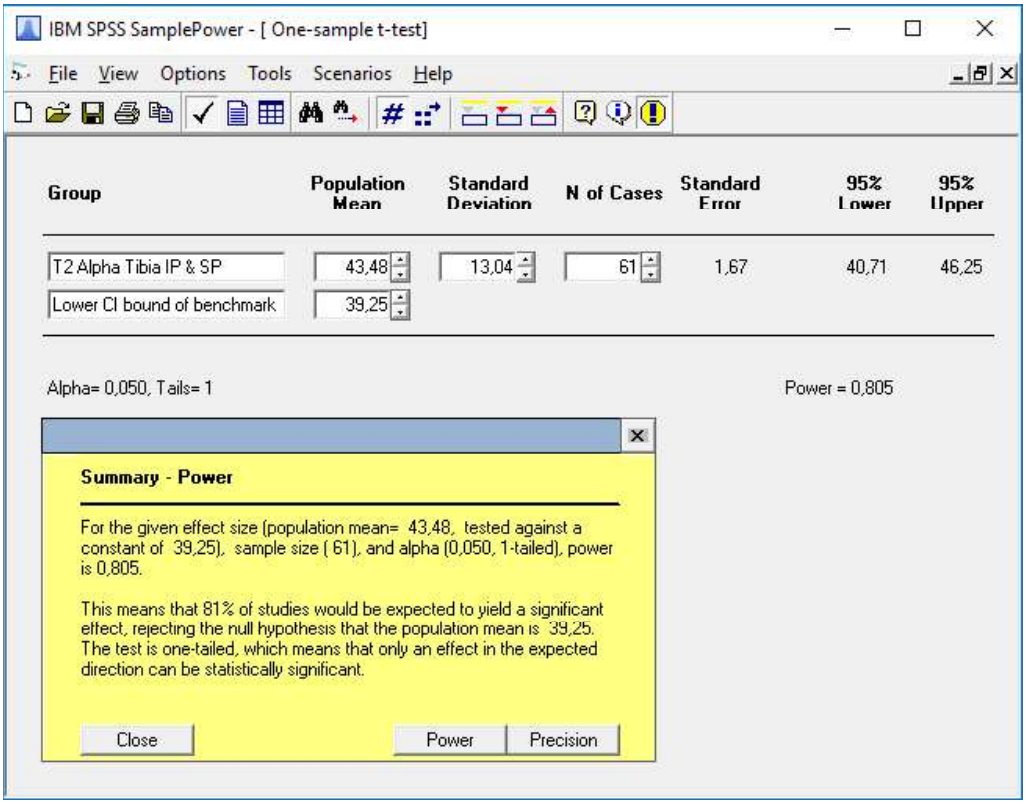
With the proposed sample size of 61 subjects, the clinical investigation will have power of 80.0% to yield a statistically significant result.

This computation assumes that the population from which the sample will be drawn has a mean of 43.48 with a standard deviation of 13.04. The observed value will be tested against a theoretical value (constant) of 39.25.

This effect was selected as the smallest effect that would be important to detect, in the sense that any smaller effect would not be of clinical or substantive significance.

A second goal of this clinical investigation is to estimate the mean in the population. On average, a clinical investigation of this design would enable us to report the mean with a precision (95.0% confidence level) of plus/minus 2.77 points.
The precision estimated here is the median precision. Precision will vary as a function of the observed standard deviation (as well as sample size), and in any single clinical investigation will be narrower or wider than this estimate.

**IBM SPSS Sample Power Output – Screenshot**




Estimated drop-out rate is 20% which leads to the requirement of enrolling additional 13 subjects into the clinical investigation.

| | |
|---|---|
| **Sample Size** | **Overall number of subjects to be enrolled: 74 subjects (rounded up to 80 subjects)** |

11.2. ANALYSIS POPULATIONS

It is expected, that during this clinical investigation only one population for T2 Alpha Tibia will exist and all subjects will be analyzed “Per Protocol” (PP). However, it cannot be fully avoided that in theory subjects might need to be excluded from the PP population. In this occasion, there will be two groups being fully analyzed to ensure transparency and avoid bias.

The groups are defined as follows:

- **Intent-to Treat Population**

  The Intent-to-Treat (ITT) Population is defined to be all enrolled subjects. An enrolled subject is a subject that has signed informed consent, all screening procedures have been successfully completed, is eligible and can receive treatment. The ITT population will not be analyzed for the annual reports and will only be included in the final report.

- **Per Protocol Population**

  The Per Protocol (PP) Population is defined to be all subjects in the ITT Population with no major protocol violations. The protocol violations that will exclude a subject are as follows:

  - The subject does not receive the Tibial Nail of the T2 Alpha Tibia Nailing System

- The subject does not meet all eligibility criteria
- The subject has a protocol violation that is considered likely to affect subject outcomes.

After the clinical investigation has been completed, a review of the data will be conducted to determine which subjects are to be excluded from the PP population.

## 11.3. ANALYSIS PLAN BY CLINICAL INVESTIGATION ELEMENT AND EVALUATION

### 11.3.1. Statistical Analysis

Evaluation elements are defined as the questions on the CRF/eCRF. The SAP lists all evaluation elements and secondary elements which will be based on calculations between two or more evaluation elements.

All quantitative variables, including those based on calculations (secondary elements), will be analyzed with a case summary evaluation before the detailed characteristics and parameter can be evaluated. A case summary contains a listing of the number of valid cases/values, missing cases/values (if any) and total cases/values in the specific analysis. In general, as central position parameter for quantitative variables the mean, median and mode will be analyzed. As variation parameter the standard deviation, 95% confidence interval of the mean, interquartile range and range (based on maximum and minimum) will be calculated. All quantitative variables will be assessed for normality used the Shapiro-Wilk test. For optional visualization of quantitative variables, box-and-whisker plots will be used. Additional analyses like skewness and kurtosis measures of standard errors are also optional.

All qualitative variables, including those based on summaries (secondary elements), will be analyzed listing the proportions, frequencies, column and row totals and missing proportion (if any).

The SAP reflects this approach and specifies the variables characteristics (quantitative or qualitative) in detail together with the related analysis strategy. This also includes calculation and summaries based on primary elements and the required analysis.

### 11.3.2. Primary Analysis / Endpoint

This analysis is only part of the final report. The primary endpoint analysis will only be executed once at the end of the clinical investigation and will not be part of any interim or annual reports or presentations given in front of the final report.

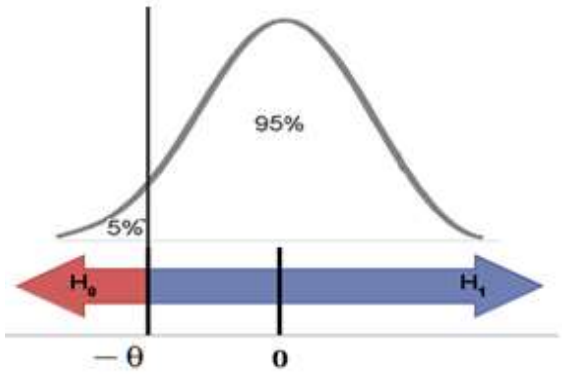
The 12 months post-operative results for subjects implanted with the T2 Alpha Tibia Nailing System will be compared to Sanders et al: Semiextended intramedullary nailing of the tibia using a suprapatellar approach: radiographic results and clinical outcomes at a minimum of 12 months follow-up. J Orthop Trauma, 2014; Sun et al: The outcome comparison of the suprapatellar approach and infrapatellar approach for tibia intramedullary nailing. Int Orthop, 2016; and Chan et al: Suprapatellar Versus Infrapatellar Tibial Nail Insertion: A Prospective Randomized Control Pilot Study. J Orthop Trauma, 2016“. Specifically, the SF-36 score results reported by Wang, et al. (2017), Sanders, et al. (2014), Sun, et al. (2016) and Chan, et al. (2016) will serve as the control groups for the T2 Alpha Tibia group.

Higher SF-36 PCS and MCS score results are linked to better subject results and vice versa.

The clinical investigation endpoint is non-inferiority to the control, meaning the clinical investigation result should be equal or better than the control. In this clinical investigation, an equal or better SF-36 score result means equal or greater ($\geq$). As only results from samples will be captured, results are mostly estimates of the true population parameter. These estimates vary by a certain area, where it is expected that the true population parameter falls within. Based on this, it is required to specify a lower limit for the acceptable difference or zone of indifference, denoted as $-\theta$.

Hypotheses were developed to allow for a comparison of the 12 months post-operative SF-36 PCS to evaluate effectiveness / performance. The 12 months post-operative SF-36 PCS is the primary endpoint of this clinical investigation. Hypothesis tests will be one-sided with a significance level α of 5%.

| Hypothesis | Equations | Interpretation |
|---|---|---|
| Null ($H_0$) | $A - B < -\theta$<br>T2 Alpha Tibia (A) – Control (B, pooled benchmark results) < -θ | Central tendency of A is inferior to the central tendency of B. |
| Alternative ($H_1$) | $A - B \geq -\theta$<br>T2 Alpha Tibia (A)⁻ Control (B, pooled benchmark results) ≥ -θ | Central tendency of A is non-inferior to the central tendency of B. |




| Possible Evidence (p) | Possible Decisions | Possible Conclusions – SF-36 PCS |
|---|---|---|
| p-value > α (0.05) | Fail to reject null hypothesis ($H_0$) | T2 Alpha Tibia < Control (pooled benchmark results)<br>Insufficient evidence to reject the null hypothesis ($H_0$: $A - B < -\theta$) at the pre-determined significance level of 5%. |
| p-value ≤ α (0.05) | Reject null hypothesis ($H_1$) | T2 Alpha Tibia ≥ Control (pooled benchmark results)<br>Sufficient evidence to reject the null hypothesis ($H_0$: $A - B < -\theta$) at the pre-determined significance level of 5%. |

To test non-inferiority, the 12 months mean SF-36 PCS result of the T2 Alpha Tibia group will be compared to the mean estimate of the control group, 43.48 points.

To be able to identify an acceptable difference or zone of indifference (-θ), the lower 90% confidence interval (CI) of the SF-36 PCS result at 12 months post-operative in the control group (Sanders, et al.; Sun, et al.; Chan, et al.) was used as lower limit (lower 90% CI of control is 39.25 points). The maximum acceptable difference in the negative direction is 4.23 points.

Based on the underlying distribution of the data and the result of the normality assessment, either the parametric one-sample t-test or the non-parametric one-sample sign test will be used to compare the 12 months post-operative SF-36 PCS result of the T2 Alpha Tibia group against the value of 39.25 points (mean of control - θ or 43.48 – 4.23 = 39.25 points).

11.3.3. Secondary Analyses

For efficacy/performance, bone consolidation will be assessed by 12 months as measured by Investigator assessment. For Safety, the incidence of device-related adverse events/incidents by 12 months will be monitored through collection and analyses. Both analyses will be part of the annual and final reports.

Furthermore, device related adverse events/incidents and the time to (earliest) Device Related Adverse Events/incidents will be analyzed as well. Considered variables, the level of measurement and the planned analysis steps are listed in detail in the SAP.

11.3.4. Additional Analyses

Additional Analyses are outlined in the subsequent sections. Analysis details (variables, level of measurement, planned steps) are listed in-depth in the SAP.

- **Weight-bearing status**

  The weight bearing status will be evaluated and analyzed at the pre-operative visit and at 3 months, 6 months and 12 months. The within subject changes from visit to visit will be analyzed in addition. This analysis will be part of the annual and final reports.

- **External Support**

  The status of the subject using external support will be evaluated at the pre-operative visit and at 3 months, 6 months and 12 months. The within subject changes from visit to visit will be analyzed in addition. This analysis will be part of the annual and final reports.

- **Mortality**

  For analysis of the time to death or mortality, the Kaplan-Meier method will be used. The times between the date of surgery and the date of the 12 months assessment will be used together with the times between surgery and the date of death. This analysis will be part of the annual and final reports.

- **Reoperation**

  For analysis of the time to the reoperation, the Kaplan-Meier method will be used. The times between the date of surgery and the date of the 12 months assessment will be used together with the times between date of surgery and the date of reoperation (earliest reoperation in case that one subject experienced more than one reoperation). This analysis will be part of the annual and final reports.

- **SF-36 Total Score – Within subject changes by visit**

  The within subject score changes of the SF-36 Total Score from visit to visit will be analyzed to help identify the changes on the subject level. This analysis will be part of the annual and final reports.

11.4. MISSING DATA / SAP DEVIATIONS

The intent is to collect as complete a dataset as possible. Nevertheless, in some situations missing data cannot be avoided. The reports and tables therefore will show the number and percentage of missing cases for each analyzed variable in relation to the enrolled cases for each post-operative assessment

Any deviations from Statistical Analysis Plan will be listed in the annual or final reports.

11.5. REPORTS

11.5.1. Interim Analysis and Reports

Interim analyses will be performed on a yearly basis. The progress of the clinical investigation will be reported together with the interim results on the variable level according to the analysis plan. The only exception is the analysis of the primary endpoint will not be part of the interim reports.

11.5.2. Final Analysis and Reports

The full final report with complete analysis and progress and conduct reporting will be created at the end of this clinical investigation.

# 12. Clinical Investigation Plan Deviations

A Clinical Investigation Plan (CIP) deviation is a departure from the approved CIP that is not implemented or intended as a systemic change. All CIP deviations are recorded and reported to each site's IRB/EC in accordance with the respective site's IRB/EC policies.

# 13. Adverse Events/Incidents

As this CIP is being carried out to satisfy the post-market requirements to support safety and efficacy/performance according to the Council Directive 93/42/EEC concerning medical devices (Annex X (1.1c)) (MDD 93/42/EEC) and Regulation 2017/745 on medical (MDR 2017/745), categorization and definition of device related adverse events will follow the guidelines outlined in the MDR 2017/745 as "incident" reporting. The following AE terminology will apply:

**An Adverse Device Effect (ADE)** is defined as any untoward or unintended response to the clinical investigation treatment; and/or a medical response which may have a causal relationship to the treatment.

- **An Incident** is defined as any malfunction or deterioration in the characteristics or performance of a device made available on the market, including use-error due to ergonomic features, as well as any inadequacy in the information supplied by the manufacturer and any undesirable side-effect.

- **A Serious Adverse Device Effect (SADE)** is defined as any ADE that results in consequences characteristic of a SAE or might lead to the consequences if suitable action or intervention is not taken; causes considerable interference with the subject's usual activities and may be incapacitating or life-threatening, including those events resulting in a subject's disability or permanent damage, or required intervention to prevent disability or permanent damage; results in a life-threatening illness or injury; and/or results in death (fatal).

- **A Serious Incident** is defined as any incident that directly or indirectly led, might have led or might lead to any of the following:

    - the death of a patient, user or other person;

    - the temporary or permanent serious deterioration of a patient's, user's or other person's state of health;

    - a serious public health threat

- **An Unanticipated Adverse Device Effect (UADE)** is defined as an Adverse Event not described in the informed consent, Clinical Investigation Plan or device labeling which has resulted in any of the

consequences of a SAE or which might have led to any of the consequences of a SAE if suitable action had not been taken, intervention had not occurred, or if circumstances had been less opportune. Anticipated Adverse Events will be those listed in the T2 Alpha Tibia Nailing System device labeling (Operative Technical Manual and Instructions for Use).

13.1. ADVERSE EVENT/INCIDENT SEVERITY

The severity of all AEs/incidents is assessed by the Investigator utilizing the following categories:

- **Mild:** The AE/incident is transient and easily tolerated by the subject.
- **Moderate:** The AE/incident causes the subject discomfort and interrupts the subject's usual activities.
- **Severe:** The AE/incident causes considerable interference with the subject's usual activities and may be incapacitating or life-threatening. This includes those events that result in a subject's disability or permanent damage, and/or required intervention to prevent permanent disability or damage.
- **Life-threatening:** The AE/incident results in a life-threatening illness or injury.
- **Fatal:** The AE/incident results in death.

13.2. RELATIONSHIP TO THE DEVICE

Only adverse events/incidents that are considered possibly, probably or definitely related to the device will be captured for this clinical investigation.

13.3. FORESEEABLE ADE AND SADE

ADEs, SADEs and incidents which may be expected as part of the surgical interventions include:

- Axial malalignment
- Chondromalacia
- Compartment syndrome
- Deep vein thrombosis
- Delayed union
- Fat embolism
- Hematoma
- Iatrogenic fracture
- Implant breakage (nail)
- Implant breakage (screw)
- Implant failure (nail)
- Implant failure (screw)
- Implant loosening (nail)
- Implant loosening (screw)
- Infection (deep)
- Infection (superficial)
- Malunion

- Necrosis
- Non-union
- Pain
- Peripheral nerve injury without specification
- Pressure ulcer
- Pre-tibial fistula
- Pulmonary embolism
- Rotational malalignment

13.4. ADVERSE DEVICE EFFECT/INCIDENT REPORTING AND ANALYSIS

In the event that a SADE, UADE or serious incident occurs, the Investigator is required to notify the Sponsor within 48 hours of being made aware of the event. The Investigator is also required to notify their IRB/EC in accordance with the policies of their local laws and regulations.

# 14. Reoperations

Reoperations and reason(s) for reoperations will be collected throughout the course of the clinical investigation. A reoperation may include, but not limited to, irrigation and debridement, revision surgery, and/or implant removal.

# 15. Ethics

This clinical investigation is to be conducted according to International Conference of Harmonisation of Good Clinical Practice (ICH-GCP), applicable regulations, institutional research policies and procedures, Declaration of Helsinki and in compliance with the Clinical Investigation Plan (CIP). Investigators will be trained on the clinical investigation devices and surgical techniques prior to implanting clinical investigation subjects.

This CIP and any amendments will be submitted to a properly constituted independent ethics board, in agreement with local legal prescriptions, for formal approval of the clinical investigation conduct. The decision of the ethics board concerning the conduct of the clinical investigation will be made in writing to the Site Principal Investigator before commencement of this clinical investigation. Clinical investigations shall not begin until the governing regulatory authority has provided full, unconditional approval. Off-label use of the T2 Alpha Tibia Nailing System is not permitted.

15.1. INSTITUTIONAL REVIEW BOARD (IRB)/ETHICS COMMITTEE (EC)

IRB/EC approval will be obtained at each of the investigational sites prior to enrolling clinical investigation subjects at that site. In addition, any SADE, UADE or serious incident that meets the reporting criteria of the IRB/EC, will be reported to the IRB/EC. During the clinical investigation, the Investigator should promptly provide written reports to the IRB/EC of any changes that affect the conduct of the clinical investigation and/or increase risk to the subjects, unless otherwise submitted by the Sponsor.

15.2. INFORMED CONSENT

The Investigator, or qualified clinical investigation personnel designated to perform this task, will explain the nature of the clinical investigation to the subject, and answer all questions regarding participation in this clinical investigation. Prior to any clinical investigation procedures being performed, the ICF will be reviewed, signed and dated by the subject, and by the person administering the informed consent. A copy

of the ICF will be given to the subject, and the original will be placed in the subject's clinical investigation records. Subjects will need to sign updated versions of the ICF if required by the Investigator's IRB/EC during the course of the clinical investigation.

## 16. Data Collection Process

The Sponsor will collect clinical data for this clinical investigation utilizing eCRFs through an EDC system. All clinical data is entered into the EDC system by designated personnel at each of the Investigator sites. All data entered in the eCRFs are supported by source documentation.

## 17. Clinical Investigation Monitoring

It is the responsibility of the Site Principal Investigator to oversee the safety of the clinical investigation at his/her site, to include the careful assessment and appropriate reporting of AEs/incidents as noted above as well as the implementation of site data safety. The Sponsor, or designee, will monitor the sites to ensure informed consent has been documented appropriately, to ensure the information documented on the completed case report forms match the medical records and to resolve any differences. The Sponsor will take all steps necessary to ensure data integrity. The Sponsor will also review significant new information, including unanticipated adverse device effects/incidents and ensure that such information is provided to all Investigators, their IRBs/ECs, and applicable regulatory authorities. Additionally, a quality assurance check will be performed to ensure the investigator is complying with the Clinical Investigation Plan and applicable regulations in the collection of all clinical investigation data.

## 18. Data Handling and Record Keeping

Information about clinical investigation subjects will be kept confidential. In the event a subject revokes authorization to collect or use protected health information, the Site Investigator, by regulation, retains the ability to use all information collected prior to the revocation of subject authorization. The Health Insurance Portability and accountability Act (HIPAA) will apply in order to ensure data protection and document anonymization. Records are to be stored in a secure location. Retention of records shall be maintained through the clinical investigation duration as well as specified years following the clinical investigation completion as required by local regulatory authority.

## 19. Reports

Analysis will be executed and interim reports will be prepared on a yearly basis. Upon the completion of all subjects final post-operative assessment, data freeze will take place and the final report will be prepared.

## 20. Public Registration

The clinical investigation and summary of results will be registered on ClinicalTrials.gov and/or European Database on Medical Device (EUDAMED).

## 21. Completion of the Clinical Investigation

The Investigator will conduct this clinical investigation in compliance with the Clinical Investigation Plan, and will complete the clinical investigation within the timeframe specified in the contract.

Continuation of the clinical investigation beyond this time must be mutually agreed upon in writing by both the Investigator and Stryker. The Investigator will provide a summary of the clinical investigation results in accordance with the IRB/EC guidelines.

Stryker may terminate this clinical investigation prematurely, either in its entirety or at this site, for reasonable cause provided that written notice is submitted a reasonable time in advance of the intended termination. The Investigator may also terminate the clinical investigation at their site for reasonable cause, after providing written notice to Stryker a reasonable time in advance of the intended termination. If Stryker terminates the clinical investigation for safety reasons, it will immediately notify the Investigator by telephone and subsequently provide written instructions for clinical investigation termination.

## 22. Essential Documents

All essential documentation will be stored as specified under the Sponsor's Standard Operating Procedures.

## 23. Publication Policy

Refer to the clinical investigation agreement for the publication policy.

## 24. References

Chan DS, Serrano-Riera R, Griffing R, Steverson B, Infante A, Watson D, Sagi HC, Sanders RW. Suprapatellar Versus Infrapatellar Tibial Nail Insertion: A Prospective Randomized Control Pilot Study. J Orthop Trauma. 2016; 30(3):130-4.

Sanders RW, DiPasquale TG, Jordan CJ, Arrington JA, Sagi HC. Semiextended intramedullary nailing of the tibia using a suprapatellar approach: radiographic results and clinical outcomes at a minimum of 12 months follow-up. J Orthop Trauma. 2014; 28(5):245-55.

Stannard JP, Bankston L, Futch LA, McGwin G, Volgas DA. Functional Outcome Following Intramedullary Nailing of the Femur. A Prospective Randomized Comparison of Piriformis Fossa and Greater Trochanteric Entry Portals. JBJS. 2011; 93: 1385-91.

Stryker Trauma GmbH. Instructions for Use T2 Alpha Tibia Nailing System. [L22000044 Rev. AA, 03-2018].

Stryker Trauma GmbH. Instructions for Use IMN Instruments. [L22000035 Rev. AB, 11-2017].

Stryker Trauma GmbH. Instructions for Use IMN Screws System. [L22000045 Rev. AA, 03-2018].

Sun Q, Nie X, Gong J, Wu J, Li R, Ge W, Cai M. The outcome comparison of the suprapatellar approach and infrapatellar approach for tibia intramedullary nailing. Int Orthop. 2016; 40(12):2611-2617.

Wang Z, Cheng Y, Xin D, Liu T, Qu W, Wang D, Zhao Y, Zhao J. Expert Tibial Nails for Treating Distal Tibial Fractures With Soft Tissue Damage: A Patient Series. J Foot Ankle Surg. 2017; 56(6):1232-1235.

Ware JE Jr, Kosinski M, Gandek B. SF-36 Health Survey: manual and interpretation guide. Lincoln, RI: QualityMetric Inc. 2000; B6-B11.

## 25. Clinical Investigation Plan Signature Page

A Post-Market Clinical Evaluation of the Treatment of Tibia Fractures with the T2 Alpha Tibia Nailing System

# T2 Alpha

I have read this Clinical Investigation Plan and agree that this clinical investigation is ethical. I agree to conduct this clinical investigation in accordance with this Clinical Investigation Plan, as well as all applicable regulations and guidelines. I agree to maintain the confidentiality of all information received or developed in connection with this Clinical Investigation Plan.

_____ _____

Signature of Investigator Date of Signature

_____

Name of Investigator (Printed)

# 26. Document Version History

| Version | Effective Date | Description | Revised/Created by |
|---|---|---|---|
| 1 | 27-Aug-2018 | Initial version | Colleen Bordeaux |
| 2 | 24-Jan-2020 | See tracked version for changes | Christine Youssif |
| 3 | 23-Nov-2020 | See tracked version for changes | Susanne Höfer |

## Certificate Of Completion

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Signatures: 4
Certificate Pages: 5
Initials: 0
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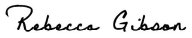
| Rebecca Gibson<br>rebecca.gibson@stryker.com<br>Manager, Clinical Research<br>Stryker Corporation - Trauma & Extremitites<br>Security Level: Email, Account Authentication (Required) |  <br>Signature Adoption: Pre-selected Style<br>Signature ID:<br>B69B71B0-C1FA-437D-B216-59BFBEB69FE2<br>Using IP Address: 52.154.71.15<br><br>With Signing Authentication via DocuSign password<br>With Signing Reasons (on each tab):<br>I approve this document | Sent: 11/24/2020 9:24:19 AM<br>Viewed: 11/24/2020 4:41:00 PM<br>Signed: 11/24/2020 4:42:34 PM |
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| Certified Delivered | Security Checked | 11/26/2020 1:54:46 AM |
| Signing Complete | Security Checked | 11/26/2020 1:55:06 AM |
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i. decline to sign a document from within your DocuSign account, and on the subsequent page, select the check-box indicating you wish to withdraw your consent, or you may;
ii. send us an e-mail to rebecca.gibson@stryker.com and in the body of such request you must state your e-mail, full name, IS Postal Address, telephone number, and account number. We do not need any other information from you to withdraw consent.. The consequences of your withdrawing consent for online documents will be that transactions may take a longer time to process..

**Required hardware and software**

| | |
|---|---|
| Operating Systems: | Windows2000? or WindowsXP? |
| Browsers (for SENDERS): | Internet Explorer 6.0? or above |
| Browsers (for SIGNERS): | Internet Explorer 6.0?, Mozilla FireFox 1.0, NetScape 7.2 (or above) |
| Email: | Access to a valid email account |
| Screen Resolution: | 800 x 600 minimum |
| Enabled Security Settings: | •Allow per session cookies<br>•Users accessing the internet behind a Proxy Server must enable HTTP 1.1 settings via proxy connection |

** These minimum requirements are subject to change. If these requirements change, we will provide you with an email message at the email address we have on file for you at that time providing you with the revised hardware and software requirements, at which time you will

have the right to withdraw your consent.

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